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Administration and Dose of the Most Frequently Used Drugs in Paediatrics

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1. Introduction

Though the main aim of modern medicine is the prevention of healthy people, the most of the medical service for treatment today is applied as medical treatment of patients. One of the very important reasons of the service of medical treatment is choice of wrong drugs, and the other is not be able to use the planned treatment truly. The patients may not take the drugs that clinicians suggested themselves. This situation is known to be closely related to the presence of social health organization of patients. The patients may misuse a true treatment. Also the clinicians may cause the problem of drug misuse, especially the antibiotics. Whatever the reason is, the drug misuse causes the public health to deteriorate and economical loses and, this is inevitable. Moreover, some of the drug misuses, like of antibiotics, may imbalance the ecology and cause the problem to convey to next generations (Gokalp & Mollaoglu, 2003).

World Health Organization has defined the use of rational medication as "providing medication to individuals easily, at the lowest prices, and for the most suitable dosages and periods according to clinical findings and personal characteristics of individuals" (Baytemur, 2005; Cetinkaya et al, 2010; Ozdemir, 2010). Antibiotics are among the most important discoveries of the past century (Çetinkaya et al, 2010; Karabay, 2009).

Antibiotic use among the infants at newborn intensive care units is gradually increasing. In a study conducted over 29 newborns in USA, it was determined that 43% of the patients used antimicrobial during their stay. Undergoing microbial application poses a risk in terms of resistance. To avoid the use of antibiotics, in this sense, there have been training programs developed by the American Society of Infection (Patel & Saiman, 2010).

Antibiotics sits atop in the list of most frequently used medication in all countries. Similarly in Turkey, antibiotics are placed on the top in terms of the average per capita medication with a ratio of 17-19% (Çetinkaya et al, 2010; Özdemir, 2010; Ozgunes, 2005). The frequency of antibiotics usage in Turkey for in-patients is over 30%. This ratio increases over 50% for intensive care units (Çetinkaya et al, 2010; Sardan, 2005). While the consumption costs of antibiotics in USA exceed 7 million dollars per year, such medications establish the 30% of the total medication budgets of all hospitals. Nearly half of the antibiotics usage is still not

appropriate despite strict control programs and such effort (Akan, 2006; Çetinkaya et al, 2010). In Turkey, antibiotic treatment is prescribed too frequently (Bal, 2005; Celen et al, 2005; Çetinkaya et al, 2010; Özgüneş, 2005;). In a study it is stated that antibiotics are being prescribed to significant portion of the patients who apply to clinics (15-48%) and only 2-2.5% of those prescribed medication was based on culture results (Çetinkaya et al, 2010; Özgüneş, 2005).

Since the prevalence of drug errors are high, it is that imperative that nurses understand the factors leading to errors, and avoid them to the best of their ability (Dinc, 2011).

Without considering by whom it was prescribed, nurses are responsible for the every each medication that is administered personally on legal grounds, moral grounds, and ethical grounds (Dinç, 2011).

All professional nurses should take these issues seriously. Safe and correct medication is one of the principal responsibilities of a nurse during patient care. For a nurse to make free decisions over right medication, correct administration, and providing appropriate means for measurement and monitoring is important for the assessment of the side effects of medication and the patient reactions against it. Reliable medication requires knowledge synthesis, experience, critical approach and intellectual norms (Dinç, 2011).

Comparing to that on an adult, medication administration greatly differs on children, while bringing along responsibilities. It is of the physician's responsibility to write down the doses into drug master file. Nurse, on the other hand, is responsible for administering the medication at the correct amount and on the correct time. Nurse has to know when this medication would start to be effective, for how long it would be effective, what side-effects it might cause, any toxic indications, and counter-measures in respect thereof (Kavakli et al, 1998).

In a study carried out to analyze the knowledge and behavior of pediatricians regarding to the rational use of antibiotics, as well as the socio-demographic factors that might be affecting, 89.8% of the participants reported that, when prescribing antibiotics, they need to see the patient first, whereas, 78.1% indicated that they were prescribing antibiotics according to the patient's clinical condition, 71.1% reported that they had paid attention to the appropriateness of the symptoms, and 67.2% told that they were going to take microbiological culture samples for examination. As for the question '*who should give education about antibiotics*' 32.1% replied as the physician who had prescribed the medication, 23.4% said the junior doctors, 21.9% said pharmacists, 17.2% said the pediatric nurse, 9.4% said nurses (Çetinkaya et al, 2010).

The pediatrics nurses auditing the medication use, evaluation by them if the importance of regular use of the medication is understood or not, to obtain the suitable feedback from the patent and the patient's family by the prescribing physician, adverse effects and what they should do under such circumstances etc., providing training and consultancy on all these are among their duties (Çetinkaya et al, 2010; Çetinkaya &Tengir, 2006).

2. Pharmacological concepts

If taken by a living organism, drug is an agent that brings changes in body functions. Administration of drugs is of the principal practices in nursing. Safety of the patient is the

basis in preparation of medication, and during their administration. Along with the nurse's skill in administering drugs, he / she has to possess adequate information about the drug (Gorgulu & Ulusoy, 1996).

2.1 Sources of drugs

These are the basic sources of drugs:

- **Natural sources:** Minerals (like Iron), animals (such as insulin), and plants (such as opium)
- **The synthetics** (*chemical agents manufactured in laboratories*): Synthetic drugs have the same chemical composition with the natural ones, and they are obtained much cheaper; just not every drug could be acquired in this way, though (Görgülü & Ulusoy, 1996).

2.2 Drug nomenclature

Drugs have multiple names:

- "*Chemical Name*" shows its chemical composition.
- "*Generic Name*" (family, registry name) describes the common name of the drug, given by its first manufacturer. This name is given after its chemical name.
- "*Official Name*" is the name for the official publications that would certificate the drug
- "*Trade Name*" or sometimes "Brand Name" is given by the drug's authenticated manufacturer. There can be more than one trade names.

Nurses can recognize the drugs they used frequently by their generic names and trade names (Çavuşoğlu, 2000; Dinç, 2011; Görgülü & Ulusoy, 1996). Because nurses happen to be facing the drugs under good deal of different names, they need to be careful about the name before its administration (Dinç, 2011).

2.3 Classification of drugs

Drugs are classified in various ways. As some could be classified by the body systems, such as "affecting respiratory system", "affecting cardiovascular system", some could be grouped by the syndromes they eliminate (Dinç, 2011; Görgülü & Ulusoy, 1996). Any drug may belong to more than one categories, as in the aspirin, which is an analgesic, antipyretic and anti-inflammatory drug (Dinç, 2011).

2.4 Pharmaceutical type of drugs

A pharmaceutical drug or medicine refers to the final state of medical substances, intended or ready for use in medical applications. The active element of the drug is processed to become useable with other solids or liquids. Drugs are available in different forms so they could be easily taken according to varying needs and conditions:

1. Solid Pharmaceutical Types: powder, cachet, package, capsules, tablet, pastille, pilular, sugar-coated pill, extracts.
2. Semi-liquid semi-solid Pharmaceutical Types: Suppository, ovular, ointments.
3. Liquid Pharmaceutical Types: Solutions, solution for injections, syrup, potion, elixirs, lotions, enema (Çavuşoğlu, 2000; Yüncü, 1994).

2.5 Drug effects

Nurse should be aware of the curing, thus, desired effect of a drug before administering it. Since drugs are chemical compounds they may result in more than one effect, therefore, they may not react the same way for every patient (Dinç, 2011).

2.5.1 Curing effects

These are the desired physiological effects of a drug. Every drug has an intended curing purpose. Aspirin can be used to wear off a pain, reduce fever, help inflammations over edema. It is important for a nurse to know about the curing effects of prescribed medicines. By this way, nurse can properly brief the patient and assess the desired effects of medicine. (Dinç, 2011).

2.5.2 Side effects / adverse effects

Drugs can result in undesired, and sometimes, unexplained reactions in the body. No drug is completely safe. The side-effects can be predictable; these effects can show up even if drug is taken at the appropriate doses. Should the severity of side-effects start exceeding the desired effects, this medication should be abandoned by whom it was prescribed (Dinç, 2011).

Adverse drug reactions are undesired, and, most often, unpredictable effects. They may result in anomalies which would incapacitate the patient. Some of them may show up at short notice, some may take even months (Dinç, 2011).Side effects are those which surface as an unsettling effect to the patient although the dose was appropriate. These may result from the preservatives and other ingredients, or even the drug itself (Çetinkaya &Tengir, 2006).

Nurses should be alarmed for any side effects especially when dealing with new drugs. A nurse should be aware of the fact that even mildly occurring adverse effects may result in severe allergic reactions with high toxicity. Early detection of adverse effects may prevent the patient from getting harmed (Dinç, 2011).

2.5.2.1 Toxic effects

Toxicity determines the level of toxication a substance can cause. The toxicity occurs with the accumulation of drug in the blood due to either high dosage, or oral administration and digestion of an non-oral medication, or failure in metabolism and excretion mechanism. Depending on the drug activity, toxic effects can be deadly (Dinç, 2011).

2.5.2.2 Idiosyncratic reactions

These are unusual reactions in which the patient shows either excessive or too little reaction against a medication. These are unpredictable and it is not possible to determine which patient might develop an idiosyncratic reaction (Dinç, 2011).

2.5.2.3 Allergic reactions

Drug reaction, according to the UN World Health Organization, is defined as "unexpected and harmful reactions that a medicine provided with appropriate doses for the intent of diagnosis, treatment, or preservation is causing" (Çetinkaya et al, 2008; Sin, 2005). Allergic reactions constitute only one part of undesired drug reactions (Çetinkaya et al, 2008; Sin,

2005). Due to lack of feedback, the frequency of reactions on the patients obtaining their medication at outpatient services cannot be determined (Çetinkaya et al, 2008; 2005; Sin, 2005; Tomaç & Üstündağ). As for the hospitalized incidents, the observation rate for drug reactions is 15 – 30% (Çetinkaya et al, 2008; Sin, 2005).

Allergic reactions can be mild as well as they could be serious. Allergic symptoms vary according to patient and medication. With respect to different drug types, antibiotics have the highest incidence rate for allergic reactions (Dinç, 2011).

Allergic medicine reactions, to get her with the most common form of skin reactions constitute 5-10% of the medicine side effects. It is presumed that the hospital expenses due to medicine reactions are 7000 per unit bed year and morbidity and mortality costs are presumed to be more than 136 million dollars only in USA (Çetinkaya & Tengir, 2008).

Antibiotics like Vancomycin, Cephalosporins, and Penicillins, besides, anticonvulsant drugs, narcotic analgesics, and anti-emetics are of the examples to the drugs that cause undesired effects on children. Because most of these effects proceed mildly, the situation can be brought under control easily. However, every three out of ten reactions last longer and require hospitalization. An example to such most serious reactions is "respiratory arrest" which is caused by anaphylaxis, or application of benzodiazepine – narcotic analgesic combination, following a Cephalosporin antibiotic treatment (Pala & Baktir, 2011).

Penicillin was found by Fleming in 1928. Penicillin group of drugs are the most frequently prescribed antibiotic, and they usually are the most common reasons of medicine allergy (Çetinkaya & Tengir, 2008).

Indeed, penicillin allergy is one of the most encountered problems (Çetinkaya et al, 2008; Tomaç & Üstündağ, 2005). It was determined in a study that three out of five antibiotics prescribed in the world in 1999 were derivatives of penicillin. For this reason, penicillin, among all drugs, constitutes the most researched antibiotic group for their allergic reactions (Çetinkaya et al, 2008; Mungan, 2005).

It is estimated that the chance for an allergic reaction to occur following penicillin is 2% for every treatment cure (Çetinkaya et al, 2008; Mungan, 2005). Among children, rate for penicillin allergy is not determined (Cetinkaya & Cag, 2004; Çetinkaya et al, 2008). For the children having medical history of their parents with penicillin allergy, the rate of allergy development by the age of 16 is 26%. The 39% of children who were hospitalized due to drug reactions later showed life-threatening incidents (Çetinkaya et al, 2008; Park & James, 2005).

A research to analyze the knowledge and application of nurses in Penicillin Allergy Test and the factors underlying has been conducted; a total of 161 nurses and midwifes working in twenty-two healthcare centers located in Konya, Turkey has participated. The 83.5% of the participants told that penicillin should be administered at the healthcare centers, 92.1% opted for a nearby medical facility in case of an emergency, and 91.3% of them told that a doctor, at least, should be present at the site of administration for the same reasons. In the end, it was suggested that nurses and midwifes should acquire knowledge about the penicillin test before any penicillin treatment was placed in order, so as precautionary actions could be taken during the application (Çetinkaya et al, 2008).

Patients should definitely be given adequate written material. They should be asked to carry special id cards indicating what drugs they had allergic reaction against. On these allergy

cards, name of the active agent, drug's trade name, severity of the reactions that was observed, assessment tests (history, skin test, IgE test, IPT), suggested alternative drug and its doses should be indicated (Çetinkaya et al, 2008; Dursun & Bavbek, 2005).Administration method, the treatment and its length may affect allergic reactions' development. This is what all healthcare personnel should adequately know about. Physicians should monitor these reactions very carefully, because it will be decisive in respect to patient's future drug regime; and if ignored, the treatment will become more and more complicated, effectively requiring much higher costs (Çetinkaya & Tengir, 2008).

2.5.2.4 Drug tolerance and addiction

Any decrease in physiological response following the repeated use of medication or chemical compounds is called "drug tolerance". This tolerance is discovered when the patient starts requiring new doses after steady use of lower doses for a long period. For acute cases, this is not often the case, and tolerance does not develop. The time period required to observe such development can be one month, or even more. Moreover, "cross tolerance" may develop should any drug tolerance occurred initially, and caused other drugs of the similar pharmaceutical properties fail over the same receptor area (Dinç, 2011).

Drug tolerance is not drug addiction. There are two types of drug addictions: psychological and physical. In psychological addiction patient requires the medication not for its desired effects, but for other benefits (Dinç, 2011).

Opioid resistance develops among the long-time opioid users. Despite the increasing doses it gets never enough, and patient gradually starts showing abstinence syndrome (Anand, 2007).

2.5.2.5 Drug interactions

If a drug alters the effect of another drug, the matter at hand is a drug interaction. The occurrence of such is frequent among the people taking multiple medicines at once. Any drug can increase or decrease the effectiveness of another drug, can affect the metabolism and alter the rate of absorption and / or excretion (Dinç, 2011).

If the combined effects of two drugs equal to the sum of the effect of each drugs individually, drug accumulation takes place (Dinç, 2011).

Synergistic effect is told when two drugs are taken simultaneously. By this effect, the physiological effectiveness is increased comparing to that if taken one by one (Dinç, 2011).

2.6 Dose responses of drugs

The differences in people's drug responses are called polymorphism. Factors contributing to this can be environmental, genetic or cultural ones (Dinç, 2011).

The reason for treatment with medicine is to prevent diseases, decrease the effect of a disease or keep that under control. To this end, sufficient amount of medicine should be delivered to the targeted tissues without causing intoxication. Pharmacokinetics studies the period of time a medicine is absorbed, distributed inside, metabolized, and egested from the body. This period involves a steady and dynamic interaction between the human bodies and drugs (Çetinkaya &Tengir, 2006).

The term “bio-availability” is used for the part of the dose that reaches to the circulatory system. The dose interval between the beneficial part of a drug and that causing side effects is called “therapeutic index”. The time it takes for drug concentration in blood serum to be halved is called “half-life”. Half-life is affected by other drugs, tissue perfusion and organ functions. Determination of the blood level is easier than that of a tissue, in most of the cases. Volume of distribution is a parameter, used to determine the relation between the applied dose and blood concentration of a drug. Volume of distribution is affected by the chemical properties of the drug and patient's physiological condition. “Stable drug level” indicates the egested amount of drug matching the amount of drug which was taken. Usually in clinical practices, stable drug level is attained following 4-5 half-lives.

“Clearance” is the term showing the excretion rate of a drug. Clearance of any drug depends on the volume of distribution, half-life, and patient’s physiology, blood circulation of organs, the organ functions, and drug's chemical properties. In clinical terms, clearance is studied in two types: linear (first degree) and nonlinear (zero degree). A drug showing linear pharmacokinetics results in proportional increase to blood and tissue concentrations as the dose increases. Most of the drugs used in newborns (amino glycosides, Vancomycin, Phenobarbital, caffeine, catecholamine) are egested this way. As for the drugs showing nonlinear pharmacokinetic properties, there will be a sharp increase in blood concentration even if there is a mild change in the dose level. Such an unpredictable change is related to enzyme saturation levels in the liver. Therefore, almost all of the drugs egested from liver have nonlinear pharmacokinetics. These drugs, on the other hand, tend to show linear excretion properties if given in therapeutic doses. Approaching to the toxicity levels, this relation becomes nonlinear. Phenytoin is a good example to such drugs (Ovali, 2008).

In order to measure the effects of some drugs, checking blood levels may be required. In the use of amino glycosides, the measurement of both the lowest and the highest concentrations in the blood might be useful. Should the lowest concentration be observed above expected, an excretion problem can be considered, thus, dose intervals are extended (or narrowed when the concentration was lower). Deviations in the maximum values, on the other hand, require changes in the dose amount, not in the interval. Because those inspections require considerable amount of blood taking, for the infants, it is a better idea to make with clinical overview instead of following the routine, unless the drug levels are required in case of necessity (Ovalı, 2008).

Factors related to the growth and development of a child may affect the drug effect and its excretion. Maturation lag or natal disorders do affect the drug absorption, its effect and excretion (Kavaklı et al, 1998).

Comparing to adults, newborns exhibit great differences physiologically, anatomically, and pharmacologically. Renal functions in the newborn are reduced since the glomerular and tubular functions are infrequent, and blood circulation at the kidneys is low. Glomerular filtration and tubular functions reach to their mature levels after 20 weeks from delivery, whereas, this is 2 years for renal functions. Newborn's ability for water-retention and excretion of solutes are insufficient. All of these reasons cause extended half-lives. On a full-term infant the liver is immature. Enzymes playing role in drug mechanisms are not sufficient. Only through the infant's growth, the blood circulation in liver increases, and the

enzyme maturation is completed. Glycogen stores are minimal at the liver of premature infants; they cannot stockpile large protein molecules. The albumin and other proteins which are involved in drug metabolism are kept in minimum amounts; subsequently, the free fractionation of drugs increases (Ozcengiz, 2011).

Drug response in infants varies according to the body's muscle – fat – water distribution, protein binding, body temperature, the cardiac outflow, physiological maturation of heart, maturation of blood – brain barrier, efficiency of the liver and kidneys, and whether a congenital malformation exists or not. Total body water is higher in premature newborns comparing to a newborn, and in newborns in comparing to a 2 years old. The rate of fat and muscle increases with the age, a significant characteristic for the clinical applications of newborn. Water-soluble drugs have higher volume-distribution. Thus, starting doses are greater to attain desired blood-levels. Because the fat-rate is lower in newborns, drugs redistributed to the fatty tissues, as well as those redistributed to muscle-tissues have longer effects. There are also other factors affecting a newborn's drug-response. Since the volume-distribution is wider, the excretion is delayed. Liver and kidney functions are insufficient; the rate of protein binding is low. Moreover, the presence of prematurity, sepsis, congestive cardiac failure, increased intra-abdominal pressure, controlled ventilation, and insufficient nutrition do affect the drug response adversely. Ultimately, reviewing the drug pharmacokinetics and pharmacodynamics are required for each and every newborn (Özcengiz, 2011).

For a drug to be used in the body, first, it should be absorbed (should pass to the blood from its entry point), be distributed (its delivery through circulation to the impact area) and be transformed to its active state. Later on, it is broken up with the metabolism, and egested from body as a drug metabolite. This mechanism prevents the toxicity of regular medication due to accumulation in body. For infants and children, absorption, distribution, metabolism, and excretion mechanisms differ from those in adults due to the immaturity of their body systems (Çetinkaya &Tengir, 2006).

3. Drug pharmacokinetics

The term *pharmacokinetics refers to the way a drug is handled by the body. Pharmacokinetic* measures, such as area under the curve (AUC) and concentration at the maximum (Cmax) and parameters calculated from those measures, such as clearance, half-life, and volume of distribution, reflect the absorption (A), distribution (D), and elimination (E) of a drug from the body. A drug can be eliminated by both metabolism (M) to one or more active and inactive metabolites and excretion of the unchanged drug. The overall set of processes is often referred to as ADME, which ultimately controls systemic exposure to a drug and its metabolites after drug administration (Buxton & Benet, 2011).

This systemic exposure, reflected in plasma drug and/or metabolite concentrations, is generally used to relate dose to both beneficial and adverse effects. All drugs show inter- and intra-individual variance in pharmacokinetic measures and/or parameters (Buxton & Benet, 2011). Variances can sometimes be substantial. In the pediatric population, growth and developmental changes in factors influencing ADME also lead to changes in pharmacokinetic measures and/or parameters. To achieve AUC and Cmax values in children similar to values associated with effectiveness and safety in adults, it may be

important to evaluate the pharmacokinetics of a drug over the entire pediatric age range in which the drug will be used. Where growth and development are rapid, adjustment in dose within a single patient over time may be important to maintain a stable systemic exposure.

Developmental changes in the pediatric population that can affect absorption include effects on gastric acidity, rates of gastric and intestinal emptying, surface area of the absorption site, and gastrointestinal enzyme systems for drugs that are actively transported across the gastrointestinal mucosa, gastrointestinal permeability, and biliary function.

3.1 Absorption

Absorption is the period of a drug to pass into body-liquids and to be brought to its receptor zone (Çetinkaya &Tengir, 2006).

Similarly, developmental changes in skin, muscle, and fat, including changes in water content and degree of vascularization, can affect absorption patterns of drugs delivered via intramuscular, subcutaneous, or percutaneous absorption (Buxton & Benet, 2011).

Drugs are delivered through intravascular (*intravenous*) or extravascular (*intramuscular, oral, sublingual, subcutaneous, or rectal*) routes. A drug administered via extravascular route should be absorbed in order to reach its receptor zone (Çetinkaya &Tengir, 2006).

The absorption of most drugs at the gastrointestinal system is through passive diffusion. Absorption is affected by the delivery route, drug density, medium's acidity, and the local circulation. For newborns and infants, the drugs given orally usually have a belated absorption (Çetinkaya &Tengir, 2006).

A drug to pass from cell-membrane shouldn't be ionized. Acidic drugs ionize at alkaline medium. Since these drugs do not ionize at the acidic medium they are absorbed well. The stomach pH of a newborn is acidic (1-3); by the 4th month the acidity approaches to that of an adult's 50%, and around the age of 3 it gets near-adult-values (0.9-1.5) (Çetinkaya &Tengir, 2006).

Decreasing stomach activity for newborns and infants affect the drug absorption, too. For newborns, stomach is empties in 6-8 hours; this number reaches to adult values of 2 hours at the age of 6-8 months. Irregular peristaltic movements until the 8th month cause this procrastination, also delaying drug's blood-levels. Furthermore, newborns do not exhibit efficient absorption since their intestinal enzyme developments were delayed (Çetinkaya &Tengir, 2006).

Absorption of intramuscular or subcutaneous drugs depends on the tissue perfusion at the primer application zone. Since the circulation at muscles and various tissues are less than sufficient, the absorption of intramuscular or subcutaneous drugs is decreased (Çetinkaya &Tengir, 2006).

Slow blood circulation can also affect the drug absorption in newborns. Drug distribution can be limited for the infants carrying cardiovascular disease (Çetinkaya &Tengir, 2006).

Oral use: Although oral use is the most frequent drug administration type, this is not preferred for newborns. Stomach acids secretion in newborns and infants is low; their digestive juice is close to neutral. The bioavailability of basic drugs is decreased, whereas

that of acidic ones (*Ampicillin*) is increased. Moreover, gastro-intestinal motilities are irregular; these are slower in newborn and infants, while they are faster than adults in children (Pala & Baktır, 2011).

Rectal use: It is an alternative route when oral use is not applied due to nausea, vomiting, or other reasons. Some analgesic – antipyretic drugs, valproic acid, Diazepam, Phenobarbital, and some corticosteroids can be administered this way. Absorption of the drugs that are applied as a suppository in the rectum is neither regular, nor exact (Pala & Baktır, 2011).

Intramuscular use (IM): it is weak and irregular for newborns and infants. This is caused by the irregularities in blood circulation and vasomotor functions (Pala & Baktır, 2011).

Percutaneous use: With the stratum corneum layer too thin, skin hydration is excessive in newborns. Therefore, locally applied drugs are absorbed more than that in the adults, making undesired toxicity quite possible. Especially, topical preparations containing corticosteroid require significant attention (Pala & Baktır, 2011).

3.2 Distribution

Distribution of a drug may be affected by changes in body composition, such as changes in total body water and adipose tissue, which are not necessarily proportional to changes in total body weight. Plasma protein binding and tissue binding changes arising from changes in body composition with growth and development may also influence distribution (Buxton & Benet, 2011).

Prior to the absorption, drug is carried to organs and tissues through blood-circulation. Composition of body liquids and the drug's level of protein-binding affect the distribution level. Plasma albumin is a primer binding-place for drugs. This binding phenomenon delimits the amount of free drug in circulation, hence, preventing drug to attain at toxic levels (Çetinkaya &Tengir, 2006).

The amount of binding to plasma protein differs from one drug to another. Therefore, density and the amount of the drug that reached to the receptor zone are not proportional to dose. Neonatal albumin has lower binding capacity to some drugs (*Phenytoin*).

Should the active free drugs remain at high levels in blood, the chances for toxic effects to surface become more likely. The water amount in body is a significant parameter used to determine the highest attained drug density. The total water amount of premature infants constitutes the 80-85% of their total weight, whereas this ratio is 75% for interm infants, and it is at adult-like levels (50-60%) by the end of age two. Given the amount of total weight to adjust proportional dose levels, administering drugs that are water-soluble results in insufficient drug density in blood-plasma; thus, more appropriate doses are used for infants (Çetinkaya &Tengir, 2006).

The ability to metabolize drugs in newborns (especially premature infants) is quite limited due to physiological immaturity (Çetinkaya &Tengir, 2006).

Once metabolized, drugs transform into water-soluble compositions for excretion at kidneys. Most of this bio-transfer takes places in the liver. Two-to-three weeks from

delivery, liver enzymes begins to maturate; at about the 4th week liver functions are fully developed and the excess drugs can be metabolized. If this period is not taken into account, the non-metabolized drugs begin to accumulate at toxic levels (Çetinkaya &Tengir, 2006).

Because the metabolism rate of an infant (and small child) is faster than an adult, certain drugs can be metabolized also faster. Another factor is the change in liver size. Fetal liver is the 4% of total weight in infants, while this is 2% for adults. This alone explains why many drugs are disposed more quickly, and, accordingly, why the children require medication in higher-doses (Çetinkaya &Tengir, 2006).

The volume of body liquids vary comparing to adults. Comparing to total weight, body liquids in children are more than they are in adults (Pala & Baktır, 2011).

The relative mass of fatty tissues and skeleton muscle tissues are less than those at adults. Especially fat-soluble drugs have greater distribution volume; they should be used in lower doses (Pala & Baktır, 2011).

The rate of drugs' protein binding is lower since the total protein concentration is lower than that in adults. Since the free drug concentration in the blood is higher, so is for the toxicity risk (Pala & Baktır, 2011).

The blood-brain barrier isn't fully developed. There is a risk for hypersensitivity against the drugs affecting the central (Pala & Baktır, 2011).

3.3 Metabollsm

Drug metabolism usually occurs in the liver, but may also occur in the blood, gastrointestinal wall, kidney, lung, and skin. Developmental changes in metabolizing capacity can affect both absorption and elimination, depending on the degree to which intestinal and hepatic metabolic processes are involved. Although developmental changes are recognized, information on drug metabolism of specific drugs in newborns, infants, and children is limited. In general, it can be assumed that children will form the same metabolites as adults via pathways such as oxidation, reduction, hydrolysis, and conjugation, but rates of metabolite formation can be different (Buxton & Benet, 2011).

There are qualitative and quantitative differences in biotransformation between a newborn and other age groups. (Pala & Baktır, 2011).

The metabolism capacity of most drugs is rudimental in newborns; on the contrary, various metabolism pathways show significant development during the first one year (Pala & Baktır, 2011).

In some cases, the dominant metabolic route differs at the infants and children. Caffeine synthesis due to the methylation of teophylline is developed well at infants (Pala & Baktır, 2011).

Glucuronidation at infants is insufficient (Pala & Baktır, 2011).

Sulfide conjugation is developed at infants. Paracetamol absorption is similar to adults (Pala & Baktır, 2011).

3.4 Protein binding

Protein binding may change with age and concomitant illness. In certain circumstances, an understanding of protein binding may be needed to interpret the data from a blood level measurement and to determine appropriate dose adjustments. In vitro plasma protein binding studies can determine the extent of binding of the parent and the major active metabolite(s) and identify specific binding proteins, such as albumin and alpha-1 acid glycoprotein. Optimal estimates of the degree to which protein binding is linear may be obtained by testing maximumand minimum observed concentrations (Buxton & Benet, 2011).

The main reason that age affects drug action is that drug elimination is less efficent in newborn babies and in old people, so that drugs commonly produce greater and more prolonged effects at the extremes of life. Other age-related factors, such as variation in pharmacodynamic sensitivity, are also important with some drugs.

3.5 Excretion

Drug excretion by the kidney is controlled by glomerular filtration, tubular secretion, and tubular re-absorption (Buxton & Benet, 2011). Because these processes mature at different rates in the pediatric population, age can affect systemic exposure for drugs where renal excretion is a dominant pathway of elimination. Consideration should also be given to the maturation of other excretory pathways, including biliary and pulmonary routes of excretion. Glomerular filtration rate (GFR) in the newborn, normalized to body surface area, is only about 20% of the adult value, and tubular function is also reduced. Accordingly, plasma elimination half-lives of renal eliminated drugs are longer in neonates than in adults. In babies born at term, renal function increases to values similar to those in young adults in less than a week, and indeed continues to increase to a maximum of approximately twice the adult value at 6 months of age. The increase in renal function occurs more slowly in premature infants. Renal immaturity in premature infants can have a very large effect on drug elimination. For example, in premature newborn babies the antibiotic Gentamicin has a plasma half-life of 18 hours or greater, compared with 1-4 hours for adults, and approximately 10 hours for babies born at term. It is, therefore, necessary to reduce and/or space out doses to avoid toxicity in premature babies.

Drugs and their metabolites are excreted through sweat, urine, stools, or enzymes. By the time kidney functions develop, disposing drugs via urinary system is limited. The glomerular filtration speed and the circulation in kidneys are 30-40% of adults; this ratio is even smaller for infants delivered before 34 weeks. Following the first two weeks, the glomerular filtration speed is doubled, eventually reaches to adult-levels in 2.5 – 5 months (Çetinkaya &Tengir, 2006). Glomerular filtration speed meets adult levels in 6 – 12 months (Pala & Baktır, 2011). The half-lives of drugs also change (Pala & Baktır, 2011).

4. Pharmacodynamic changes in children

Results obtained from clinical trials and experimentation with the animals show that receptor development leads to changes in drug response. Serotonin is a neurotransmitter paying important role in the behavioral and psychiatric disorders. Serotonin at the brain steadily decreases with the increasing age. The pharmacodynamic response of Dopamine,

also an important neurotransmitter, varies largely in the newborn and adult test animals. Many neurological, psychiatric and behavioral disorders are related to the dopamine at SSS. Among the pharmacodynamic responses of the drugs which are being used against this type of disorders may show significant differences during infancy and childhood.

Major factors affecting the newborn's response to a treatment: Gestation age, chronological age, weight, development phase, liquid-electrolyte balance, disorder level at the organ systems and functions, presence of co-existing diseases, accompanying other medication (Ovalı, 2008).

5. Principles of pharmacotherapy for the pediatric patients

- Assessment of clinical / laboratory findings regarding to the drugs used,
- Confirmation of patient's age, body weight, and dose regime; making out the discrepancies in drug absorption, distribution, metabolism and excretion between the infants and children,
- Choosing the most suitable dose type and regime,
- Preparation of a stabile and suitable dose form if no commercial package is available,
- Using the most affective, safest, and fine tasted economic drugs by use of comparative tests,
- Monitoring adverse effects and drug reactions, recognizing the undesired outcomes on children,
- Applying changes in the drugs, dose, or dose intervals when necessary,
- Regular communication with the patient and patient relatives during the treatment (Pala & Baktır, 2011).

5.1 Major problems of pediatric patients related to drug use

- They have inadequate prospectus knowledge
- Dose forms are insufficient for the pediatric population
- Pharmacokinetics, effectiveness, and reliability data through clinical tests are either insufficient or completely absent
- The parameters regarding primary activity for each age groups should be determined
- Duration of disease, age groups, and maturation period should be considered
- Oral suspensions should be developed
- Tablets and capsule sizes should be at appropriate sizes for pediatric patients
- Appropriate dose types should be improved for individual use (Pala & Baktır, 2011).

The drug manufacturers design drugs according to adult population. With the increasing doses on pediatric patients, the drugs used in adults generally cause trouble (Schultheis et al, 2006). Although most drugs in the market are steadily used on pediatric patients today, only one fourth of these drugs have actually been approved by the FDA (Food and Drug Administration) for their use on infants (Pala & Baktır, 2011). FDA has a website in order to give assistance for who might be willing to carry out clinical tests on pediatric patients (Schultheis et al, 2006).

5.1.1 Dose forms

Regarding new products in the market, drug manufacturers generally take little interest in the production of liquid forms that are to be used on infants and children. Among the

reasons, likely obligations, limited sources, and the little market share of pediatric drugs can be told. Not having been approved, most of the products are kept being used on the infants and children. Formulation of these medications may not be appropriate for pediatric patients just because they are fit for adults. Liquid forms are preferred for oral use on infants. Infants have difficulty in swallowing capsules and tablets. Besides they are too sized for them, their active ingredients are equally too much. Measuring the appropriate dose becomes, therefore, difficult. Most drugs do not dissolve in the water entirely. To make use of some drugs on the infants orally, suspensions should be formed. Carboxymethylcellulose and methylcellulose are used to achieve this. Most of the intravenous drugs used in adults are very concentrated. Therefore, their use on infants and children are quite difficult. Due to difficulties in dosing, toxic reactions are reported related to digoxin and morphine use on infants. The parenteral drugs to be used on infants, but are used in adults, are diluted in injection water or in 0.9% NaCl. The stability of these drugs should be tested for their active components and sterilities. The excipient components used in drug production are often inert matters, some of which might result in undesired effects. The benzyl alcohol used as preservative show serious toxic properties on infants; sorbitol used in high volumes as excipient may result in diarrhea. In addition, the propylene glycol used in preparations such as Phenytoin, Phenobarbital, digoxin, diazepam, vitamin D, and hydralzine, leads to hyperosmolarity on infants (Pala & Baktır, 2011).

5.1.2 Dosing in children

Calculation according to body weight is a preferred way of measuring the infant dose, especially using the Clark formula (Pala & Baktır, 2011).

Clark Formula:

Infant dose = Infant weight (kg)/ 72 x adult dose

Many clinic experiments show that the dose calculations according to the surface area (m^2) are more suitable than those using body weights for their least erroneous, thus, preferred aspect. Respiration metabolism, blood volume, extracellular liquid amount, glomerular filtration speed, and renal blood circulation are among the physiological parameters showing strong correlation with the body surface. Most of these functions have a direct affect on drug elimination (Pala & Baktır, 2011).

Since the metabolism is faster in children, infant doses (per kg. weight) can be greater than that of adults (Pala & Baktır, 2011).

Among the drugs given to infants in greater amount (per kg.) are as follow: Phenytoin, Diazepam, Imipramine, Phenobarbital, Teophylin, Chlomypramin, Carbamazepine, Enprophylin, Haloperidol, Ethosuximide, Digoxin, Chlorpromazine, Clonazepam, some anti-cancerogenic drugs (Pala & Baktır, 2011).

With the lower renal and hepatic functions, infants require longer drug intervals comparing to children and adults. For children to get appropriate doses, thorough clinical tests and drug's blood level studies are required. Due to certain ethical reasons, carrying out clinical studies over the children is difficult. In addition to the outstanding ethical reasons, too little size of the samples resulting in inefficiency in determination, insufficient experimental

equipment specific to children, other varying parameters on a long-term study, contribute to such difficulties (Pala & Baktır, 2011).

6. Drugs

6.1 Antibacterial drugs

Antibacterial (chemical agents which cease the reproduction of microorganisms or kill them) agents are the most frequently used group of pediatric drugs. These drugs are to be influential as bactericide or bacteriostatic corrupting the structure or the functions of the microbial cell (Eroğlu, 2002; Ovalı, 2002).

6.1.1 Penicillin

Penicillin influences the gram-positive coccus, some gram-negative microorganisms and spirochetes. They are used in order to provide prophylaxis in streptococcus, pneumococcus, staphylococcus, salmonella, shigella infections, venereal diseases and also in rheumatic fever (Kavaklı et al, 1998).

6.1.1.1 Oral preparations

Penicillin G has a variable absorption level as it is acid-labile. *Penicillin V* is acid-resistant and absorbed better (Eroğlu, 2002).

400.000 U=250 mg penicillin, 25.000-50.000 U/kg/day rheumatic fever prophylaxis; 400.000 U/day (every 12 hours) (Eroğlu, 2002).

6.1.1.2 Parenteral preparations

6.1.1.2.1 Benzyl penicillin (crystallized penicillin G)

The antibacterial spectrum is limited. It cannot be administered by oral route as it is decomposed in gastric acid and is not well-absorbed by digestive tract (Rang et al, 1998; Dökmeci 2000).

Newborn: IV 15-30 min. 6 dose/day every 4 hours established optimal treatment.
Newborn: <2000g: 50.000 U/kg/day (every 12 hours)
In Meningitis: 100.000 U/kg/day (every 12 hours)
Newborn: >2000g: 75.000 U/kg/day (every 12 hours)
In Meningitis: 150.000 U/kg/day (every 12 hours)
Infant (I), child (C): 100.000-250.000 U/kg/day (every 4-6 hours)
In Serious Infections: 200-400.000 U/kg/day (every 4-6 hours)
Higher doses are required in B group streptococcal meningitis (Apak, 1996).
Side effects are as follows: allergy, shock, anaphylaxis, serum disease, rash, gastrointestinal system (GIS) (Eroğlu, 2002).

6.1.1.2.2 Procaine penicillin G

After IM injection it is a slowly absorbed, water-insoluble crystal salt of penicillin G. It is used in pneumococcus, streptococcus and meningococcal infections. Newborn: 50.000 U/kg/day IM (single dose); the others 25-50.000 U/kg/day IM (single dose) (Dökmeci, 2000).

Side effects: Allergy, shock (Apak, 1996).

6.1.1.2.3 Benzathine penicillin G

It is a salt of penicillin G which establishes quite low serum levels, which is water-insoluble and whose effect however remains for 3-4 weeks. In rheumatic fever prophylaxis, 600.000-1.200.000 U/dose IM (each month) is applied. Penadur LA, Deposilin are its derivatives. It does not cause shock (Apak, 1996; Dökmeci, 2000; Eroğlu, 2002).

Monitoring: Shall high doses be applied in patients with renal failure the serum sodium and potassium levels should be monitored. They should be monitored in terms of extravasation (Kanmaz, 2010).

Caution: The crystallized penicillin G should only be used IV. Procaine and benzathine penicillin G should only be used IM (Kanmaz, 2010).

Incompatible Drugs: Amphotericin B, aminophylline, aminoglycosides, metoclopramide (Kanmaz, 2010).

The things to be considered by nurse applying the drug: Nurse should know whether child is allergic to the drug or not (Kavaklı et al, 1998).

After the vial is diluted with sterile water the drug should be well dissolved before the desired dose is taken from the vial.

In case that high dose of Penicillin G is rapidly administered by IV route it can cause such electrolyte imbalances as potassium and sodium. So the drug should be administered very slowly. When administered by IM route, the injection area should be carefully selected; the drug should be administered deep and the area should be frequently changed (Kavaklı et al, 1998).

After the drug is administered by parenteral route the children should at least be monitored for an hour especially in terms of allergy and anaphylaxis. The presence of erythema and pallor in the injection area of IV and IM can be a sign of sensitivity. And also in case that the child is observed with anxiety, nausea, vomiting, dyspnea, tremor, instant febrility, and rash it should be considered that it might be an allergic reaction. Allergic reactions should immediately be notified to doctor. Drug, tools and equipment should all be available for an emergency (Kavaklı et al, 1998).

In case of an extravasation hyaluronidase can be used (Kanmaz, 2010).

Toxicity symptoms should be closely monitored in newborns, infants and people with renal failure. Bleeding time should be monitored (Kavaklı et al, 1998).

In oral route the best is to administer the drug with water pre-meals. Administering the drug 1 hour before, or 2 hours later than the meals decreases the effect of gastric acid or the possibility that foods delay the absorption of drugs. Child should be prevented from drinking acid beverages 1 hour before and after the administration of drug (Kavaklı et al, 1998).

Tablet drugs should be protected against light. Oral suspensions and syrups should be preserved in refrigerator. The infusion solutions of penicillin G can stay for 24 hours under room temperature (Kavaklı et al, 1998).

6.1.2 Penicillines resistant to penicillinase enzyme

This group of penicillin cannot hydrolyze with staphylococcal penicillinase. This antibiotic is preferred in staphylococcal infections resistant to penicillin (Eroğlu, 2002; Küçüködük, 1994).

6.1.2.1 Methicillin

In newborn,

IM, IV (15-30min.), <2000g <14 days: 50 mg/kg/day (every 12 hours),
<2000g >14 days: 75 mg/kg/day (every 8 hours),
>2000g <14 days: 75 mg/kg/day (every 8 hours),
>2000g >14 days: 100 mg/kg/day (every 6 hours),
For others: IV (15-30 min.), IM 100-200 mg/kg/day (every 4-6 hours), PO: 50-100 mg/kg/day (every 6 hours) (Eroğlu, 2002; Küçüködük 1994).
Side effects: It can cause interstitial nephritis. The dose should be adjusted in renal failure. Along with other penicillin it can produce cross allergic reaction (Apak, 1996).

6.1.2.2 Aminopenicillin

6.1.2.2.1 Amoxicillin

Even if administered with meals through GIS amoxicillin is absorbed faster and almost completely and has fewer side effects compared to ampicillin. It is an acid resistant ampicillin derivative and administered at a dose of PO; 25-50 mg/kg/day (every 8 hours) (Longo et al, 2002).

In a study where Feder and his friends (1999) compared the effects of Amoxicillin and Penicillin V it has been found out that amoxicillin does better than penicillin V in the treatment of angina caused by group a beta-hemolytic streptococcus (Feder et al, 1999).

6.1.2.2.2 Ampicillin

It covers the gram negative spectrum of penicillin. Newborn: IM, IV (15-30 min.), <7 days <2000 g: 50 mg/kg/day (every 12 hours), >2000 g: every 8 hours, >7 days <2000 g: 100 mg/kg/day, >2000 g: every 6 hours.

Infant, child: 50-100 mg/kg/day, PO (every 4-6 hours), Sepsis: 100-200 mg/kg/day IV (every 4 hours), Meningitis: 200-400 mg/kg/day IV (every 4 hours), in other infections: 100-200 mg/kg/day IV (every 4-6 hours) (Eroglu, 2002; Dokmeci, 2000; Kucukoduk, 1994).

Mode of Administration: IV slow
Preparation: Vials are prepared with 5-10 ml sterile water.
Miscible Serums: 5% Dex, SF
Drugs to be confronted at the end point: Fat emulsions, Acyclovir, Aminophylline, Calcium gluconate, Cefepime, Furosemide, Heparin, Insulin, Magnesium sulfate, Metronidazole, Potassium chloride, Vancomycin.
Incompatible Drugs: Dex/Amino acid, Amicasin, Dopamine, Epinephrine, Fluconazole, Gentamicin, Midazolam, Sodium bicarbonate.
Storage Conditions: Should be consumed in 1 hour.

6.1.2.2.3 Ampicillin sodium sulbactam

Dose: Dose is determined by your doctor. Typically, adults and children weighing over 30 kg - 375-750 mg 2 times daily for 5-14 days. Children under 30 kg body weight, have completed one year of age - 25 - 50 mg /kg body weight per day in two divided doses every 12 hours.

Uses: Broad-spectrum antibiotic useful against group *B. streptococcus, Listeria monocytogenes*, and suscetible *E coli* species

Adverse Effectes: Very large doses may results in CNS excitation or seizure activity. Moderate prolongation of bleeding times (by approximately 60 second) may occure after repeated doses. Hypersensitivity reaction (maculopapular rash, ulticarial rash, off fever) are rare in neonates (Young & Mangum, 2010).

6.1.3 Side effects of penicillin

6.1.3.1 Allergic reactions

Penicillin allergy can be diagnosed by taking a skin test. Acute allergic reactions can be such delayed reactions as anaphylaxis, angioneurotic edema and urticarial; and also be fever, eosinophilia, hemolytic anemia, serum disease, urticarial and maculopapular rash. The presence of rash is not indication to cease drug use (Eroğlu, 2002).

6.1.3.2 Dose-related effects

High doses can cause CNS toxicity, hypopotassemia and coagulation impairments (Apak, 1996; Eroğlu, 2002).

6.1.4 Cephalosporins

Their mechanisms of action resemble to penicillin. They are grouped in four generations. As the generation increases the activity against gram (-) also increases. The ones aside from cefuroxime and third-generation are not able to penetrate CNS. They cannot be used in bacterial meningitis treatment. Cephalosporins are commonly used because of their clinical utilities in the treatment of common infections (Rang et al, 1998; Zeph, 2002).

While maculopapular rash, drug-related fever and positive Coomb's test are the major side effects such reactions and anaphylaxis as urticarial and serum diseases are rarely seen (Rang et al, 1998; Zeph, 2002).

Cephalosporins cause allergic reactions in patients allergic to Penicillin. With the use of cephalosporin side effects are observed in 10% of the patients allergic to Penicillin (Puchner & Zacharisen, 2002).

6.1.4.1 First-generation cephalosporins

They are active against gram (+) cocci including staphylococcus aureus, and such gram (-) organisms as *E. coli* and *Klebsiella*. They are inactive against enterococci and H. influenzae. First-class cephalosporins cannot cross the blood-brain barrier and so are not effective in the treatment of central nervous system infections (Apak, 1996; Behrman & Kliegman, 2001; Dökmeci, 2000; Eroğlu, 2002).

6.1.4.1.1 Cephadroxil

Administered at the dose of 30 mg/kg/day (every 12 hours) PO, It has such side effects as hypersensitivity reactions, rarely renal toxicity, neuropathy, and eosinophilia (Apak, 1996; Behrman & Kliegman, 2001; Eroğlu, 2002).

6.1.4.1.2 Cephalothin

Newborn; IV (15-30 min.), IM <7 days; 40 mg/kg/day administered every 12 hours; >7 days; 60 mg/kg/day administered every 8 hours. The side effects are the same as in cephadroxil (Apak, 1996; Eroğlu, 2002).

6.1.4.1.3 Cefazolin sodium

Newborn; 40 mg/kg/day IM-IV administered every 6 hours. Cefazol, Cefamezin, Maksiporin, Cefozin are its derivatives. It rarely has such side effect as rash, positive Coomb's test, coagulopathy in uremic patients (Apak, 1996; Eroğlu, 2002).

6.1.4.2 Second-generation cephalosporins

They are used in gram (+) cocci, penicillinase producing and not producing H. influenzae, in *Klebsiella pneumonia* related bronchopulmonary infections, in E. Coli or proteus related nosocomial infections, in urinary infections caused by enterobacters and in the treatment of sinusitis and otitis media for the ones allergic to amoxicillin (Dökmeci, 2001).

Unlike others Cefuroxime is the only second-generation cephalosporin to cross blood-brain barrier. In case of an infection it is able to penetrate CNS. It is especially used in H. influenzae meningitis and sepsis treatment (Eroğlu, 2002).

6.1.4.2.1 Cefaclor

It is used in the treatment of upper and lower respiratory tract, urinary tract, skin and soft tissue infections as well as in otitis media and susceptible organisms. And it is administered every 8 hours at a dose of 20-40 mg/kg/day (Behrman & Kliegman, 2001; Eroğlu, 2002).

6.1.4.2.2 Cefoxitin

In children older than 3 months it is administered every 6-8 hours at a dose of 60-80 mg/kg/day either as IV or IM. It can cause thrombophlebitis, diarrhea and pseudomembranous colitis (Apak, 1996; Eroğlu, 2002).

6.1.4.3 Third-generation cephalosporins

Compared to first-generation cephalosporins they are less active against gram (+) cocci; however more active against most of the strains of gram (-) cocci. While they are moderately active against *Pseudomonas aeruginosa* they are more active against *H. influenza* and *N. gonorrhoeae*. They can easily penetrate into CNS from inflamed meninges. They are usually discharged from kidneys (Dökmeci, 2000).

6.1.4.3.1 Cefotaxime sodium

Treatment of neonatal meningitis and sepsis caused by susceptible gram-negative organisms (e.g. *E coli, H influenzae,* and *Klebsiella*), Treatment of disseminated gonococcal infections.

Dose: 50 mg/kg IV (Young & Mangum, 2010).

Newborn; < 7 days: (100 mg/kg/day) 12 hours interval, > 7 days; (150 mg/kg/days) IV-IM 8 hours interval, others; 100-200 mg/kg/days IV-IM 6-8 hours interval, for Meningitis; 200 mg/kg/days IV 6 hours interval (Apak, 1996; Eroğlu, 2002; Küçüködük, 1994).

Adverse Effects: neurotoxicity risk increases if used with Aminoglykosides. It may result in hypersensitivity for penicillin sensitive people (Apak, 1996; Eroğlu, 2002). Side effects are rare but include rash, phlebitis, diarrhea, leukopenia, granulocytopenia, and eosinophilia (Young & Mangum, 2010).

6.1.4.3.2 Ceftazidime

Treatment of neonatal meningitis and sepsis caused by susceptible gram-negative organisms (e.g. *E. coli, H. influenze, Neisseria, Klebsiella,* and *Proteus* species), especially *Pseudomonas aeruginosa*. Resistance among strains of *Serratia* and *Enterobacteriaceae* is increasing (Kanmaz, 2010; Young & Mangum, 2010).

Dose: 30 mg/kg per dose IV infusion by syringe pump over 30 minutes, or IM. To reduce pain at IM injectione site, ceftazimide may be mixed with 1% lidocaine without epinephrine (Kanmaz, 2010; Young & Mangum, 2010).Newborn; IM-IV <7 days and <2000 g; 100 mg/kg/days every 12 hours, >2000 g; 100 mg/kg/days every 8 hours, >7 days; 100-150 mg/kg/days every 8 hours, for others; 100-150 mg/kg/days (max 6 g) IV-IM every 8 hours (Apak, 1996; Eroğlu, 2002).

Adverse Effects: Reported adverse effects are uncommon but include rash, diarrhea, elevated hepatic transminases, eosynophilia, and positive Coombs' test (Kanmaz, 2010; Young & Mangum, 2010).

Administration and Storage Conditions: When the drug in powder gets diluted it can be stored for 24 hours under room temperature; and 7 days in refrigerator. It has not been approved to use preparations containing L-Arginine on children. As the forms administered to children contain sodium carbonate it releases carbon dioxide bubbles when diluted (Kanmaz, 2010).

Incompatible Drugs: Fluconazole, Midazolam, Vancomycin (Kanmaz, 2010).

6.1.4.4 Fourth-generation cephalosporins

6.1.4.4.1 Maxipime

Administered at a dose of 50-100 mg vial every 8 hours (Eroğlu, 2002).

6.1.5 Aminoglycosides

They inhibit the protein synthesis ribosomes. They have bactericidal effects on gram (-) enteric bacilli and *S. aureus*. And they are discharged from kidneys. Dose adjustment is important even in minor renal failures (Eroğlu, 2002).

6.1.5.1 Amicacin

Uses: Amicacin belongs to the aminoglycoside family of antibiotics. It has a very broad spectrum of activity. Bactericidal effect on bacteria of the strains of Gram-positive and Gram-negative and are resistant to certain enzymes produced by bacteria - betalactamase. Amicacin bacteria disrupts protein synthesis (Young & Mangum, 2010).

Newborn ; Gestation age ≤ 27 → 18 mg/kg/dose every 48 hours
28-30 → 18 mg/kg/dose every 36 hours
31-33 → 16 mg/kg/dose every 36 hours
≥ 34→ 15 mg/kg/dose every 24 hours (Kanmaz, 2010).

Side Effects: Nephrotoxicity, ototoxicity, arthralgia, rash, eosinophil, neuromuscular block may develop (Apak, 1996).

> 1/100- Dizziness, sense of hearing and balance.

1/1000- Fever. Rash and itching. Disturbances in liver function. Changes in the blood picture.

<1/1000- Headache. Lowering blood pressure. Reducing the number of white blood cells, platelet count. Anemia. Tingling. Convulsions. Arthralgia (Young & Mangum, 2010).

Incompatibility: Lipid solution, Ampicillin, amphotericin B, phenytoin (Kanmaz, 2010).

6.1.5.2 Gentamicin

It is one of the most commonly used aminoglycosides (Kırdak & Kilicturgay, 1996; Rang et al, 1998).

Uses: Treatment of infections caused by aerobic gram-negative bacilli (e.g. *Pseudomonas, Klebsiella, E. coli*). Usually used on combination with a B-lactam antibiotic (Young & Mangum, 2010). High serum levels are required for bactericidal effect. Side effects are less seen with longer dose intervals. The volume of distribution increases in patients with PDA and clearance decreases. In premature and asphyxiated infants serum half-life prolongs (Kanmaz, 2010).

Gestation age ≤29 weeks→ 0-14 mg/kg/dose every 72 hours
30-36 weeks →0-14 mg/kg/dose every 48 hours
>14 mg/kg/dose every 24 hours
37-44 weeks→ 0-7 mg/kg/dose every 48 hours
>7 mg/kg/dose every 24 hours
≥45 weeks every 24 hours for all (Kanmaz, 2010).

Adverse Effects: The most frequently reported adverse reactions are occular burning and irritation upon drug instillation, non-specific conjunctivitis, conjunctival epithelial defects, and conjunctival hyperemia.

Other adverse reactions which have occurred rarely are allergic reactions, thrombocytopenic purpura, and hallucinations (Young & Mangum, 2010).

Garamycin, Genta, Gensif, Gentamicin, Gentrex are its derivatives. It has ototoxic and nephrotoxic side effects (Kırdak & Kılıçturgay, 1996; Rang et al, 1998). Temporary tubular dysfunction: loss of calcium, magnesium and sodium via the urinary system. Vestibular and auditory toxicity. When used with patients using pancuronium neuromuscular blockage may increase. In the event that extravasation develops hyaluronidase can be used. Other concomitant ototoxic and nephrotoxic drugs increase the toxicity (Kanmaz, 2010).

Incompatible Drugs: Amphotericin B, Ampicillin, Furosemide, Heparin (>1 U/ml), Imipenem/Cilastatin, Indomethacin, Methicillin, Mezlocillin, Nafcillin, Oxacillin, Penicillin G, Propofol, Cefepime, Ticarcillin/Clavulanate (Kanmaz, 2010).

6.1.5.3 Streptomycin sulfate

It is an antibiotic and anti-tuberculostatic drug. It affects some gram negative and positive microorganisms (Kavaklı et al, 1998). It is used with Isoniazid and other tuberculosis drugs in tuberculosis meningitis and progressive tuberculosis. In tuberculosis meningitis it is administered by IM route every 12 hours 20-40 mg/kg/day. The maximum dose is 1 g/day. The length of treatment period is usually 2-3 months. Higher doses and/or more prolonged therapy may result to destruction in 8th cranial nerve (Eroğlu, 2002).

Side effects: Myocarditis, Ataxia, nuisance, vomiting, ototoxicity, nephrotoxicity and hypersensitivity can be seen (Kavaklı et al, 1998).

6.1.5.4 tobramycin

It is more active against P. Aeruginosa than gentamycin. Newborn; IV (30-60 min.) , IM; <7 days <34 weeks <1500g; 3 mg/kg every 24 hours, >1500g; 2.5 mg/kg every 18 hours, >34 weeks >1500g; 2.5 mg/kg every 12 hours, >after 7 days; 5 mg/kg every 12 hours, for older people; 5-7.5 mg/kg/day IM, IV every 6-8 hours (Eroğlu, 2002; Küçüködük, 1994).

6.1.5.5 Netilmicin

Treatment of infections caused by aerobic gram-negative bacilli (Young & Mangum, 2010). It is antimicrobial effective and indicated for the treatment of sepsis caused by susceptible E. *coli, Klebsiella, Enterobacter, Pseudomonas, H. influenza, Salmonella, Shigella, Staphylococci* and of respiratory tract and surgical infections. And it is used in the treatment of complicated urinary system infections, sepsis, skin and skin joint infections, lower respiratory infections and intra-abdominal infections (Köksal & Mangum, 2010).

Uses: Serious life-threatening infections with bacteria sensitive to Netromycin (sepsis, endocarditis) (Young & Mangum, 2010).

Dose: The dose to be used in the first week ≤29 gestational weeks 5 mg/kg/dose every 48

The dose to be used in the first week ≤29 gestational weeks 5 mg/kg/dose every 48 hours

30-33 weeks 4.5 mg/kg/dose every 48 hours

34-37 weeks 4 mg/kg/dose every 36 hours

≥38 weeks 4 mg/kg/dose every 24 hours

After the first week 4 mg/kg is administered as first dose. After 12-24 hours following the end of infusion the dose interval is calculated on the basis of serum concentration (Kanmaz, 2010).

Side Effects: 1/100- Rash, pruritus. Protein in the urine, an increase of uric acid in urine. Dizziness and balance disorders. The deterioration of hearing. 1/1000- Changes in blood picture. Urticaria. Changes in the liver. <1/1000- Headache. Anemia. Lowering blood pressure. Kidney damage (Young & Mangum, 2010).

Administration and Storage Conditions: Ampoules should be diluted before use. The drug diluted with SF can be stored for 3 days in refrigerator (Kanmaz, 2010).

Incompatible Drugs: Amphotericin B, Ampicillin, Furosemide, Heparin, Methicillin, Mezlocillin, Nafcillin, Oxacillin, Penicillin G, Propofol, Ticarcillin/Clavulanate (Kanmaz, 2010).

6.1.6 Macrolides

6.1.6.1 Erythromycin

It inhibits the protein synthesis by binding to ribosome. It can be used with sulphonamide for otitis media treatment (Eroğlu, 2002; Gallardo & Thomas, 1999).

Uses: Erythromycin is used alternatively instead of penicillin to treat bacterial infections, especially in patients allergic to penicillin. The drug is effective in the treatment of diphtheria treatment of whooping cough, pneumonia caused by Mycoplasma pneumonia (including infants), Legionnaires' disease, the treatment of Chlamydia, Gonorrhea, Syphilis, endocarditis, urinary tract inflammation, conjunctivitis (Young & Mangum, 2010).

Dose: 10 mg/kg PO (Young & Mangum, 2010). While erythromycin estolate should be administered every 3 hours; ethylsuccinate one should be administered every 6 hours with food. In chlamydia treatments: Estolate form 12.5 mg/kg/dose every 6 hours for 14 days. In serious infections 5-10 mg/kg/dose every 6 hours with a slow infusion for 60 min. or 10 mg/kg/dose PO. In ophthalmia neonatorum treatment: 0.5% cream for each conjunctiva (Kanmaz, 2010).

Side effects: It is accepted as one of the most dependable antibiotics. The side effects are rarely seen and usually light and limited to skin. However in several occasions angioedema and urticarial have been observed to develop (Gallardo & Thomas, 1999).

Drug Interaction: The plasma clearance of midazolam decreases by 50%. Theophylline and carbamazepine serum concentration may increase. When used together with sisapride, it causes serious dysrhythmias (Kanmaz, 2010).

Monitor: Heart rate and blood level should be monitored during IV use. Liver function tests should be carried out. Hemogram can be used for eosinophilia (Kanmaz, 2010).

6.1.6.2 tetracyclines

It inhibits bacteria protein synthesis. It has wide-spectrums active against gram (+) and gram (-) bacteria (Behrman & Kliegman, 2001; Eroğlu, 2002). Its use is limited in infants and children because of the side effects. Tetracycline prevents growth accumulating in bones and teeth. It should be used on ones older than 8 years old. It may increase intracranial pressure in infants (Eroğlu, 2002).

6.1.6.2.1 Chlortetracycline hydrochloride

PO: administered every 6 hours at a dose of 25-50 mg/kg/day (Köksal & Reisli, 2002).

6.1.6.2.2 Oxytetracycline

Child; PO: 25-50 mg/kg/day every 8 hours, IM: 15-20 mg/kg/day every 8-12 hours, IV: 10-20 mg/kg/day every 12 hours (Eroğlu, 2002).

6.1.7 Other antimicrobial drugs

6.1.7.1 Clindamycin

It is a derivative of lincomycin. It inhibits protein synthesis. It is active against gram (+) cocci and anaerobes (Köksal & Reisli, 2002). Its metabolism in premature is highly variable (Kanmaz, 2010).

Dose: 5-7.5 mg/kg/dose IV slow infusion for 30 min. or PO (Kanmaz, 2010).

Newborn; (IM/IV), <7 days <2000g: 10 mg/kg/day every 12 hours >2000g: 15 mg/kg/day every 8 hours, >7 days <2000g: 15 mg/kg/day every 8 hours, >2000g: 20 mg/kg/day every 4 hours, infant and children; 10-25 mg/kg/day (PO) every 6-8 hours or 25-40 mg/kg/day IV, IM every 6-8 hours (Eroğlu, 2002).

Side effects: Such gastrointestinal symptoms as nausea, vomiting, nuisance, and diarrhea are frequent (Apak, 1996; Eroğlu, 2002). Pseudomembranous enterocolitis may develop. Given fast by infusion it may cause syncope and respiratory arrest. Cleocin, Clindan, Klinoksin are its derivatives (Eroğlu, 2002).

6.1.7.2 Chloramphenicol

It inhibits protein synthesis. It has wide spectrum. It is bacteriostatic for many organisms in low concentrations. Newborn; <14 days 25 mg/kg/day PO, IV, every 12 hours >14 days <2000g: 25 mg/kg/day PO, IV, every 4 hours, >2000g: 50 mg/kg/day PO, IV every 4 hours, infant and children; 50-100 mg/kg/day PO, every 6 hours IV 100 mg/kg/day every 4 hours (Eroğlu, 2002; Dökmeci, 2001).

Side effects: Non dose-related aplastic anemia is a rarely seen; but a serious complication. Dose-related bone marrow suppression is frequently seen and reversible (Eroğlu, 2002).

6.1.7.3 Rifampicin

It is an antimicrobial and antibacterial agent. It is used with at least one more antituberculosis agent in tuberculosis treatment. And administered as single dose 10-20 mg/kg/day PO (Dökmeci, 2001).

6.1.7.4 Vancomycin

It inhibits cell wall synthesis in gram (+) bacteria (Dökmeci, 2001).

Uses: Drug of choice for serious infections caused by Methicillin-Resistant Staphylococcus (e.g. S. Aureus and S. Epidermidis) and Penicillin-Resistant Pneumococci (Dökmeci, 2001; Young & Mangum, 2010). Dose restriction is required in case of a renal failure. It cannot be administered

by oral route as it cannot be absorbed well enough. IM administration causes tissue necrosis. It is administered only by IV route in systemic infection treatments (Dökmeci, 2001).

Dose: IV infusion by syringe pump over 60 minute. Meningitis: 15 mg/kg per dose. Bacteremia: 10 mg/kg per dose (Young & Mangum, 2010). Newborn; IV, <7 days <1200g; 15 mg/kg/day every 24 hours, >1200g; 30-45 mg/kg/day every 12 hours, >7 days <1200g; 15 mg/kg/day every 24 hours, >7 days >1200g; 30-45 mg/kg/day every 8-12 hours. For others; 45-60 mg/kg/day every 6-8 hours (Dökmeci, 2001; Ekenel et al, 2001; Eroğlu, 2002).

Adverse Effects: Nephrotoxity and ototoxity: Enhanced by aminoglycoside therapy. Rash and hypotension (red man syndrome): Appears rapidly and resolves within minutes to hours. Lengthening infusion time usually eliminates risk for subsequently doses. Neutropenia: Reported after prolonged administration (more than 3 weeks). Phlebitis: May be minimized by slow infusion and dilution of the drug. (Eroğlu, 2002; (Young & Mangum, 2010).

Preparation: The maximum concentration should be 5 mg/ml.

Miscible Serums: 5% Dex, 10% Dex, SF

Drugs to be confronted at the end point: Dex/Amino acid mixture, Lipid solution, Acyclovir, Aminophylline, Ampicillin, Amicasin, Fluconazole, Heparin (concentration ≤1 U/ml), Calcium gluconate, Meropenem, Midazolom, Potassium chloride, Ranitidine, Sodium bicarbonate.

Incompatibility: Cefazolin, Cefepime, Cefotaxime, Ceftazidime, Ceftriaxone, Dekort, Heparin (concentration >1 U/ml)

Storage Conditions: The solution diluted with sterile water as 50 mg/ml can be stored for 14 days in refrigerator.

6.1.7.5 Sulphonamide

The main indications are non-complicated urinary infections. Erythromycin-sulphonamide combination is effective in the treatment of otitis media. It is used in acute rheumatic fever prophylaxis. However it is not effective in group A streptococcus infection. Such drug-related reactions as fever and rash may develop (Dökmeci, 2001).

6.2 Antiviral drugs

6.2.1 Acyclovir

Acyclovir is one of the most commonly used antiviral drugs (Kavaklı et al, 1998). Treatment of neonatal herpes simplex infections varicella zoster infections with CNS and pulmonary involvement, and herpes simplex encephalitis (Kavaklı et al, 1998; Young & Mangum, 2010).

It can be used for the treatment of herpes simplex virus infections of newborn, varicella infections of children taking immunosuppressive and of immunodeficient children (Kavaklı et al, 1998).

Dose: 20 mg/kg per dose Q8 hours IV by syringe pump over 1 hour. Prolong the dosing interval in prematures infant <34 weeks PMA, or in patients with significant renal impairment or hepatic failure. Treat localized herpes simplex infections for 14 days,

disseminated or CNS infections for 21 days (Young & Mangum, 2010).As this drug's intestinal absorption is not that good it should be taken by oral route at high doses. The drug reaches its peak after 1.5-2 hours following being administered by oral route. Almost 30-90% of it is discharged by urinary system (Kavaklı et al, 1998).

Adverse Effects: The most common side effects are nausea, vomiting, diarrhea and headache. Other reported side effects include agitation, confusion, rash, anemia, and muscle pain. Hypersensitivity reactions, seizures, agitation, confusion, anemia, hepatitis, and muscle pain have also been reported (Apak, 1996; Kavaklı et al, 1998; Young & Mangum, 2010).

The things to be considered by nurse applying the drug: In application by IV route a vial of 500 mg is diluted with 10 ml sterile water. The vial is shaken until the drug is fully dissolved. The desired dose is taken into syringe. In order to decrease concentration a single dose should be administered every 1 hour with infusion solution and if possible with infusion pump. Fast application may result in phlebitis and kidney destruction. The infusion area should be changed in order to avoid thrombophlebitis. The prepared solution should be used within 12 hours.

As the drug gets discharged from urinary system the child should be provided with adequate hydration pre-application and during application. The nephrotoxicity risk decreases after 2 hours following infusion application.

Nurse should attentively observe the observable side effects of the drug and should notify doctor if any is observed. If necessary, drug use should be ceased at once (Kavaklı et al, 1998).

6.2.2 Gansklovir

It is an antiviral drug used for the prevention of hearing loss in infants with symptomatic congenital CMV infection (Dökmeci, 2001; Kanmaz, 2010).

Children; first line treatment, 10 mg/kg/day IV (1 hour, slow) every 8-12 hours, 14-21 days; Maintenance, 5-6 mg/kg/day IV every 12-24 hours for 5 days in a week (Dökmeci, 2001). The dose should be halved in case of a serious neutropenia (<500/mm3) (Kanmaz, 2010).

Side Effects: Granulocytopenia, anemia, thrombocytopenia (Kanmaz, 2010).

Incompatible Drugs: Enalaprilat, Fluconazole, Linezolid, Propofol, Remifentanil, Aztreonam, Cefepime, Piperacillin-Tazobactam (Kanmaz, 2010).

6.2.3 Interferons

These composites produced by body cells against viral infections can be synthesized via recombinant DNA technology in our day. The activities of these substances in the treatment of virus infections are a matter of research (Biçer, 2008).

6.3 Antifungal drugs

6.3.1 Amphotericin B liposome

It destroys the cell membrane permeability. It is used in progressive and fatal infections as a result of toxicity (Apak, 1996; Dökmeci, 2001; Eroğlu, 2002).

Uses: Treatment of systemic fungal infections resistant to conventional amphotericin B therapy or in patients with renal or hepatic dysfunction (Young & Mangum, 2010).Dose: 5 to 7 mg/kg dose Q24 hours IV infusion by syringe pump over 2 hours (Young & Mangum, 2010).

It is administered by IV route every 2-6 hours in a 5% dextrose solution. It is started with 0.25 mg/kg/day and increased by 0.25 mg/kg/day in 1-2 days and can be advanced up to 1-1.5 mg/kg/day (Apak, 1996; Dökmeci, 2001; Eroğlu, 2002).

Side Effects: Anemia, thrombocytopenia, hypokalemia, nausea/vomiting, and fever/chills (Young & Mangum, 2010).

6.3.2 Fluconazole

It is active against oropharynx, esophagus, urinary and systemic candidiasis. It is orally well- absorbed. It interacts with Warfarin, Phenytoin, Cyclosporine and Rifampin (Eroğlu, 2002).

6.3.3 Nystatin

It is used in skin and mucosal candidiasis infections (Apak, 1996; Kanmaz, 2010). It resembles to Amphotericin B as structure. It cannot be absorbed via gastrointestinal channels, skin and mucosae. It may have fungicidal or fungistatic effect (Kanmaz, 2010).

Dose: Topical: cream or ointment can be used on the affected area every 6 hours. Therapy should be maintained even after symptoms disappear (Kanmaz, 2010).

PO: from 100.000 U/ml solution 2 ml for term infants, 1 ml for preterm ones every 6 hours for each side of mouth. Therapy should be maintained even after symptoms disappear (Kanmaz, 2010).

Side effects: Cream or ointment related rash (Kanmaz, 2010).

Administration Properties: Oral suspension must be shaken well before use. This suspension includes <1% alcohol, saccharin, 50% sucrose (Kanmaz, 2010).

6.4 Other drugs

6.4.1 Acetaminophen

It is a drug whose analgesic and antipyretic effect is almost equal to aspirin. However it does not resemble to aspirin in terms of gastric mucosa destruction and bleeding. It has no antirheumatic effect being only active against mild and moderate fever. It is used in cases of nuisance, muscle and joint pain, neuralgia and fever. It is also advised in situations where aspirin is contraindicated or not tolerated (Kavaklı et al, 1998).

The dose, route of administration, duration and discharge of drug:

Oral: loading dose 24 mg/kg, maintenance dose 12 mg/kg/dose
Rectal: loading dose 30 mg/kg, maintenance dose 20 mg/kg
Maintenance dose intervals
Preterm ≤32 weeks: 12 hours

>32 weeks: 8 hours
Term 6 hours (Kanmaz, 2010).

age-appropriate daily dose:
0-1 month→ 40 mg
4-11 months →80 mg
1-2 age →120 mg
2-3 age →160 mg
4-5 age →240 mg
6-8 age →320 mg
9-10 age→400 mg
11 years old and older→480 mg (Kavaklı et al, 1998).

The drug is administered every 4-6 hours. It should not exceed more than 5 doses within 24 hours. The drug can be in tablet, capsule, drop, suspension, syrup and suppository forms. The drug gets absorbed by gastrointestinal system, reaches the highest level in blood within half an hour-one hour and sustains its effect for almost 5 hours.

It is metabolized in liver and discharged from body via urinary system. It reaches fetus through placenta (Kavaklı et al, 1998).

Side effects of the drug: As a result of higher dose intake and more prolonged therapy vomiting, nausea, confusion, fever, coma, hepatic and renal tubular necrosis can be observed (Kavaklı et al, 1998). Liver toxicity occurs with excessive doses or after prolonged administration (>48 hours) of therapeutic doses. Rash, fever, thrombocytopenia, leupenia, and neutropenia have been reported in children (Young & Mangum, 2010).

The things to be considered by nurse applying the drug: Nurse should be warned not to exceed recommended dose. For children who have received higher doses and more prolonged therapy liver, kidney and hematopoietic functions should be analyzed.

In case of children with nutritional deficiency it may result in toxicity in liver even if higher doses are not administered.

If the drug is used to reduce fever it should not be forgotten that it can mask the serious disease condition.

The drug should be stored in tight-closed, light-proof bottles and kept away from the reach of children (Kavaklı et al, 1998).

6.4.2 Adenosine

Acute treatment of sustained paroxysmal supraventricular tachycardia. It may also be useful in establishing the cause of the SVT.

Dose: 50 mcg/kg rapid IV push (1 to 2 seconds). Increase dose in 50 mcg/kg increments Q2 minutes until return of sinus rhythm.

Adverse Effects: > 1 / 100 Pain in the chest. Shortness of breath. Dizziness and headache. The in flow of hot face. Speeding up heart rate. Tingling in the extremities. Nausea. 1/100-1/1000 Sweating. Lowering blood pressure. Anxiety. Seeing the fog. >1/1000 The attack of an asthma attack.

6.4.3 Adrenaline

As a bronchodilator in asthma attack it is administered 2 times at 20 minutes intervals by SC route at a dose of 0.01 mg/kg/dose. Higher dose Administration may result in arrhythmia and/or hypotension (Kartal, 2002).

Uses: The resuscitation - the cessation of the heart - together with other measures. Injections performed only by health services, which provides further information about the drug.

Dose: 0.0.1 to 0.03 mg/kg. IV push or SC (Young & Mangum, 2010).

6.4.4 Activated charcoal

It is used as absorbent in oral drug overdose treatment. The dose of 0.25-1 gr/kg can be administered by PO route every 4 hours if necessary (Eroğlu, 2002).

6.4.5 Albuterol

Albuterol is used as a bronchodilator in the treatment of bronchospasm developed in children with reversible respiratory tract disease. It affects the smooth muscles (Kavaklı et al, 1998).

The dose, route of administration, duration and discharge of drug:

The age-appropriate daily dose of albuterol:

2-6 age → 0.1-0.2 mg/kg/dose 3 times a day, 4 mg 3 times a day (the highest applicable dose)

6-12 age → 2 mg/dose 3 times a day, 24 mg/day (the highest applicable dose)

12 ages and older → 2-4 mg/dose 3-4 times a day, 8 mg 4 times a day (the highest applicable dose).

The drug is administered every 4-6 hours as 0.5% solution 0.01-0.05 ml/kg by inhalation via nebulizer. It can be administered more frequently on children with need.

Aerosol inhalation is administered on children above 12 at 90 µ/sprey and the drug reaches the highest level in blood after ½- 2 hours. It is metabolized in liver and discharged from body via urinary system (Kavaklı et al, 1998).

Side effects of the drug: Tachycardia, peripheral vasodilatation, tremor, nervousness, hyperactivity, hypokalemia, irritation in oropharynx are potential side effects (Kavaklı et al, 1998).

The things to be considered by nurse applying the drug: The drug should be well shaken before inhaler application. Mouth should be washed with water after each application in order to avoid mouth and throat dryness.

It should be administered with precaution in children with hyperthyroidism, diabetes, mellitus and heart disease. Addictiveness may develop in prolonged therapy and the usual dose may not be enough.

It has more effect when used with drugs decreasing congestion.

The serum potassium level, heart rate, respiration rate, blood gases of children should be closely monitored when the drug is administered (Kavaklı et al, 1998).

6.4.6 Aminophylline

Treatment of neonatal apnea, including post-extubation, post-anesthesia, and prostaglandin E1-inducted. Bronchodilator. May improve respiratory function (Kavaklı et al, 1998; Young & Mangum, 2010).

Dose: Loading dose: 8 mg/kg IV infusion over 30 minutes, or PO. Maintenance: 1.5 to 3 mg/kg per dose PO, or IV slow push Q8 to 12 hours. In preterms infants, changing from IV aminophylline to PO theophylline requires no dose adjustment (Young & Mangum, 2010).

The dose of 20 mg/kg/day should not be exceeded in rectal application. IM administration of drug is not advised as it causes long-term pains in the injection area (Kavaklı et al, 1998). When the drug is administered by IV route it reaches the highest level in blood within 30 minutes; by oral route it reaches within 1-2 hours.

The drug is metabolized in liver and discharged from body via urinary system. It reaches fetus through placenta in pregnancy period and is transmitted to child through natural nutrition in lactation period (Kavaklı et al, 1998).

Side Effects: An allergic reaction (difficulty breathing; closing of your throat; swelling of your lips, tongue, or face; or hives); seizures; increased or irregular heartbeats; or severe nausea or vomiting (Kavaklı et al, 1998; Young & Mangum, 2010).

The things to be considered by nurse applying the drug: The solution should be given in 20-30 minutes in IV administration. In infants younger than 6 months it should be slowly administered by infusion prepared in 5% dextrose. And it should not be mixed with other drugs.

In oral administration the drug should be administered with water half an hour or one hour before or 2 hours after meals as drug absorption is faster when child is hungry. Child should not break or chew the tablet; but swallow it as a whole. Tablet is not advised for children under the age of 12. Rectal route of administration is used for children who cannot take by oral route. If possible, drug use should be adjusted according to the excretion times of children as drug absorption is faster when rectum is empty. After the administration of drug child should be laid in supine position for 15-20 minutes. As the absorption via rectal route in children is way faster than adults the probability of toxicity is also higher. So nurse should be warned not to exceed recommended dose.

Vital signs and inputs/outputs are observed and recorded at frequent intervals. Instant and clear tachycardia is one of the symptoms of toxicity.

When side effect-related symptoms appear the drug should not be administered and doctor should be notified. In the event that the symptoms are light it can be administered with higher doses.

Such commonly consumed beverages as coffee, tea, coke can increase the reactions. While a diet rich in protein increases the output of drug; a diet rich in carbohydrate decreases the output of it. These conditions result in changes in the drug level in blood. So it may be required to readjust the dose.

The drug should be stored in refrigerator. Suppository forms should be stored either outside or in refrigerator according to the recommendation of the manufacturer (Kavaklı et al, 1998).

6.4.7 Acetylsalicylic acid

As an antipyretic and analgesic it is administered 4-6 times a day at a dose of 30-65 mg/kg/day via PO route in infants and children (Dökmeci, 2000).

6.4.8 Atropine

Reversal of severe sinus Bradycardia, particularly when parasympathetic influences on the heart predominate. Also used to reduce the muscarinic effects if neostigmine when reversing neuromuscular blockade.

Dose: IV: 0.01 to 0.03 mg/kg per dose IV over 1 minute, or IM. Dose can be repeated Q10 to 15 minutes to achieve desired effect, with a maximum total dose of 0.04 mg/kg (Young & Mangum, 2010).

Endotracheal: The same dose can be administered from ET tube. Right after ET tube, 1 ml SF should be given and PPV should be applied for homogenous distribution.

Oral: 0.02 mg-0.09 mg/kg/dose every 4-6 hours (Kanmaz, 2010).

Adverse Effects: Cardiac arrhythmias can occurs, particularly during the first 2 minutes following IV administration; usually a simple A-V dissociation more often caused by smaller rather than larger doses. Fever, especially in brain-damaged infants. Abdominal distention with decreased bowel activity. Esophageal reflux. Mydriasis and cyclopedia (Young & Mangum, 2010).

6.4.9 Calcium gluconate 10%

Uses: Treatment and prevention of hypocalcaemia, usually defined as a serum ionized calcium concentration less than approximately 4 mg/dL. Treatment of asymptotic infants is controversial.

Dose: Symptomatic hypocalcaemia – acute treatment: 100 to 200 mg/kg per dose. Maintenance treatment: 200 to 800 mg/kg per day (Young & Mangum, 2010).

The things to be considered by nurse applying the drug: The drug should be administered by IV route in a way not to exceed 0.5 ml per minute. Besides, 1000 ml serum, prepared in physiologic, can be administered every 12-24 hours. The temperature of solution should be close to the body temperature. The fast delivery of calcium to heart at higher concentrations may result in fatal cardiac arrest. So the drug should be administered very slowly when parenteral route is used. The heart rate should be checked and monitored. When the drug is administered by non-diluted IV route paresthesias, peripheral vasodilatation and hypotension can be observed. If the child is observed with any symptom drug administration should be ceased and the child should be ensured to rest for half an hour or one hour. It can cause extravasation (the process of exuding or passing out of a vessel into surrounding tissues) tissue irritation and necrosis. Nurse should closely monitor the injection area.

In order to ensure well absorption by oral route the drug should be administered 1-1.5 hours after meals. In order to promote intestinal absorption the use of milk and milk products should be decreased. As calcium gluconate increases the digital toxicity it should be attentively administered in patients receiving digital.

The effect of drug on tetany treatment is evaluated by neuromuscular recovery (Kavaklı et al, 1998).

Administration: It can be either slowly administered by IV route in 10-30 minutes or used as continuous infusion.

Miscible Serums: 5% Dex, 10% Dex, SF

Drugs to be confronted at the end point: Dex/Amino acid, Lipid solution, Aminophylline, Ampicillin, Amicasin, Dobutamine, Furosemide, Heparin, Midazolom, Meropenem, Potassium chloride, Vancomycin

Incompatibility: Amphotericin B, Fluconazole, Sodium bicarbonate

Side effects: Bradycardia, cardiac arrest, tissue necrosis, intestinal bleeding, diarrhea, gastric irritation. It should be used carefully in patients who receive digital treatment and has bradypnea.

6.4.10 Captopril

Uses: Treatment of moderate to severe hypertension. Afterload reduction in patients with congestive heart failure.

Dose: 0.01 to 0.05 mg/kg per dose PO Q8 to 12 hours. Adjust dose and interval based on response. Administer 1 hour before feeding.

Adverse Effects: Captopril produces the following side effects: Angioedema with involvement of the face, mouth, larynx, tongue, and glossitis, neutropenia, anemia and thrombocytopenia, proteinuria, acidosis, tachycardia, cardiac arrest, arrhythmias, rash and erythema multiform, exfoliate dermatitis, photosensitivity, elevated liver enzymes in serum, liver cell injury, cholestasis jaundice, gastric irritation, hepatitis, drowsiness, nervousness, depression, paresthesias of hands, confusion, ataxia, bronchitis, bronchospasm, pneumonia eosinophil, rhinitis (Young & Mangum, 2010).

6.4.11 Ceftriaxone

Uses: Treatment of neonatal sepsis and meningitis caused by susceptible gram-negative organisms (e.g. E coli, Pseudomonas, Klebsiella, H influenzae). Treatment of gonococcal infections.

Dose: Septis and disseminated gonococcal infection: 50mg/kg Q24 hours. Meningitis: 100 mg/kg loading dose, then 80 mg/kg Q24 hours. Uncomplicated gonococcal ophthalmia: 50 mg/kg (maximum 125 mg) single dose. (note: topical antibiotic therapy alone is inadequate and is unnecessary if systemic treatment is administered). IV administration: infusion by syringe pump over 30 minutes. Avoid administration of calcium-containing solution or products within 48 hours of the last administration. IM administration: to reduce pain at the injection site, reconstitute with 1% lidocaine without epinephrine.

Adverse Effects: Not recommended for use in neonatal with hyperbilirubinemia! Displaces bilirubin from albumin binding sites, resulting in higher free bilirubin serum concentration. Concurrent administration of ceftriaxone and calcium-containing solutions or products in neonates is contraindicated. Eosinophilia, Thrombocytosis, leukopenia. Increase in AST and ALT. Skin rash. Transient gallbladder precipitations occasionally associated with colicky abdominal pain, nausea, and vomiting (Young & Mangum, 2010).

6.4.12 Chloral hydrate

Uses: Sedative/hypnotic for short-term use only. Chloral hydrate has no analgesic after a feeding to reduce gastric irritation.

Dose: 25 to 75 mg/kg per dose PO. Oral preparation should be diluted or administered after feeding to reduce gastric irritation.

Adverse Effects: Chloral hydrate may lead to unpleasant side effects, including: drowsiness, nausea, vomiting, and diarrhea. Toxic doses (overdoses) can cause a marked drop in blood pressure and severely compromised respiration (breathing). Signs of an overdose of chloral hydrate can include: confusion, seizures, difficulty breathing, slurred speech, slow or irregular heartbeat, vomiting, weakness, and a lowered body temperature. Chronic use of chloral hydrate is also associated with a severe withdrawal syndrome and may induce liver damage (Young & Mangum, 2010).

6.4.13 Iron

Indication: The prevention and treatment of iron-deficiency induced anemia.

Pharmacology: Ferrous salts are preferred as they are absorbed 2-3 times better than ferric salts when administered by oral route. Ferrous sulfate, ferrous fumarate, ferrous gluconate can also be used. Absorption is better on an empty stomach. Half or one-third of it is absorbed when taken with food.

Dose: Premature infants: Elemental iron 2 mg/kg/dose PO, started after 4 weeks in doses divided into 2-3. For babies lighter than 1000 gr 4 mg/kg/day may be administered. For patients receiving EPO treatment: 6 mg/kg/day

Iron dextran: For ones who cannot take by oral route 0.4-1 mg/kg/day is administered as continuous infusion in D/AA.

Side effects: Iron treatment should not be launched as long as premature infants do not get adequate vitamin E. Hemolysis may increase in that case. Diarrhea and constipation, lethargy, hypotension, black-colored stool and erosion in gastric mucosa can be observed. It may be required to seek for occult blood in stool in suspicious cases (Kanmaz, 2010).

6.4.14 Dexamethasone

Uses: Dexamethasone is used primarily in the intensive and short-term treatment of severe allergic conditions such as asthma, also in rheumatic diseases, skin diseases, eye, blood and certain cancers.

Dose: 0.075 mg/kg per dose Q12 hours for 3 days, 0.05 mg/kg per dose Q12 hours for 3 days, 0.025 mg/kg per dose Q12 hours per 2 days, and 0.1 mg/kg per dose Q12 for 2 days IV or PO.

Adverse Effects: 1/100 Accumulation of fat around the body and face, growth retardation in children, susceptibility to infectious diseases, the activation of diabetes, muscle weakness, abnormal menstruation, body hair in women, akne. Most of these symptoms occurs as a result of long-term glucocorticoid therapy. 1/1000 Disturbances in water management, reducing the level of potassium in the body, accumulation of water in the body, raised blood pressure, heart failure, allergic reactions, accelerated blood clotting, gastrointestinal disorders, increased appetite, weight gain, damage the lining of the digestive tract, sagging skin, mental disorders manifested by extreme changes in mood, insomnia, headache, increased intraocular pressure in the eye lens opacity. If there are troublesome symptoms should seek medical attention.

6.4.15 Diazepam

It is effective as anxiolytic and muscle- relaxing agent. In treatment of status epilepticus 0.1-0.5 mg /kg/dose is administered 2 times at 5-15 minutes intervals by IV route in newborns-infants-children. Its effect by IM route is limited. To decrease anxiety: 4 times 0.2-0.3 mg/kg/day PO (Eroğlu, 2002).

6.4.16 Digoxin

Digoxin is an antiarrhythmic and cardiac glycoside drug (Kavaklı et al, 1998). It is a highly active cardiac glycoside with a half-life of 48 hours (Dökmeci, 2000; Küçüködük, 1994).

Uses: Treatment of heart failure caused by diminished myocardial contractility. Treatment of SVT, atrial flutter, and atrial fibrillation (Young & Mangum, 2010).

Dose:	*Old*	*Dose*	*Maintenance*	*Interval*
	29 <	*0.015 mg/kg*	*0.004 mcg/kg*	*24*
	30-36	*0.02 mg/kg*	*0.005 mg/kg*	*24*
	>37	*0.035 mg/kg*	*0.006 mg/kg*	*12 (Young & Mangum, 2010).*

Total digoxin dose; premature baby: 0.02 mg/kg PO, after birth of newborn; 0.01-0.03 mg/kg IM, IV / 0.04 mg/kg PO, infant; 0.03-0.04 mg/kg IM, IV / 0.05 mg/kg PO, children; 0.010-0.015 mg/kg IM, IV, PO. Higher doses result in fatal arrhythmias (Dökmeci, 2000; Küçüködük, 1994).

Adverse Effects: Toxic Cardiac Effects: PR interval prolongation, sinus bradycardia or SA block, trail or nodal ectopic beats, ventricular arrhythmias. Nontoxic Cardiac Effects: QTc interval shortening, ST segment sagging, T-wave amplitude dampening, heart rate slowing (Young & Mangum, 2010).

The things to be considered by nurse applying the drug: Before nurse administers Digoxin to a child he or she should very carefully obtain prior Digoxin use history. Serum digoxin, potassium, magnesium and calcium levels should be determined by laboratory investigations before digoxin administration. Nurse should measure radial heart rate for a minute before administrating the drug to child and if any abnormality presents he or she

should check apical pulse and its rate, rhythm and properties and notify doctor. The drug can be administered by IV route either directly or via a solution including 5% dextrose or 9% sodium chloride. Absorption may delay if the drug is administered by oral route after meals. And absorption may also delay when administered with antacids. IM administration of drug is not advised especially for children with diabetics or mild tissue perfusion as it causes pain. When IM route is used the drug should be administered deep into a large muscle mass and then the area should be massaged after injection. No more than 5 mL should be administered in one area. In case that digoxin is administered with such drugs as diuretics which decrease potassium level and some antibiotics toxicity may develop. Besides, calcium should not be administered to digitalized children. It may have fatal consequences. If the drug is used for atrial fibrillation treatment purposes nurse should check heart rate and if it is below 60 or above 100 beats per minute then he or she should notify doctor. The drug should be administered with precaution and at fewer doses in children with hyperkalemia having kidney and hepatic impairment. The inputs/outputs of child should be followed, edema should be monitored and daily weight check should be ensured. Cardiac arrhythmia and anorexia in children are early symptoms of toxicity. Nurse should pay attention to those symptoms. If it is suspected of toxicity blood digoxin level should be measured and EGK should be performed. Nurse should store the drug in tight-closed and light-proof bottles. If any color change is observed the drug should not be used (Kavaklı et al, 1998).

6.4.17 Dobutamine

It is used in temporary treatment of heart failures related to the depression caused by cardiac rigidity. 0.0025-0.010 mg/kg/min is administered by IV infusion according to the patient's response (Eroğlu, 2002).

Dose: 2 to 20 mg/kg per minute continuous IV infusion. Begin at a low dose and titrate by monitoring effects. Use a large vein for IV (Kanmaz, 2010).

Side Effects: Volume replacement should be performed before drug use as it may cause hypotension in hypovolemic patients. Tachycardia may develop at higher doses. Arrhythmia, hypertension and vasodilatation in skin may also develop. If it exudes or passes out of a vessel it causes tissue ischemia (Kanmaz, 2010).

Administration and Storage Conditions: Diluted drug can be stored for 6 hours under room temperature and 48 hours in refrigerator. Slight color change does not mean that the drug is spoiled (Kanmaz, 2010).

6.4.18 Dopamine

It is indicated for all kinds of hypotension, heart failure and circulatory impairments. To increase cardiac output and to improve organ perfusion it is started to be administered by IV infusion at a dose of 0.002-0.005 mg/kg/min (100 mg dopamine in 250 ml 5% dextrose) as 0.400 mg/ml solution. It can be advanced up to 0.020 mg/kg/min (Apak, 1996).

Uses: Treatment or hypotension

Dose: 2 to 20 mcg/kg per minute continuous IV infusion. Begin at a low dose and titrate by monitoring effects. Use a large vein for IV.

Adverse Effects: > 1/100 Headache. Additional heartbeat, increased heart rate. Pain in the chest. Nausea and vomiting. Shortness of breath. 1/1000 Heart arhythmia. Changes in the ECG. Lowering blood pressure. Allergic reactions. Pulmonary edema (Young & Mangum, 2010).

Monitor: Heart rate and intra-arterial blood pressure should continuously be monitored. Urinary output and peripheral perfusion should be observed. A large vein is recommended to use. Extra care should be shown in terms of extravasation. Pallor may be observed through the subject vein. If it exudes or passes out of a vessel it causes necrosis, in which case 1 mg/ml phentolamine should be injected around lesion (Kanmaz, 2010).

Administration and Storage Conditions: The opened ampoule should be stored in refrigerator and consumed within 24 hours. Ampoules with color change should not be used (Kanmaz, 2010).

Miscible Serums: 5% DX, 5% DSF, SF, D/AA, fat emulsions (Kanmaz, 2010).

Incompatible Drugs: Amphotericin B, Acyclovir, Furosemide, Indomethacin, Insulin, Sodium bicarbonate (Kanmaz, 2010).

6.4.19 Fentanyl

Uses: Anelgesia, sedation, anesthesia.

Dose: Sedation and analgesia: 0.5 to 4 mcg/kg per dose IV slow push. Repeat as require (usually Q2 to 4 hours).

Infusion rate: 1 to 5 mcg/kg per hours. Tolerance may develop rapidly following constant infusion.

Anesthesia: 5 to 50 mcg/kg per dose (Young & Mangum, 2010).

Neonatal dose: IV slow 0.3-2 mcg/kg/dose
IV infusion dose: 0.3-5 mcg/kg/hour (Anand, 2007).

Adverse Effects: Respiratory depression, Sometimes nausea, Vomiting, Bradycardia, Hypotension, Extremely bronchospasm. At high doses observed in a small chest muscle stiffness, which may hamper rescue breathing (Young & Mangum, 2010).

Preparation: 1 ml fentanyl from 50 mcg/ml ampoules gets diluted with 4 ml SF.

Miscible Serums: 5% DX, 10% DX, SF

Drugs to be confronted at the end point: Dex/Amino acid mixture, Dekort, Dobutamine, Dopamine, Furosemide, Heparin, Midazolam, Potassium Chloride.

Incompatible Drugs: Phenytoin, Azithromycin.

Storage Conditions: It should be protected against light. Diluted ampoules can be stored for 24 hours in refrigerator.

6.4.20 Furosemidum

Uses: Diuretic that may also improve pulmonary function. It is used in pulmonary edema, in heart failures and for increasing urinary discharge

Dose: 1 mg/kg IV slow push, IM or PO. May increase to a maximum of 2 mg/kg per dose IV or 6 mg/kg per dose PO.

Adverse Effects: > 1 /100 Decreased blood potassium levels, which implies a weakening of the muscles. Decreased levels of magnesium, calcium and sodium. Increasing levels of uric acid in the blood. Reduce the volume of blood in case of longer treatment. 1/1000 Digestive disorders. <1/1000 Phlebitis. Changes in the blood picture. Allergic reactions. If you get a rash you should immediately contact your doctor and stop taking the drug. Dizziness and tinnitus. Increased blood sugar levels (Young & Mangum, 2010).

It develops hypotension, hyponatremia, hypokalemia, alkalosis and hypercalciuria. It is highly ototoxic especially when administered fast.

Administration and Storage Conditions: The ampoules should be protected against light.

Compatible: SF and sterile water.

Incompatible: Dopamine, Dobutamine, Erythromycin, Fluconazole, Midazolam.

6.4.21 Glucagon

Uses: It is used in patients with diabetes in decline due to excessively low blood sugar. This condition usually occurs as a result of too much insulin.

Dose: 200 mcg/kg per dose IV, IM, SC

Adverse Effects: 1 /100 Nausea and vomiting. 1/1000- <1/1000 Allergic reactions (Young & Mangum, 2010)

6.4.22 Heparin

Uses: Preventing blood clots, the risk of their formation is increased, e.g. after surgical procedures in acute myocardial infarction. Heparin is also used to treat blood clots in the legs and lungs in congestion of the arteries. The use of heparin also gives good results in the treatment of frostbite and burns (Young & Mangum, 2010). Prevention of peripheral and central catheters from congestion. Its use in renal vein thrombosis is still a matter of discussion (Kanmaz, 2010).

Dose: IV for each ml of liquid 0.5-1 Unit

For thrombosis treatment 70 Unit/kg bolus in 10 minutes, 28 Unit/kg/hour continuous infusion (Young & Mangum, 2010). 75 units/kg bolus over 19 minutes.

Adverse Effects: Side effects in the form of bleeding occurs in approximately 10% of patients. >1/100 Bleeding. A decline in platelet count. Changes in the functions of the liver. <1/1000 Allergic reactions, allergic shock. Disturbances in the function of the adrenal cortex. Hair loss (Young & Mangum, 2010).

Preparation: Added onto the solution as half of the total.

Miscible Serums: SF, 5% DX, 10% DX

Drugs to be confronted at the end point: Dex/Amino acid mixture, Acyclovir, Amphotericin B, Ampicillin, Calcium gluconate, Cefazolin, Cefepime, Cefotaxime, Ceftazidime, Ceftriaxone,

Dekort, Dobutamine, Dopamine, Fentanyl, Fluconazole, Furosemide, Insulin, Meropenem, Midazolom, Penicillin G, Potassium chloride, Sodium bicarbonate, Bactrim (Young & Mangum, 2010).

Incompatible Drugs: Amicasin (if concentration is intense), Diazem, Gentamicin (if concentration is intense), Phenytoin, Vancomycin (Kanmaz, 2010).

Storage Conditions: It should be stored at room temperature under 25°C in its package (Young & Mangum, 2010).

6.4.23 Hydroxyzine hydrochloride

Uses: Sedative/hypnotic. Anesthesia induction. Treatment of refractory seizures.

Dose: IV: 0.05 to 0.15 mg/kg over at least 5 minutes. Repeat as required, usually Q2 to 4 hours. May also be given IM. Dosage requirements are decreased by incurrent use of narcotics.

Adverse Effects: Pediatric patients: desaturation 4.6%, apnea 2.8%, hypotension 2.7%, paradoxical reactions 2.0%, hiccough 1.2%, seizure like activity 1.1% and nystagmus 1.1%. The majority of airway-related events occurred in patients receiving other CNS depressing medications and in patients where midazolam was not used as a single sedating agent (Young & Mangum, 2010).

6.4.24 Ibuprofen

It is a non-steroidal anti-inflammatory agent with analgesic and antipyretic effect. As an analgesic and antipyretic it is administered at a dose of 10-15 mg/kg/dose every 4-6 hours by PO route and 40-60 mg/kg/day at maximum (Dökmeci, 2000).

Uses: Rheumatic Diseases. Menstrual pain. Pain of different origins.

Dose:

3-6 months > 5 kg 50 mg 3-4 times a day

6-12 months 50 mg 3 times a day

1-4 ages 100 mg 3-4 times a day

The maximum dose for children and newborns is:

3 months– 4 age 30 mkg 3-4 times a day (Pursell, 2010).

Adverse Effects: >1/100 Abdominal pain, burning sensation in the throat, nausea, diarrhea. Fatigue.
Headache. Rash. 1/1000 Allergic reactions. Symptoms of allergy may be asthma, rhinitis, and rash. Bleeding from the gastrointestinal tract. Gastric ulcer. Blurred vision. The deterioration of hearing. Anxiety. Insomnia (Young & Mangum, 2010).

6.4.25 Indomethacin

Uses: Closure of ducts arteriosus. Prevention of intraventricular hemorrhage.

Dose:(mg/kg)

Age at 1st dose	1st	2nd	3rd
<48	0.2	0.1	0.1
2 to 7 d	0.2	0.2	0.2
>7 d	0.2	0.25	0.25

Adverse Effects: The most common side effects are nausea, vomiting, diarrhea, stomach discomfort, heartburn, rash, headache, dizziness and drowsiness (Young & Mangum, 2010).

6.4.26 Imipenem

Uses: Restricted to treatment of no-CNS infections caused by bacteria, primarily Enterobacteriaceae and anaerobes, resistant to other antibiotics (Kanmaz, 2010; Young & Mangum, 2010).

Dose: 20 to 25 mg/kg per dose Q12 hours IV infusion over 30 minutes

Adverse Effects: Seizures occur frequently in patients with meningitis, preexisting CNS pathology, and severe renal dysfunction. Local reaction at the infection and increased platelet counts are the most frequent adverse effects. Other including eosinophilia, elevated hepatic transaminases, and diarrhea also occur in more than 5% of patients (Young & Mangum, 2010).

Incompatible Drugs: Amicasin, Fluconazole, Gentamycin, Clonazepam, Sodium bicarbonate, Tobramycin (Kanmaz, 2010).

6.4.27 Insulin

Indication: For adjuvant treatment in hypoglycemia and hyperpotassemia.

Pharmacology: It ensures intracellular glucose transmission. It converts glucose into glycogen, ensures amino acid intake and transmission of K into muscle tissue and cell. It increases fat synthesis. It inhibits lipolysis and the conversion of protein to glucose. It is decomposed in liver and kidneys. Serum half-life is 9 minutes for adults.

Dose: Intermittent dose: 0.1-0.2 U/kg, every 6-12 hours SC

Continuous infusion: 0.01-0.1 U/kg/hour

Only regular insulin can be given IV. The dose is adjusted according to blood sugar.

Side effects: Hypoglycemia and increase in insulin resistance. It can cause normoglycemic hyperinsulinemia and metabolic acidosis.

Monitor: Blood sugar should be monitored at 15-30 min. intervals after infusion and dose adjustment.

Administration and Storage Conditions: A solution of 1 U/ml concentration should be prepared by diluting with sterile water or SF. Should wait for 20 minutes to give time for connection of plastic to IV catheters before continuous infusion. It should be stored in refrigerator.

Incompatible Drugs: Aminophylline, Dopamine, Phenytoin, Phenobarbital, Pentobarbital (Kanmaz, 2010).

6.4.28 intralipid

Uses: Parental nutrition source of calories and essential fat acids.

Adverse Effects: 1/100- 1 / 1000 Fever. Chills. Nausea. Redness of the skin. <1/1000 Allergic shock. Changes in the blood picture, which occur most frequently in infants. Increase or decrease in blood pressure. Rash. Changes in liver function. Shortness of breath. Long-term painful erection (Young & Mangum, 2010).

6.4.29 Caffein

It is MSS stimulator and vasoconstrictor of cerebral vessels. It is used for vascular headache and as analeptic. Neonatal apnea loading dose: 10 mg/kg, maintenance 5-10 mg/kg/day (Biçer, 2008).

6.4.30 Ketamine

General anesthetic, sedative, hypnotic, analgesic and amnestic. IV, IM. It protects cardiovascular functions. It improves lung compliance, has bronchodilator effect. As ketamine favorably alters the heart and respiratory functions it can be used as a sedative agent in patients who receive mechanical ventilation and have myocardial depression induced by benzodiazepines and opiates. It can be used in cases where spontaneous ventilation is requested while sedation is provided (Biçer, 2008).

Neonatal Dose:

IV slow	0.5-2 mg/kg/dose
IV Inf. Dose	0.5-1 mg/kg/h
IM, SC	2 mg/kg/dose
Oral	5-8 mg/kg/dose (Anand, 2007).

Sedation: 0.5-2 mg/kg/dose IV, can be repeatedly administered at doses of 0.5 mg/kg/dose at 2-5 min. intervals or with 1-2 mg/kg/hour infusion until adequate sedation is achieved (Max. 5 mg/kg). 4-5 mg/kg/dose IM (if adequate sedation is not achieved within 10 minutes), one more dose of 2 mg/kg/dose can be administered. Rapid sequential intubation: 0.5-2 mg/kg/dose IV or 3-7 mg/kg/dose IM (1 dose). Caution: It acts fast; but slow. Aspiration and laryngospasm can be observed in patients who ventilate spontaneously in the unprotected airway. Atropine and glycopyrronium bromide are advised to use before ketamine as it increases saliva and bronchial secretions. It should not be administered in cases of increase in intracranial pressure, suspected head trauma and in convulsions whose etiology is unknown and where intracranial pressure may have increased. It can cause such reactions as hallucination and delirium and these phenomena increase by age and dose. The administration of benzodiazepines 5 minutes before ketamine is active against these phenomena (Biçer, 2008).

Side Effects: Laryngospasm, out-of-anesthesia reaction, tachycardia, hypertension, increase in intracranial pressure (Biçer, 2008).

6.4.31 Levothyroxine

Uses: Treatment of hypothyroidism

Dose: PO: 10 to 14 mcg/kg. IV 5 to 8 mcg/kg

Adverse Effects: Prolonged over treatment can produce premature craniosynostosis and acceleration of bone age (Young & Mangum, 2010).

6.4.32 Magnesium sulfate

Uses: Postpartum eclampsia. Tetanus.

Warning: Injection should not be administered in renal failure. Injections should be done slowly by controlling the breath of the patient (Young & Mangum, 2010).

6.4.33 Meropenem

Uses: Limited to treatment of pneumococcal meningitis and other serious infections caused by susceptible gram-negative organisms resistant to other antibiotics, especially extended-spectrum beta-lactamase producing *Klebsiella pneumonia* (Young & Mangum, 2010).

Dose: 20 mg/kg per dose IV

Less than 32 weeks GA, less than or equal to 14 days PNA: administered Q12 hours; after 14 days PNA: administered Q8 hours. 32 weeks and older GA, less than or equal to 7 days PNA: administered Q12 hours; after 7 days PNA: administered Q8 hours. Meningitis and infections caused by Pseudomonas species, all ages: 40mg/kg per dose Q8 hours. Give as an IV infusion over 30 minutes. Longer infusion times (up to 4 hours) may be associated with improved therapeutic efficacy (Young & Mangum, 2010).

Adverse Effects: Diarrhea (4%), nausea/vomiting (1%) and rash (2%). May cause inflammation at the injection site. The use of carbapenem antibiotics can result in the development of cephalosporin resistance in *Enterobacter, Pseudomonas, Serration, Proteus, Citrobacter,* and *Acinetobacte*r species. The risk of pseudomembranous colitis and fungal infections are also increased (Young & Mangum, 2010).

Administration: IV 30 min. infusion

Preparation: 500 mg meropenem is diluted with 10 ml proper solution. 50 mg/ml concentration is obtained.

Miscible Serums: 5% Dex, 10% Dex, SF

Drugs to be confronted at the end point: Dex/Amino acid, Lipid solution, Acyclovir, Aminophylline, Dopamine, Dobutamine, Fluconazole, Gentamicin, Heparin, Sodium bicarbonate, Vancomycin.

Incompatibility: Amphotericin B, Metronidazole, Acyclovir, Calcium gluconate, Diazepam, Zidovudine.

Storage Conditions: Diluted with sterile distilled water it can be stored for 2 hours under room temperature, 12 hours in refrigerator; diluted with SF for 2 hours under room

temperature, 18 hours in refrigerator; diluted with 5% Dex for 1 hour under room temperature, 8 hours in refrigerator. These periods of time are valid for 50 mg/ml concentration (Kanmaz, 2010).

6.4.34 Metronidazole

Uses: Reserved for treatment of meningitis, ventriculitis, and endocarditis caused by Bacteroides fragilis and other anaerobes resistant to penicillin; treatment of serious intra-abdominal infections; and treatment of infections caused by Trichomonas vaginalis. Treatment of C. difficile colitis.

Dose: Loading dose: 15 mg/kg PO or IV infusion by syringe pump over 60 minutes Maintenance dose: 7.5 mg/kg per dose PO or IV infusion over 60 minutes. Begin one dosing interval after initial dose. Adverse Effects: Seizures and sensory polyneuropathy have been reported in a few adult patients receiving high doses over a prolonged period. Drug metabolites may cause brownish discoloration of the urine (Young & Mangum, 2010).

6.4.35 Phenobarbital

It is a long-term effective MSS depressant. For sedation: infants and children; 2-3 mg/kg/day PO every 8-12 hours. For sleep: infants and children; 2-3 mg/kg/dose PO, if IM required it is repeated after 12-24 hours (Eroğlu, 2002).

Dose: 20 mg/kg IV, given slowly over 10 to 15 minutes. Refractory seizures: Additional 5 mg/kg doses, up to a total of 40 mg/kg.

Neonatal Abstinence Syndrome: 16 mg'kg PO on day 1.

Uses: Epilepsy, seizures primarily large, so called and grand mal seizures, which cover only part of the brain. Seizures in newborns.

Adverse Effects: Respiration and respiratory depression (Kanmaz, 2010). > 1 / 100 Drowsiness. Disturbances in attention. Irritability, especially in young children. The difficulty of concentration of vision. The difficulty in coordinating movements. Changes in the blood picture. Rash. Confusion, especially in older patients. 1/1000 The risk of mucous membrane of the mouth and teeth, especially during prolonged treatment. <1/1000 – Anemia (Young & Mangum, 2010).

Follow: The therapeutic concentration is 15-30 mcg/ml. Respiratory depression is observed in concentration exceeding 60 mcg/ml. The serum half-life is longer in the first 1-2 weeks. The serum half-life differs in patients taking phenytoin and valproate (Kanmaz, 2010).

Administration and Storage Conditions: The ampoules should be used within 30 minutes after opening (Kanmaz, 2010).

Incompatible Drugs: Fat emulsions, Hydralazine, Hydrocortisone, Insulin, Clindamycin, Methadone, Midazolam, Morphine, Pancuronium, Ranitidine, Vancomycin (Kanmaz, 2010).

6.4.36 Phenytoin

Uses: Anticonvulsant often used to treat seizures refractory to phenobarbital.

Dose: 15 to 20 mg/kg IV infusion over at least 30 minutes, after that 4 to 8 mg/kg Q24 hours IV or PO. Max 0.5 mg/kg/minute.

Adverse Effects: Due to the central nervous system: Nystagmus, slurred speech, impaired motor coordination, may rarely occur: dizziness, insomnia, irritability, involuntary muscle spasms, headache, in very rare cases you may experience dyskinesia.

Due to the gastrointestinal tract: most - nausea, vomiting, constipation, in rare cases can lead to hepatotoxicity.

On the part of the skin: various forms of skin rashes, systemic lupus erythematous, Stevens - Johnson syndrome, toxic epidermolysis.

On the part of the hematopoietic system: in rare cases there may be abnormal blood cell production - thrombocytopenia, leukopenia, granulocytopenia, and anemia Megaloblastic makrocytosis (equivalent of treatment with folic acid) (Young & Mangum, 2010).

Administration Type: Loading dose IV 30 minutes infusion, Maintenance dose IV slow.

Preparation: The maximum concentration should be 10 mg/ml when it is diluted with SF. 5 mg/ml concentration is obtained diluting 50 mg/ml with 9 ml SF.

Miscible Serums: SF. Stability is ruined with most of the IV liquids.

Drugs to be confronted at the end point: Fluconazole, Sodium bicarbonate

Incompatible Drugs: 5% Dex, 5% with Dextrose, Dex/Amino acid, Lipid emulsions, Aminophylline, Amicasin, Dobutamine, Fentanyl, Heparin, Potassium chloride, Vitamin K1.

Storage Conditions: Unopened ampoules should be protected against light under room temperature. Opened ampoules should not be delayed.

6.4.37 Potassium chloride

Uses: Potassium deficiency. Prevention of excessive potassium smothering as a result of taking diuretics, diabetes, long-term diarrhea.

Dose: 0.5 to 1 mEq/kg per day divided an administered with feedings. 1g KCl = 13.4 mEq K+

Adverse Effects: Confusion, anxiety, feeling like you might pass out; uneven heartbeat; extreme thirst, increased urination; leg discomfort; muscle weakness or limp feeling; numbness or tingly feeling in your hands or feet, or around your mouth; severe stomach pain, ongoing diarrhea or vomiting; black, bloody, or tarry stools; or coughing up blood or vomit that looks like coffee grounds (Young & Mangum, 2010).

Administration: IV infusion

Preparation: Maximum concentration via peripheral line is 40 mEq/L. and 80 mEq/L. through central vein. The desired amount is added to total solution.

Miscible Serums: Compatible with all standard IV solutions.

Incompatibility: Amphotericin B, Diazepam, Phenytoin.

6.4.38 Sodium bicarbonicum 8.4%

Uses: Treatment of normal anion gap metabolic acidosis caused by renal or GI losses. Sodium bicarbonate is not a recommended therapy in neonatal resuscitation guidelines. Administration during brief CPR may be determinal.

Dose: 1 to 2 mEq/kg IV over at least 30 minutes

Adverse Effects: Excess sodium in the body, which can manifest itself in the body of water retention, swelling, weakness, anxiety, swollen tongue, dizziness and headaches, fever, decrease in saliva and urine, pressure drop, rapid heart rate, apnea (Young & Mangum, 2010).

6.4.39 Ranitidine

Dose: PO: 2 mg/kg per dose Q8 hours. IV: 1.5 mg/kg per dose Q8 hours.

Uses: Prevention and treatment of stress ulcers and GI hemorrhage aggravated by gastric acid secretion.

Adverse Effects: 1/100 Fatigue. Diarrhea, rash, dizziness. 1/1000 Allergic reactions such as swelling of the skin rash, fever, seizures or asthma. Changes in the blood picture and liver function. Jaundice. Depression, hallucinations, disorientation, especially in debilitated and elderly patients. Seeing the fog. Pain in muscles and joints (Young & Mangum, 2010).

6.4.40 Steroids

Steroids are used as anti-inflammatory, immunosuppressive or in rheumatic diseases in order to increase sensitivity against beta adrenergic, chronic ulcerative colitis, nephrotic syndrome, tuberculosis meningitis and asthma.

Dose:

Hydrocortisone	10-20 IV, IM, Oral
Methylprednisolone	0.4-2 IV, IM, Oral
Prednisone	1-2 Oral

The drug can be administered 1-2 times a day by oral route. Hydrocortisone should be administered deeply IM and delta frame should not be performed. Steroids should be administered by SC route as they cause sterile abscess and pseudoatrophy. The duration of therapy may differ from 3-5 days to weeks or months depending on the diagnosis of child. The drug is metabolized in liver and discharged from body via urinary system.

Side Effects: Edema, hypertension, headache, convulsion, acne, skin atrophy, hypokalemia, alkalosis, Cushing syndrome, hyperglycemia, peptic ulcer, nausea, vomiting, cataract, glaucoma and muscle weakness are observed side effects (Kavaklı et al, 1998).

The things to be considered by nurse applying the drug: The recommendation of manufacturer on the route of administration should be taken into consideration. Nurse should administer the drug slowly by IV route. In oral administration it should be administered at meal intervals or after meals to decrease gastric irritation of drug. Salt is limited in foods. If possible diets rich in potassium and protein are prepared. The blood pressure and other vital signs, input-output, sleeping condition and daily weight check of child is observed in recorded. Oral and

hygienic care is provided at frequent intervals. Steroid can cause hyperkalemia when used with certain diuretics. Phenobarbiturates decrease the effect of steroids. Urinary and blood glucose investigations should be carried out especially in children with diabetics. It may be necessary to increase insulin dose. As it is a drug decreasing hypophyseal stimulation for a long-term it may cause adrenal insufficiency, in which cases such symptoms as loss of appetite, nausea, anorexia, pain, fever and painful urination may appear in children. The drug should be administered carefully in patients with previous psychological problems. The behaviors, emotional status, sleeping order and psychomotor activity changes of child should be monitored and notified to doctor especially on long-term treatments. The treatment should be ceased by gradually decreasing dose. Long-term applications should be avoided in that it has many side effects. Unless otherwise stated by manufacturer nurse should protect drug against light and frost (Kavaklı et al, 1998).

6.4.41 Surfactant

Uses: Prophylaxis of infants at high risk for RDS (those < 29 weeks gestation).

Mode of Action: Preparation obtained from the lungs of beef. Lowers the surface tension of pulmonary alveoli, allowing easy opening of the alveoli and facilitates the process of respiration (Young & Mangum, 2010).

6.4.42 Tracutil

Administration: It is added to TPN solution in order to meet daily trace element need. IV infusion: Infusion should not be less than 6 and less than 24 hours. Contains Iron, Zinc, Manganese, Copper and Selenium.

Dose: 0.2 cc/kg in first week and then 0.5 cc/kg

Preparation: It can be used by being added to parenteral nutrition solutions.

Miscible Serums: 5% Dex, 10% Dex, SF, Ringer lactate, Amino acid solution.

Incompatibility: Sodium bicarbonate

Storing Conditions: Unopened ampoules are stored at room temperature under 25°C.

6.4.43 Vecuronium

Uses: Loosening the muscles before surgery.

Dose: 0.1. Mg/kg IV

Adverse Effects: The preparation is generally well tolerated. <1/1000- Allergic reactions. Allergic shock. Irritation at the injection site (Young & Mangum, 2010).

6.4.44 Vitamin K

Uses: Prophylaxis and therapy on hemorrhagic disease of the newborn. Treatment of hypoprothrombinemia secondary to factors limiting absorption or synthesis of vitamin K.

Dose: Preterm infants, 32 weeks gestation: BW > 1000 grams: 0.5 mg/kg IM. BW < 1000 grams: 0.3 mg/kg IM (Young & Mangum, 2010).

7. Drug management in pediatric nursing

Many drugs can be stored under room temperature (5-25°C). And some drugs need to be protected against sunlight. The list of drugs to be stored and not to be stored in refrigerator should be attached on the refrigerator in service. No IV drug including the diluted ones with more than 24-hour preservation period should be kept more than 24 hours. Preservation period for oral drugs explicitly written at the prospectuses are acceptable. If there is no period stated they are discharged after 30 days. That is why the first opening and discharge dates are always noted on the oral drugs (Çavuşoğlu, 2000).

Vital signs and clinical findings should be carefully evaluated. Therapeutic and toxic drug effects should be closely monitored. Kidney functions should be evaluated by monitoring the input-output liquid. The track of serum levels on drugs with limited therapeutic boundary should be ensured. The volume of the administered drug should be continuously monitored. With drugs requiring special safety measures those measures should be followed to the letter. The drugs which are not risky to administer on infants should be tagged with catchy titles and be kept away from the preparation area. One should be careful against potential side effects of the drugs which are underutilized and have limited reported experience on infants (Çetinkaya &Tengir, 2006). In terms of dose, some drugs are readjusted for infants by breaking the tablet, opening capsules, mixing with different liquids, or weighing the raw drug. Whether the drug was given at desired dose or if its bio-availability and microbial stabilities were variable cannot be determined when this method is used. Therefore, it is recommended not to resort to these methods unless otherwise is strictly required (Young & Mangum, 2010).

When a drug is administered the aim is to get the desired effects while keeping undesired ones at minimum. Pediatric nurse evaluates the response of the infant to drug and is the one to interfere if necessary. The knowledge of medication principles for newborns ensures a reliable drug administration (Çetinkaya &Tengir, 2006).

The following information should be obtained from parents before administering any drugs:

- Is the newborn allergic to any drugs?
- How does the newborn response to drug treatment?
- What are the names, doses, schedules and taking reasons of previously administered drugs?
- If newborn is breastfed, it should be found that whether the mother uses any drug or not.
- Does the infant or family know the reason why the drug has been prescribed or what are its desired effects (as well as potential side effects)?

Drug effectiveness and the tolerance of infants can be determined by the help of these questions. Besides, infant's development level, the needle size and suitable gauge for injection, how and when infants should be prepared can also be found out.

To avoid mistakes and to ensure safe, reliable drug administration, the principle called "*eight corrects*" is of a significant importance:

1. *Correct Drug:* The nurse should know the name and commercial name of the drug given by its first manufacturer. Name and dose should be checked three times before the use (Çavuşoğlu, 2000; Çetinkaya &Tengir, 2006).
2. *Correct Dose:* The dose should be calculated according to the body weight (kg) and its surface area (m^2). It is highly important to measure all the drugs properly (Çavuşoğlu, 2000; Çetinkaya &Tengir, 2006; Ovalı 2002).
3. *Correct Route:* The recommended route is checked along with the availability of that route and the condition of infant for that route (Çetinkaya &Tengir, 2006; Eroğlu 2002).
4. *Correct Patient (infant):* Each hospital has its own way of patient identification and recognition. There may be ID cards attached to the wrists or ankles for these purposes. Name of the child should be double-checked to avoid any confusion (Çavuşoğlu, 2000; Çetinkaya &Tengir, 2006).
5. *Correct Timing:* It takes longer time to administer drug to infants than administering it to adult patients. In this sense, timing of the previous administration should be checked carefully; and if it was not timely made, a new time-schedule should be arranged accordingly (Çetinkaya &Tengir, 2006; McKinney et al, 2000).
6. *Correct Approach:* During drug administration to infants, their fears, weaknesses and their ways for dealing with them are taken into account with regards to their development levels (Çavuşoğlu, 2000; Çetinkaya &Tengir, 2006).
7. *Correct Information:* The child and family should be informed about the purpose and duration of the drug treatment along with its desired effects and potential side effects. By this way, the recommended drugs can be used more safely (Çavuşoğlu, 2000; Çetinkaya &Tengir, 2006).
8. *Correct Record:* Prior to administration the nurse writes down the name of the drug, its dose, administration hour, and administration route on the observation form. The nurse performing this administration signs up the observation form with his / her name (Çetinkaya &Tengir, 2006; McKinney et al, 2000).

Pediatric drug doses are calculated according to body weight and body surface. Body surface area of the infants in proportion to their weight is much larger than that of the children and adults. This is why the dose for infants calculated with body surface is much higher than that calculated with body weight. Therefore, during the premature term and infancy periods body surface area is not used for dose calculation purposes (Çetinkaya &Tengir, 2006).

Generally, pediatric drug doses are described as gram or milligram per kilogram of body weight. Safe dose amounts differ according to infant's age and his/her ability to metabolize the drug. Before any drug is administered the recommended dose is checked and rechecked whether it should have been calculated properly. So there should be a drug guide in each pediatric unit (Çetinkaya &Tengir, 2006).

Since the pediatric doses are relatively fewer than adult ones, any mistake in the amount may have serious consequences. The biggest responsibility in drug administration falls onto nurses. The nurse should be well aware of the pharmacokinetic and pharmacodynamic effects of the drugs in order to assess the clinical effects and risky conditions (Çetinkaya &Tengir, 2006).

For premature infants, newborns and early infants the immatureness of their body systems affects the drug administration. Among the factors accompanying toxicity of drugs are an immature enzyme system in the liver, decrease of the protein fields that drugs bind, and immature kidney system. Likewise, drugs leading to acid-base imbalance also affect toxicity. For example, overdose of salicylates can easily lead to metabolic acidosis in infants. The drug level in serum, its side effects and urinary excretion should be evaluated to avoid drug toxicity (Çetinkaya &Tengir, 2006).

The electrolyte - fluid balance is closely monitored during drug treatment. Newborns have limited ability to concentrate urine, so they should be provided with adequate liquid to discharge both drugs and metabolites. Dehydration may increase the drug toxicity risk. An immature blood - brain barrier also serves for drug toxicity. The immature myelination of the central nervous system increases the permeability of blood - brain barrier. The myelination forming this barrier is not fully mature until the infant is 2 years old. As the permeability of blood - brain barrier increases during the diseases like meningitis and brain tumor, side effects of the drugs administered into central nervous system should be monitored closely (Çetinkaya &Tengir, 2006).

The skin absorption rate of the topical drugs is significant. Infants have a thin layer of dermis and epidermis, hence their absorption rate would be greater compared to adults. Besides, greater body surface in proportion to weight is an important factor when drug is administered on wide skin surface. Infants, therefore, should be monitored for their sensitiveness to the drugs applied on skin surface (Çetinkaya &Tengir, 2006).

If the patients taking numerous drugs together yield different findings than the anticipated results in the light of laboratory findings, drug interactions should be taken into consideration. Some drugs affect the absorption of other drugs through the gastrointestinal system (GIS). This interaction or behavior results from changes in pH, changes in flora, and drug binding to intestine lumen. For example, antacids do not only cause intestinal pH to change; but also inactivate the drugs by binding to them (Çetinkaya &Tengir, 2006).

The period of drug use differs from 1 week to 5 weeks before any symptom appears; following the next dose the symptoms reappear instantly. Redness, fever, joint pain and inflammation, lymphadenopathy, eosinophilic leukopathy can be observed (Çetinkaya &Tengir, 2006).

Drug Mistakes Caused by Nurse: Administration of drugs prior to a non-official request, administration of drugs without a physician's request, administration of wrong drug because of misspelling or resemblance in appearance, miscalculation of drug dose or administration at wrong dose, inattention to information provided on the drug container or package, forgetting the administration (Çetinkaya &Tengir, 2006).

Medical mistakes have a potential of becoming 8 times more harmful at the newborn intensive care units. One of those mistakes is the administration of the similar drugs at different concentrations given in different doses, whereas other mistakes could be system-related.

These are the most common mistakes made on newborns regarding drug administration:

- Administration of wrong dose because of the resemblance between Adult Vitamin K (10 mg/ml) and Neonatal Vitamin K (1 mg/0.5 ml) ampoules
- To confuse Vancomycin and Heparin vials
- Though not exactly a drug administration, vaccination at wrong doses through mistaking adult and infant versions of Diphtheria-Tetanus vaccine. Moreover, the administration of DTaP and Hib combination vaccine on inappropriate age groups in terms of their effectiveness on infants (although pentaxim or infanrix can be received under 1 year of age, combination vaccines, in general, has low effectiveness on such infants).
- To confuse Vecuronium (1mg/ml) (preparation: 0.25 mg/0.25 ml) and Cisatracurium (2 mg/ml) (preparation: 0.5 mg/0.25 ml (Used for avoiding muscle paralysis. Sedation effective) (Sauberan et al, 2010).

In this sense, the physician requests should be re-checked, any questions in mind should be asked to physician and be well understood, and the medication should be carried out on time and be recorded appropriately; by this way, any medical or legal danger caused by the drug mistakes either by nurses or physicians can be avoided. Since the pediatric doses are relatively fewer than those for adults, any quantitative mistake may lead to serious consequences (Çetinkaya &Tengir, 2006).

The factors leading to inadequate adaptation to prescribed drugs:

- Not obtaining the prescription, or not having it at the pharmacy
- Unclearness of the purpose regarding drug use
- Surmising the ineffectiveness of the drug
- Occurrence of actual side effect, or the thought of side effects appearing
- Unclearness of the instructions regarding drug intake
- Physical difficulty during the administration (handling small tablets, or unpacking drug container)
- Repelling formulations (e.g. unpleasant taste) (Kayaalp, 2001).

It is noteworthy again that the pediatric nurse to administer drug on patients should find out first that if the dose and route of the administration asked by physician is appropriate or not. The nurse should be careful for potential drug interactions. Infant's developmental characteristics affect the techniques and approaches used in drug administration. The infant and parents should be prepared besides with the drug. Attentive observation should be performed in and after the process. Observations about administration should be recorded. Patient should be kept well-monitored against undesired effects prior to administration. It is important to provide information and consultation services to the patient and/or family about drugs.

In conclusion, any mistake in drug amount for infants may have serious consequences. Nurse should be well informed about the preparation and administration of the drugs. Nurse should know about his/her legal responsibilities that might require in the process, and the pharmacologic properties of drugs. Nurse should also know about the generic and commercial names of drugs, and remain utmost careful during the administration. Pediatric nurses, in particular, should always update their knowledge about drugs.

	Ampicilline	Cefotaxime	Ceftazidime	Gentamicin	Vancomycin	Naphthalene	Penicillin	İmpenem	Ciprofloxacin	Amphotericin	Acyclovir	Dobutamine	Dopamine	Fentanyl	Morphine	Heparin	Insulin	Lipid	Sodium Bicarbonate	Calcium	Potassium	Sodium Chloride	%5 dex	%10 dex	Ranitidine	PGEl	Propanadol	Epinephrine	Pentoxifylline
Pentoxifylline																													
Epinephrine	x											c	c			c			x		c	c	c	c		c			
Propanadol																c						c	c						
PGEl				c								c	c		c	c					c	c	c	x	c			c	
Ranitidine				c	c					x	c	c	c	c	c	c		c				c	c	c		c			x
%10 dex	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c		c	c	c		c	x		c	
%5 dex	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c	c		c	c	c	c	c	c
Sodium Chloride	c	c	c	c		c	c			x	c	c	c	c	c	c	c	c	c		c		c	c	c	c	c	c	c
Potassium	c	c	c	c		c	c			x	c	c	c	c	c	c	c	c	c			c	c	c		c	c	c	c
Calcium																			x			c	c	c					
Sodium Bicarbonate	x	x	c		c	c				c	c	x	c	c	c	c	x	c		x		c	c	c				x	
Lipid	x			c									c			c	c		c		c	c	c	c	c				
Insulin	c			c	c	x						c			c	c		c	x		c		c	c					
Heparin	c	c	c	x	c	c				c	c	c	c	c	c		c	c	c		c	c	c	c	c	c	c		
Morphine	c	c	c	c	c	c					c	c	c	c		c	c		c		c	c	c	c	c	c	c		
Fentanyl						c									c	c			c		c	c		c	c				
Dopamine	c			c						x	x	c			c	c		c	x		c	c	c	c	c	c		c	
Dobutamine											x		c		c	c	c		x		x	c	c	c	c		c			
Acyclovir	c	c	c	c	c	c						x	x		c	c			c		c	c	c	c	c				
Amphotericin				x				x					x			c			c		x	x	c	c	x				
Ciprofloxacin								x																					
Impenem	x	x	x		x	x	x		x	x												c	c						
Penicillin				x				x														c	c						
Naphthalene				x				x			c			c	c	c	x		c		c	c	c						
Vancomycin								x			c				c	c	c		c			c	c						
Gentamicin	x					x	x	x		x	c		c		c	x	c	c				c	c		c				
Ceftazidime								x			c				c	c			c		c	c	c	?					
Cefotaxime								x			c				c	c			x		c	c	c	c					
Ampicilline				x				x			c	c	c		c	c	c	x	x		c	c	c	c				x	

c : Compatible (can be given together or can be mixed)
x : Incompatible (cannot be mixed, cannot be administered consecutively through the same path)
? : Unknown

Table 1. Compatibility Chart of Some of the Most Frequently Used Drugs in Pediatrics (Katzung, 1998; Loeb, 1990; Trissel, 1992; Wong et al, 1992; Young & Magnum, 2008).

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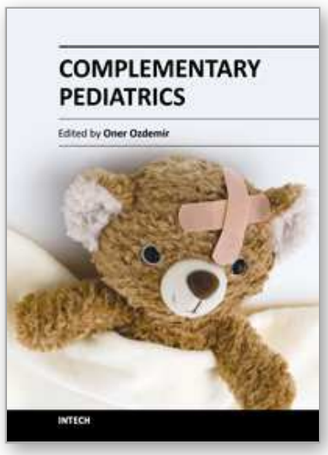
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