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14

Acetate Free Biofiltration with Potassium Profiled Dialysate (AFB-K)

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1. Introduction

Hyperkalaemia is a common, significant electrolyte disorder in uremia. Patients with chronic renal failure (CRF) undergoing haemodialysis (HD) accumulate potassium during the interdialysis period, and clearance of this potassium is one of the functions of haemodialysis. A sudden decrease in blood potassium levels during haemodialysis can induce or worsen arrhythmias, (Cupisti et al., 1999) particularly in patients already suffering arrhythmia or with risk factors for developing arrhythmia, such as heart disease of any origin, old age and diabetes mellitus, disorders which are highly prevalent in our dialysis units. Acetate Free Biofiltration with Potassium Profiled Dialysate (AFB-K) is a new haemodialysis technique that uses a potassium profiled dialysate (high at the start and low at the end of dialysis), so that by maintaining a constant potassium gradient between dialysate and blood, the decrease in blood potassium is slower – thereby contributing to prevent the appearance of arrhythmia (Santoro et al., 2002).

2. Description of the AFB technique

Acetate Free Biofiltration (AFB) is a haemodiafiltration technique (combining diffusion and convection) that uses a dialysate without acetate or bicarbonate, and in which post-dilution sodium bicarbonate is infused (145 or 167 mmol/L) throughout dialysis (Santoro et al., 2007) (Figure 1).

The primary characteristic of this haemodialysis technique is the absence of acetate. It must be taken into account that in conventional bicarbonate haemodialysis we continue to use 4 mmol/L of acetate to stabilise the acid part of the dialysate. This leads serum acetate levels to increase in conventional bicarbonate haemodialysis. Acetate is not used in AFB.

The advantages of this technique comprise improved haemodynamic stability and a reduction in the number of hypotensive episodes (Cavalcanti et al., 2004), the correction of metabolic acidosis, and improved clearance versus conventional haemodialysis (Santoro et al., 2007). Haemodynamic stability is improved by avoiding acetate (related to cytokine production, vasodilation and negative inotropic action); a solution is supplied with a high sodium content in reinfusion throughout dialysis (thereby improving vascular filling) (Tsutomu et al., 2011); the temperature is lowered (through sodium bicarbonate reinfusion at room temperature); and convection is employed (this involving the use of highly-

permeable biocompatible membranes). These advantages prove more evident in patients susceptible to suffering hypotension during dialysis, such as diabetics or elderly subjects with autonomous nervous system disorders, heart disease or liver disease, and subjects with significant comorbidity (Tsutomu et al., 2011, Sato et al., 2011). In a literature review, Santoro et al. (Santoro., 2007) described a reduction in hypotension events in AFB vs bicarbonate haemodialysis: the probability of intradialysis hypotension with AFB was reported to be close to 40% of the probability of intradialysis hypotension in the case of conventional bicarbonate haemodialysis.

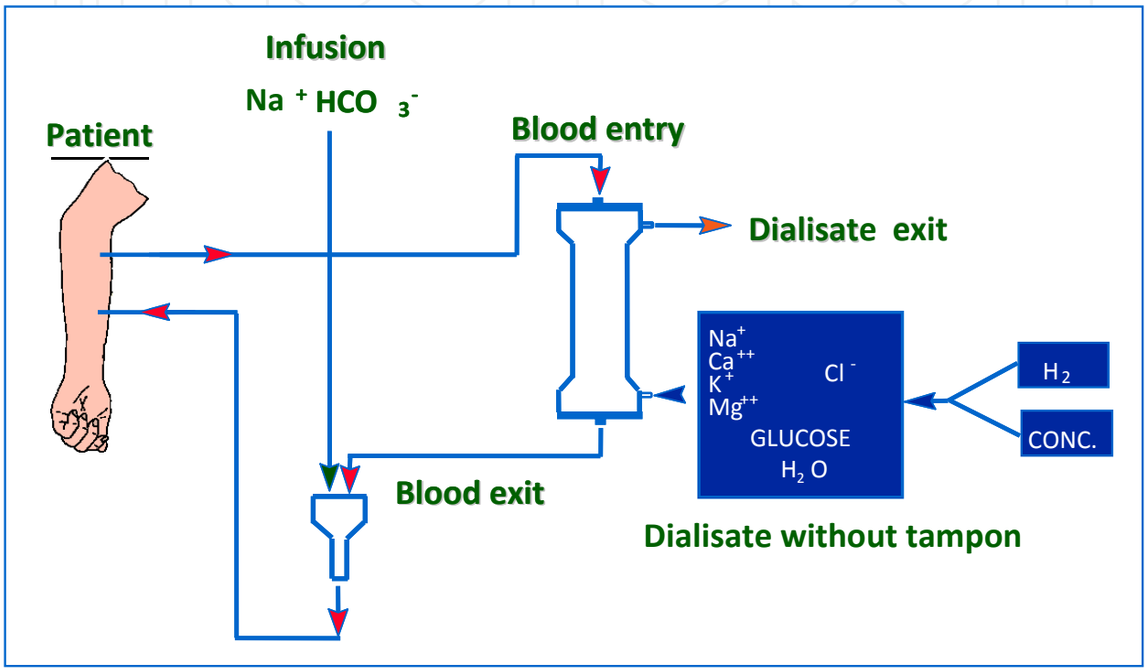


Fig. 1. AFB dialysis circuit.

3. Description of the AFB-K technique

Acetate Free Biofiltration with Potassium Profiled Dialysate (AFB-K) is the same haemodiafiltration technique free from acetate as that described above, with the addition of a potassium profiled dialysate. This is achieved with a double bag of concentrate (Santoro et al., 2002) – one bag with potassium and the other without it (Figure 2).

The dialysis machine takes concentrate from one bag or the other to form a potassium profiled dialysate: high at the start of dialysis and low at the end. The initial and final K^+ values of the dialysate are established individually for each patient (e.g., 4 mmol/L at the start of dialysis and 1 mmol/L at the end), according to a series of guidelines supplied by the manufacturer, and based on the needs of each patient. The aim is to maintain a constant K^+ gradient between the blood and dialysate bath, in order to prevent sudden K^+ reductions (Santoro et al., 2002).

The slow decrease in K^+ during dialysis is added to the advantages inherent to AFB. Dialysis with high K content in the dialysate cannot adequately reduce patient hyperkalaemia,

though symptomatically it is very well tolerated. Dialysis with low K content in the dialysate adequately reduces patient hyperkalaemia, but proves highly arrhythmogenic and is poorly tolerated by the patients. With AFB-K we are able to adequately reduce hyperkalaemia without causing arrhythmia, since blood K is gradually reduced. The patients who stand to benefit most from this dialysis technique are those with significant comorbidity and therefore with an increased risk of suffering arrhythmia.

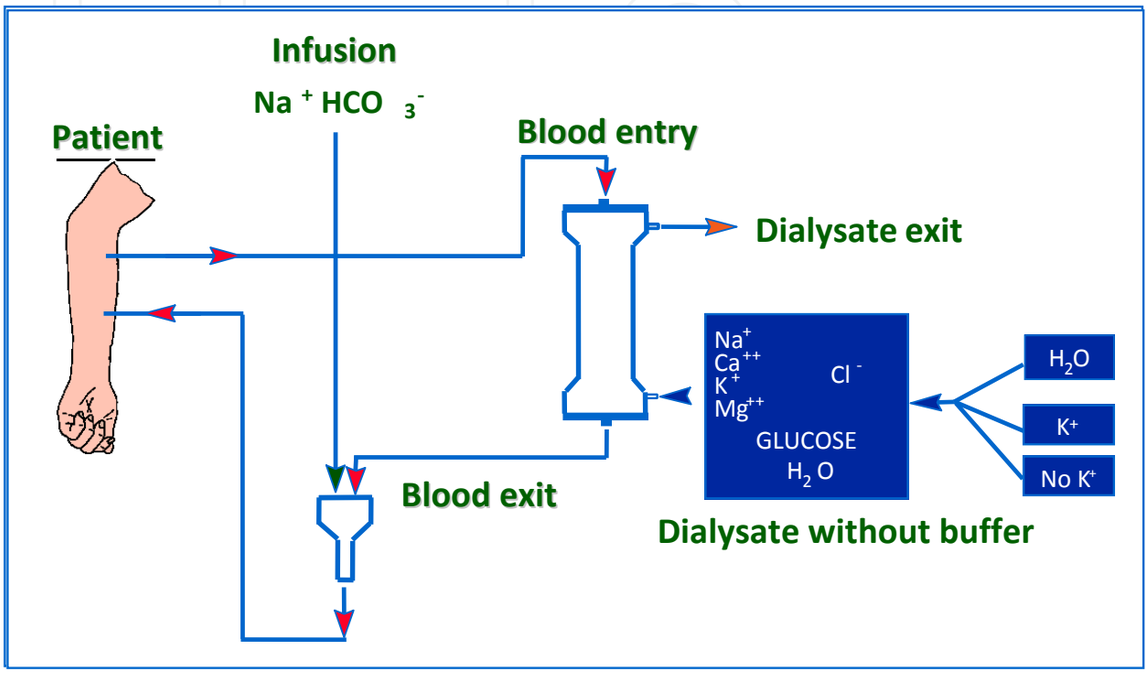


Fig. 2. AFB-K dialysis circuit.

4. Arrhythmia in patients on dialysis

Arrhythmias are very common in patients with CRF undergoing dialysis, and they are the cause of a significant percentage of sudden deaths of cardiac origin (Meier et al., 2001). Arrhythmias are more common in certain groups of patients: subjects with heart disease, left ventricular hypertrophy, coronary disease, heart valve disorders, high blood pressure or diabetes, and elderly patients.

Haemodialysis causes an arrhythmogenic effect (Meier et al., 2001). Dialysis is known to be related to QT prolongation in the ECG tracing (this being a risk marker for serious ventricular arrhythmia) (Genovesi et al., 2003).

Arrhythmia in dialysis may be related to sudden ion or blood pressure fluctuations. K^+ is a particularly arrhythmogenic ion (Kovesdy et al., 2007), related to the membrane potential, which is involved in cardiac cell depolarisation. K+ experiences sudden changes during haemodialysis, and a sharp drop can induce arrhythmia (Cupisti et al., 1999). In some cases, and despite diet advice or medical therapy, patients arrive for their dialysis session with high serum K+ levels, and experience a sudden decrease during the early part of the session. This has been related to the appearance of arrhythmias or to the worsening of pre-existing arrhythmias: induction or worsening of ventricular extrasystoles, QT prolongation (Cupisti

et al., 1999, Floccari et al., 2004) and onset of paroxysmal atrial fibrillation have been described.
Acetate Free Biofiltration with Potassium Profiled Dialysate (AFB-K) is a haemodialysis technique that attempts to obviate this problem, avoiding sudden potassium reductions during the haemodialysis session, but with due correction of the hyperkalaemia of the patients (Santoro et al., 2005).

5. Development of AFB-K

One of the first studies on potassium profiled haemodialysis was published by Readelli (Readelli et al., 1996). This multicenter, randomised, cross-over, prospective study evaluated 42 patients with a known increase in Premature Ventricular Complexes (PVC) during dialysis (Holter-ECG recording). The author compared a haemodialysis model with constant K^+ in the dialysate versus a model with decreasing K^+ that maintained a constant K^+ gradient between the blood and dialysate. A significant reduction of over 30% in PVC was recorded (both in terms of the number of PVC/h and as regards the PVC couplets/h) when performing potassium profiled dialysis. This PVC decrease is observed particularly in the first hour of dialysis, which corresponds to the greatest reduction in blood K^+ values in the case of dialysis with constant K^+. The result is obtained without affecting the K^+ levels compared with conventional constant K^+ haemodialysis.
Subsequently, Santoro (Santoro et al., 2002) published a study including 125 patients from a single centre in which dialysis with two techniques – one comprising AFB with constant K^+ and another with potassium profiled dialysate (AFB-K) – resulted in slower K^+ reduction with the latter technique (serum K^+ being greater in the first hour of dialysis with the potassium profiling procedure). Both techniques reached the same final serum K^+ levels. This study recorded a reduction in the number of intra-dialysis arrhythmias, particularly in those patients with a significant presence of ventricular ectopic beats. In conclusion, the safety and easy application of the AFT-K technique was confirmed, as well as the possibility of adapting the profile to each individual patient. In addition, this treatment was shown to reduce the impact upon repolarisation homogeneity and thus prevent cardiac arrhythmia.
Buemi et al. (Buemi et al., 2005) studied a series of 28 patients undergoing haemodiafiltration with constant K^+ (HDF), compared with HDF involving variable K (HDFK). The authors examined the ECG tracings at different times during dialysis to measure the QT-interval, and analysed serum K, intra-erythrocyte K and the electrical membrane potential at rest. Intra-erythrocyte K remained constant. The electrical membrane potential at rest decreased over time, though the reduction proved significantly greater in HDF versus HDFK. In turn, the ECG tracing showed a reduction in QT dispersion and in the QT-interval with HDFK. The authors concluded that the risk of arrhythmia may be lower when using haemodialysis with variable K.
Subsequently, Santoro (Santoro et al., 2008) published a multicenter, randomised, cross-over, prospective study in which 30 patients susceptible to arrhythmia were dialysed in a cross-over design with AFB involving constant K^+ (2.5 mEq/L) or AFB with decreasing K in the dialysate bath (AFB-K). A tendency towards fewer arrhythmias is observed with AFB-K that becomes significant in the case of patients sensitive to dialysis. A reduction in the number of PVC per hour is observed both during dialysis and hours after the end of dialysis (with a maximum reduction in the number of PVC 14 hours after dialysis). In the first hour

of treatment the serum K^+ levels of the patients were lower in AFB than with AFB-K. The study concluded that the slow clearance of K^+ may exert a protective effect.

6. Our study

Our group conducted a pilot study (Muñoz et al., 2008) at the start of the introduction of the AFB-K technique. The purpose of this study was to evaluate its efficacy and safety, analyse the decrease in blood K^+, and establish whether a decrease in arrhythmias occurs compared with AFB involving constant K^+ (AFB). We subsequently used the technique as an additional dialysis procedure in our Unit.

Twelve patients were included in the study (mean age 79 years; 5 males and 7 females). The subjects had arrhythmia or were at high risk of developing it, because of their old age, with high blood pressure (n=12), left ventricular hypertrophy (n=12), valve disease (n=8), coronary heart disease (n=3), diabetes mellitus (n=3) or paroxysmal atrial fibrillation (n=2).

A cross-over design was used, each subject serving as his or her own control. The subjects were dialysed for three weeks with AFB involving constant K^+, and for three weeks with potassium profiled AFB. At first dialysis in week 3 with each technique we conducted laboratory tests and performed ECG and Holter recordings (starting before the session and continuing until the next session).

The following dialysis regimen was prescribed: Integra® monitor (Novacor, Rueil-Malmaison, France), AN69 dialyser (Nephral® 500, Hospal), blood flow 300-350 mL/min, dialysate flow 500 ml/min and sodium bicarbonate reinfusion rate 167 mmol/L from 2100 to 2300 mL/h. The dialysate with constant K^+ was 2 mmol/L, while potassium profiling was 3.2-4 mmol/L ingoing and 1-1.3 mmol/L outgoing.

Both techniques were found to be easy to use, safe and without complications. There were no special technical requirements, and the procedures were well accepted by the nursing personnel. Patient haemodynamic tolerance was good with both techniques, with no differences in blood pressure or heart rate.

The pre- and post-dialysis results were similar with both techniques. We only observed a difference in blood K^+ determined half-way through the dialysis session, with higher values in the AFB-K group (4.0 mmol/L) than with AFB (3.6 mmol/L) ($P<0.0001$).

The ECG parameters in turn showed a significant difference in QTc (QT corrected for heart rate) after dialysis between the two techniques, with better results for AFB-K (448.8 24.2 ms vs 456.8 24 ms, p=0.039).

The mean PVC in the Holter recording was lower with AFB-K (163.5 range 21-900) versus AFB (444.5, range 23-13,565), though statistical significance was not reached (p=0.06) (Figure 3).

PVCs proved less severe (Lown grades I-II) with the AFB-K technique than with AFB involving constant K^+ (grades I-V).

All these findings were more obvious in patients with higher blood K^+ values at the start of dialysis.

In summary, K^+ decreased more slowly with AFB-K than with AFB, and a tendency towards decreased PVCs and their severity was noted (statistical significance probably not being reached because of the limited sample size), as well as a susceptibility to QTc reduction. All this is indicative of fewer arrhythmias. Our findings are similar to those previously reported by other authors (Santoro et al., 2002, Severi et al., 2003, Santoro et al., 2008).

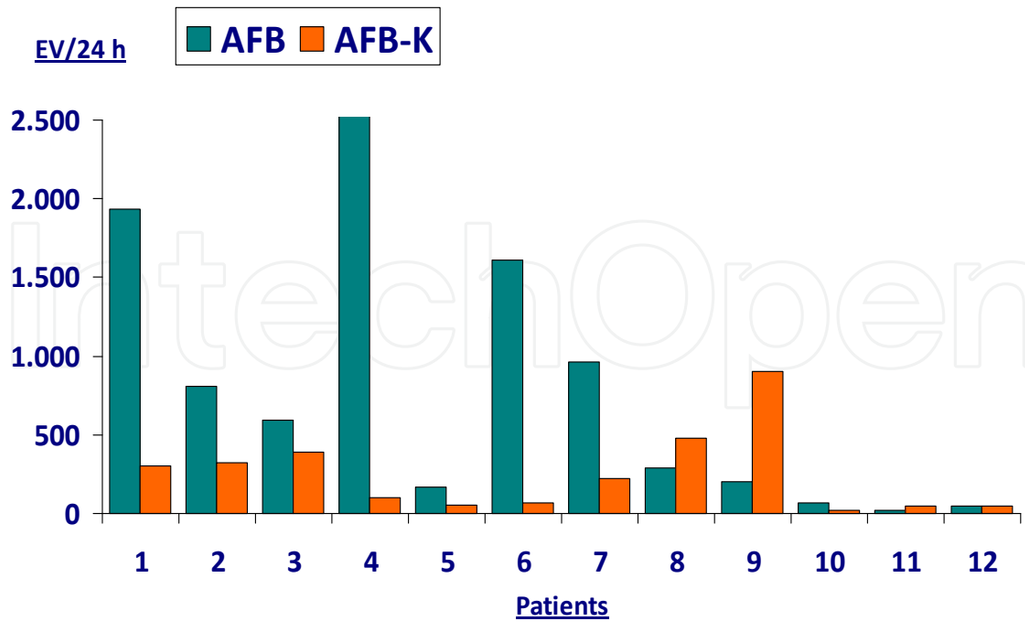


Fig. 3. PVC/24 h with both techniques (AFB and AFB-K).

In view of the results obtained, we decided to incorporate the technique to our Unit. We have indicated AFB-K in 27 patients who have been on dialysis for up to 5 years with the same technique.

We concluded that patients with arrhythmia or at risk of suffering arrhythmia benefited from potassium profiled dialysis, particularly those subjects with hyperkalaemia. Larger studies are required to confirm this reduction in arrhythmias, which could imply improved survival for patients with such a high cardiovascular risk.

7. Indications of AFB-K

Based on the literature reviewed, AFB-K is seen to be a dialysis technique offering the possibility of modulating potassium reduction according to the needs of each individual patient, with a view to ensuring slower reductions and thus preventing the appearance of arrhythmias. The indications therefore would be the following:

1. Patients with known arrhythmia, related or not to dialysis (e.g., ventricular extrasystoles detected around dialysis).
2. Patients with arrhythmia risk factors, such as subjects with heart disease of any origin, diabetes mellitus, old age, etc.
3. Patients susceptible to experiencing predialysis hyperkalaemia and markedly symptomatic dialysis sessions at the start, leading us to doubt the presence of arrhythmia.
4. Patients with indications for AFB and susceptibility to predialysis hyperkalaemia.

8. Requirements of AFB-K

The AFB-K technique has no added requirements with respect to AFB – only a different dialysate concentrate bag (double bag). AFB-K does not imply overburdening of the Dialysis

Unit or of the attending nephrologists, since it is very simple to prescribe, and likewise does not pose an added workload for the nursing personnel, since the technique is simple and easy to schedule.

9. Conclusions

One of the advantages afforded by this technology is the possibility of individualising the prescription of dialysis with a view to improving patient tolerability and prognosis (Phipps et al., 2010). Potassium profiling of the dialysate with AFB-K allows us to advance in this direction. The reduction of arrhythmias and the improved haemodynamic stability can contribute to improve the cardiovascular prognosis and survival of the patients. Larger studies (which are also more difficult to carry out) are needed to confirm improved patient survival with the new, attractive dialysis techniques.

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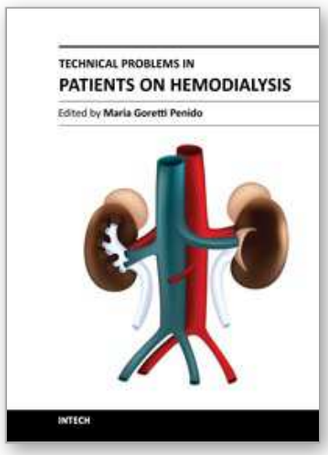
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This book provides an overview of technical aspects in treatment of hemodialysis patients. Authors have contributed their most interesting findings in dealing with hemodialysis from the aspect of the tools and techniques used.Each chapter has been thoroughly revised and updated so the readers are acquainted with the latest data and observations in the area, where several aspects are to be considered. The book is comprehensive and not limited to a partial discussion of hemodialysis. To accomplish this we are pleased to have been able to summarize state of the art knowledge in each chapter of the book.

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