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# Supraventricular Tachycardia Due to Dopamine Infused Through Epidural Catheter Accidentally (A Case Report and Review)

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## 1. Introduction

Ensuring analgesia both intraoperatively and postoperatively by the administration of local anesthetics or opioid through epidural catheter is a widespread method. On the other hand, after thoracic and major abdominal surgery, optimal perioperative anesthesia and analgesia can be provided through thoracic epidural analgesia and thus, postoperative morbidity and mortality can be decreased specifically by blocking sympathetic nerve fibers (1). In spite of the availability of epidural technique, in cases of the inadvertent administration of nonepidural medications into the epidural space, serious morbidity and mortality can be caused by a direct drug or drug-additive neurotoxic, pH, or osmolality effect (2).

In literature, there are several reports of various substances infused through epidural catheter inadvertently (2-10). However, there have been no reports describing inadvertent administration of dopamine through epidural catheter as in the case we present here. We present, review and discuss this case in the light of literature.

## 2. Case report

A 54-year-old man who was 1.68 m tall and weighed 70 kg, was admitted to cardiovascular surgery intensive care unit after 3 vessel coronary by-pass surgery. All hemodynamic data were within normal limits with the help of inotropic support. The weaning from the ventilator was uneventful. It is our policy to use thoracic epidural analgesia for all patients following open heart surgery. The catheter is placed a night before the operation after getting informed consent. The infusion liquid that is administered through the epidural catheter in order to ensure analgesia in the patient in the postoperative period in intensive care unit is prepared as 100 mg of mepedrine in 50 mL of isotonic solution and according to the clinical status of the patient, the infusion speed of the infusion device is adjusted as

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0.1-0.3 mg/kg/hour. The patient in question was receiving 0.2 mg/kg/hour of meperidine through thoracic epidural catheter by the help of an infusion device.

After 10 hours following the operation, while there was no instability regarding his hemodynamical status, he suddenly started to complain of severe abdominal pain and dizziness followed by vomiting with intervals of two or three seconds. The evaluation of vomited matter showed no abnormal material. He developed a supraventricular tachycardia (with normal QRS complex and no discernible P waves) that reached up to 180 bpm. His blood pressure was monitored as 200/120 mmHg during the constrained period. His physical findings were evaluated as normal except tachycardia and high blood pressure. He had no abnormal abdominal findings and there was no reason for projectile vomiting. All consultations were done and an emergency abdominal ultrasound was performed. Both of them, besides laboratory findings, revealed no positive answer to what caused all these suddenly developed symptoms.

The constrained period lasted for about 20 minutes until it was recognized that a nursing mistake had been made while transferring the meperidine mixed solution into microperfusion device. Dopamine solution had been placed into perfusion device instead of meperidine solution and the patient had received 5 µg/kg/min of dopamine through epidural catheter for 20 minutes. As soon as it was understood, the infusion was discontinued. The intravenous infusion liquid that contains dopamine is prepared as 200 mg of dopamine in 50 mL of isotonic solution and the infusion speed is adjusted according to the clinical status of the patient. Once the nursing mistake was discovered, the records were studied and it was understood that the patient's complaints had started about 7 minutes after the onset of the infusion of dopamine through epidural catheter.

The patient's complaints started to improve 3 minutes after the discontinuation of the infusion and eventually all the symptoms disappeared. The patient's follow-up was uneventful during his stay in intensive care unit and he was discharged from the hospital in the 5<sup>th</sup> post-operative day. A long-term follow-up including all laboratory evaluations revealed no abnormal findings. Besides, there were no pathological findings in the neurological examination of the patient during the 6-month-period following the operation.

### 3. Discussion

Thoracic epidural anesthesia which is followed by postoperative epidural analgesia is increasingly being used for abdominal, major vascular and cardiothoracic surgery. The main merit of thoracic epidural postoperative analgesia is the optimal analgesia which it provides for several days and its minimal side-effects without the need for rescue medication (11). Segmental sympathetic block and analgesia are among the potential mechanisms for thoracic epidural analgesia that may influence mortality and myocardial infarction after coronary artery bypass graft surgery in a favorable way (12). It has been reported that the use of local anesthetics in thoracic epidural analgesia may reduce myocardial oxygen demand by way of decreasing heart rate, inotropy, and systemic vascular resistance (13). It has also been reported that thoracic epidural anesthesia may improve myocardial oxygen supply by dilating stenotic coronary arteries (14). Fewer arrhythmic episodes and postoperative myocardial infarction were reported, and patients could be extubated earlier with the aid of thoracic epidural analgesia. The risk of pulmonary complications is

decreased by optimized pain control and early mobilization, and this results in a shortened stay in intensive care units. When combined with early enteral nutrition, thoracic epidural analgesia ensures an earlier return of gastrointestinal function. It has been reported that patients treated with thoracic epidural anesthesia and analgesia have a better health-related quality of life (1). However, apart from all these advantages, in patients who have undergone full anticoagulation for cardiopulmonary bypass, the risk of spinal hematoma associated with central neuraxial analgesia is still unknown (12).

Many comparisons of local anesthetic alone, opioid alone or the combination of both have been made in order to ensure thoracic epidural analgesia (11). In cases where opiates are combined with local anesthetics and given either epidurally or spinally, the opiate action is at receptors mediating pain in the dorsal horn of the spinal cord, whereas the action of the local anesthetic is at the dorsal root ganglion. Thus, the effect of combining the two produces a better quality of analgesia and a less risk of systemic toxicity or any other undesirable side effects than when compared with the use of the same degree of analgesia or anesthesia achieved with a single agent (15,16).

Various substances belonging to different pharmacological classes are used as adjuvant in regional anesthesia as they are known to enhance and prolong analgesia of local anesthetics and opioids. The dose requirements of local anesthetics and opioids may be lowered by use of such substances, and thus the dose-dependent side effects of local anesthetics and opioids (e.g. motor block, nausea) may be reduced. Such drugs may also produce analgesia themselves. The list of adjuvants studied during the review period includes adrenaline, clonidine, ketamine, neostigmine, nondepolarizing muscle relaxants, and nonsteroidal anti-inflammatory drugs (17).

Although continuous infusion is the most popular means of administration, it is generally associated with sensory block regression, notably with local anesthetic alone. The time to first analgesic rescue is increased by addition of opioid. The long-known popularity of infusion is the result of the perception that the cardiovascular and respiratory side-effects of it are less when compared to with bolus alone (11).

The following data were obtained as the result of a review on drug error in anesthetic practice: The rate of administration errors was 14%, only four of which were pre-errors. The most common errors were inadvertent arterial injection, subcutaneous injection due to tissue intravenous catheter and inadvertent intravenous injection when performing epidural and peripheral nerve blocks. The most common contributing factors cited were fault of technique (19%), haste (16%) and error of judgement (14%). In the same study, the most frequently cited factors to minimize the incident were prior experience or training (32%) and skilled assistance (11%) (18).

In another study performed, the main sources of inadvertent administration of nonepidural medications into the epidural space were found to be "syringe swap", "ampoule error", and epidural/intravenous line confusion, and it was reported that in spite of all measures that are currently undertaken, accidents would occur inevitably (2).

A literature review on human medicine identified numerous drugs that were inadvertently injected epidurally, and these included thiopental, methohexital, vecuronium, midazolam with fentanyl, morphine with dextrose, ephedrine, cefazolin, gentamicin, amoxicillin

clavulanic acid, potassium chloride, magnesium sulphate, total parenteral nutrition, intralipid infusion, phenol containing ranitidine, ether, and paraldehyde (2). Respiratory depression with remifentanyl (3), sensory blockade, muscle spasms, and hypertension with potassium chloride (4), and a significant decrease in blood glucose level with insulin (5) are among the complications which were reported in humans as a result of accidental epidural drug administration. Accidental epidural injections of vecuronium, atracurium, cisatracurium, and rocuronium were reported to have no neurological or cardiovascular side effects or other symptoms of local or systemic toxicity (6-8,10). Again, in a reported case, the inadvertent injection of a mixture of rocuronium and morphine into the caudal epidural space in awake patient showed miosis without any neurological abnormality (9). In our case, on the other hand, dopamine was administered inadvertently through epidural catheter and following the onset of administration, clinical symptoms such as abdominal pain, dizziness, supraventricular tachycardia, hypertension and vomiting were observed.

In cases of inadvertent epidural injection, some practitioners flush the epidural space with distilled water or saline in order to dilute the concentration of the drug. Some others use epidural or intravenous corticosteroids in order to reduce the inflammatory response (2). These attempts were speculative, however, and because of the upward spread of the drugs, they could potentially worsen the situation (10).

In a related study on animals, it was reported that methylprednisolone sodium succinate as a treatment for acute spinal cord injury is a commonly used but controversial practice (19). Again in other studies on animals, it has been reported that it can be used as a neuroprotective agent as it decreases lipid peroxidation (20) that may contribute to free radical formation after acute spinal cord injury (21). In a study performed by O'Kell and Ambros (22) on animals, the authors were concerned that secondary to vasoconstriction, acute inflammation and ischemia could occur, and therefore, to minimize these potentially detrimental effects, methylprednisolone sodium succinate was administered. In our case, where dopamine was administered inadvertently through epidural catheter, no pathological findings were observed as a result of the examination performed as soon as the error was discovered and in the following 6-month clinical follow-up period.

The first studies on the spread of analgesic solutions in the epidural space and penetration into the neuraxis were performed by Bromage et al (23). These studies have shown that local anesthetic appeared in the cerebrospinal fluid (CSF) very soon after epidural injection and reached a peak concentration in about 10 to 15 minutes. Plasma venous levels of epidurally administered agents are reached quickly and much sooner than after spinal anesthesia. In another study, it was reported that following lumbar epidural injection of 75 mg lidocaine (3.75 ml of a 2% solution), the drug became detectable in 1 to 2 minutes and it reached a concentration of 0.3 mcg/ml within 5 minutes (24). The rich internal vertebral venous plexus forming four extensive, longitudinal channels in the posterior and anterolateral locations constitutes the ground for rapid absorption from the epidural space. These are thin walled veins without valves. Therefore, the epidural drugs are exposed to a large vascular surface (23).

A large proportion of patients who undergo anesthesia and surgery suffer from nausea and vomiting afterwards. This may be peripheral or central in origin, vomiting may arise either from stimulation of the chemoreceptor trigger zone (CTZ) or by activation of labyrinthine



reflexes. Anti-emetic drugs are known to act centrally either at the CTZ by antagonism of dopamine receptors or at the vomiting center by antagonism of muscarinic cholinceptors or histamine receptors, or both (25). The CTZ is situated in the area postrema near the base of the 4<sup>th</sup> ventricle and, although it is found within the brain, it is not protected by the blood-brain barrier. The capillary endothelial cells are not bound tightly and therefore, they allow for relatively free passage of large and small molecules into this area. This is an important afferent limb of the vomiting reflex and when this area is stimulated by toxins or drugs in the blood or CSF, vomiting often occurs as a result. Many antiemetics are known to act at this site (26).

In the CTZ, dopaminergic fibres are found, and the stimulation of this area causes nausea and vomiting. Dopaminergic and sympathomimetic receptors have been identified in the coronary, renal, cerebral and mesenteric vessels. Dopamine receptors are also found on the presynaptic membrane of postganglionic sympathetic nerves (27). Dopamine is not only the immediate metabolic precursor of norepinephrine and epinephrine, but also a central neurotransmitter and has important intrinsic pharmacological properties. While specific dopaminergic receptors are found in the central nervous system, injected dopamine does not readily cross the blood-brain barrier and therefore, it usually has no central effects (28). In our case where dopamine was administered through epidural catheter, thus, dopamine had an influence on CTZ not through blood but through CSF, and caused the patient to vomit.

Dopamine stimulates both  $\alpha$ - and  $\beta$ -adrenoceptors as well as specific dopamine receptors in renal and mesenteric arteries. In low dosage (2-5 mcg/kg/min), dopamine reduces regional arterial resistance in renal and mesenteric vascular beds by an action on specific dopamine receptors. Besides, dopamine receptors are found in basal ganglia, the substantia nigra, corpus striatum and the limbic system. In basal ganglia, dopamine is antagonistic to acetylcholine. Dopaminergic system connects the limbic cortex, basal ganglia and hypothalamus and it is known to be concerned with behaviour (27).

In cases of overdose, adverse effects are generally attributable to excessive sympathomimetic activity. Nausea, vomiting, tachycardia, anginal pain, arrhythmias, headache, hypertension, and vasoconstriction are among effects that may be encountered during infusion of dopamine. These effects usually disappear quickly when the infusion is slowed or discontinued as the drug has an extremely short half-life in plasma (28). In our case also, symptoms such as abdominal pain, dizziness, tachycardia, hypertension and vomiting disappeared once dopamine administered through epidural was discontinued.

In a previous study, Jensen et al (29) collected related recommendations using reports of drug errors. In that study, one general and five specific strong recommendations were discussed: in order to decrease the number of drug administration errors in anesthesia, systematic countermeasures should be used; prior to the injection of a drug, the label on the drug ampoule or syringe should be read carefully; the legibility and contents of labels on ampoules and syringes should be optimized according to agreed standards; syringes should (almost) always be labeled as convenient; drug drawers and workspaces should be organized formally; before a drug is drawn up or administered, its label should be double-checked with a second person or a device.

According to Abeysekara et al (18), the reasons for drug errors in anesthetic practices include inattention, haste, drug labeling error, communication failure and fatigue. They reported that in order to minimize such events, prior experience and training, rechecking equipment and monitors capable of detecting the incident were necessary.

It is reported that with respect to epidural management, in order to detect the early signs of permanent neurological damage such as epidural hematoma or abscess and immediate life-threatening events such as respiratory and cardiovascular depression, protocols should be strictly followed by trained nurses who should also take records on an hourly basis (11). Consequently, in order to prevent inadvertent injection of drugs, nameplates or labels should be found on syringes for both test doses and drugs, and doctors and nurses should double-check before the administration of drugs (10).

#### 4. Conclusion

The area where a thoracic epidural catheter is placed has a distinctive property as it is close to heart innervation. For this reason, injection of any drug through thoracic epidural bears great importance. The drug injected through epidural directly affects the plexus in that region. If thoracic region is in question, the drug injected through epidural directly affects the sympathetic nerves innervating the heart. The drug then passes on to CSF affecting the spinal cord, and the administered drug then enters the systematic cycle and thus shows its effects.

We believe that drugs given through epidural, specifically thoracic epidural, should be used very carefully, and the name of the drug should be written on the syringe carefully. In order to prevent inadvertent administration of drugs through epidural, as the case is for all catheters used, the epidural catheter should also bear its name clearly.

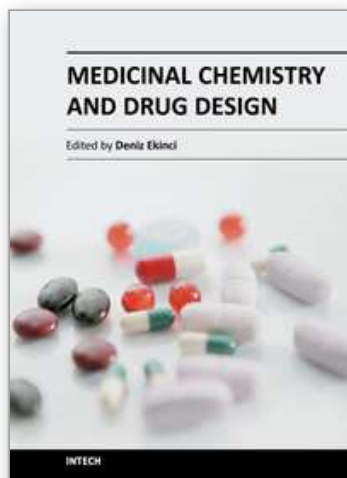
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Over the recent years, medicinal chemistry has become responsible for explaining interactions of chemical molecules processes such that many scientists in the life sciences from agronomy to medicine are engaged in medicinal research. This book contains an overview focusing on the research area of enzyme inhibitors, molecular aspects of drug metabolism, organic synthesis, prodrug synthesis, in silico studies and chemical compounds used in relevant approaches. The book deals with basic issues and some of the recent developments in medicinal chemistry and drug design. Particular emphasis is devoted to both theoretical and experimental aspect of modern drug design. The primary target audience for the book includes students, researchers, biologists, chemists, chemical engineers and professionals who are interested in associated areas. The textbook is written by international scientists with expertise in chemistry, protein biochemistry, enzymology, molecular biology and genetics many of which are active in biochemical and biomedical research. We hope that the textbook will enhance the knowledge of scientists in the complexities of some medicinal approaches; it will stimulate both professionals and students to dedicate part of their future research in understanding relevant mechanisms and applications of medicinal chemistry and drug design.

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