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Hemodialysis for Patients Bleeding or at Risk for Bleeding can be Simple, Safe and Efficient

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Abstract

Aim: Hemodialysis for patients bleeding or at risk for bleeding requires special modalities of treatment that are difficult to perform with potential side effects. A simple, safe and adequate method may be applied.

Methods: A modified way of extracorporeal circuit preparation, which focuses on minimizing the blood-air interface and negligible saline flushing of 50 ml/hr, is applied for a maximum of 3 hrs session with routine (not one-to-one) nursing attendance. Data from 16954 sessions performed with patients bleeding or at risk for bleeding (15730 retrospectively and 1224 prospectively collected) were analyzed.

Results: Cumulative failure of treatment, as defined by clotting of the extracorporeal circuit requiring termination of the procedure or replacement of the clotted part, was not more than 5% as expected for anticoagulation free hemodialysis. For the prospectively recorded sessions, blood flow was 234±30 ml/min with less than 250 ml/min in 42,4% of the sessions. Native blood access was used in 426 (34,8%), double lumen catheter in 798 (65,2%), 42 were isolated ultrafiltration sessions and 64 blood, 21 plasma, 9 platelet units were transfused. Post/pre urea ratio was 0,50±0,12. Logistic regression showed that among: duration of the session, type of dialysis, ultrafiltration rate, hematocrit, number of platelets, serum total protein, transfusions, blood flow and type of access, only blood flow significantly affected failure incidence (coefficientB=-0,041, exp(B)=0,96, p=0,04). No complications due to treatment were noted.

Conclusion: In patients with active or at risk for bleeding, hemodialysis without systemic anticoagulation can be adequately and safely performed almost as a routine session.

Keywords: Anticoagulation; Hemodialysis; Priming

Introduction

Hemodialysis treatment requires extracorporeal blood flow and some form of anticoagulation, usually with unfractionated or low molecular weight heparin. For patients with active bleeding or at risk for bleeding, the usual mode of anticoagulation is contraindicated and use of minimal dose of heparin, regional heparinization with protamine reversal, regional anticoagulation with citrate or prostacyclin and anticoagulant-free hemodialysis with or without periodic saline infusion are proposed [Vigano 1996] [Hertel 2001] [1,2]. These are difficult to perform, have side effects and require intensive nursing.

At the hemodialysis unit of our department we perform a large number of dialyses in patients with active or at risk for bleeding. Hemodialysis treatment of these patients is performed without systemic anticoagulation but with a modified way of preparation of the extracorporeal circuit and wet type dialyzers. The method described below does not require a one-to-one nursing, high blood flow, frequent large volume periodic saline infusion, special equipment and blood coagulation tests. It may also be used for patients with double lumen catheters and allows for transfusions during the session. To the best of our knowledge this modification of the priming procedure has not been previously described. We report here our experience of near 17.000 dialysis sessions.

Patients and methods

During a 7 years period, 15730 hemodialysis sessions without systemic anticoagulation were performed in patients with chronic or acute renal failure, with active or at risk for bleeding. Except for recorded failures no other analytical data were available for these sessions. To further clarify the effectiveness of the procedure used, we prospectively collected data during a 7 months period (1224 sessions). Since the expected failure rate for anticoagulant-free dialysis is established to be approximately 5% [Hertel 2001] [2], a comparative study among various modes of dialysis for patients bleeding or at risk for bleeding was not deemed necessary. Blood sampling for estimation of various parameters was done before initiation of the session (Table 1). Coagulation parameters were not evaluated because the clinical outcome was considered to be the surrogate index of success or failure of the procedure. Adequacy of treatment was assessed with the post/pre dialysis urea ratio and when the native blood access was used for treatment, the post dialysis sample was obtained with the 1 minute low flow technique. Patients under systemic anticoagulation treatment, with cirrhosis, with less than 20000 plts/μL and coagulation disorders were excluded.

Variable	N	Mean	SD	Median	Min	Max
Session duration (hrs)	1224	2,7	0,5	3	0,2	3,0
Blood flow (ml/min)	1224	234	30	250	100	300
Ultrafiltration volume (ml)	1224	891	971	700	0	5000
Ultrafiltration rate (ml/hr)	1224	341	384	250	0	2000
Hematocrit (%)	292	29,7	5,7	29,1	17,0	49,5
Hemoglobin (g/dL)	292	9,5	1,9	9,3	5,4	15,3
White Blood Cells (/μL)	292	9280	5646	8000	1100	40100
Platelets ($x10^3$/μL)	292	219	108	210	26	705
Serum Glucose (mg/dL)	292	133,5	77,2	106,0	89,0	728,0
Urea (mg/dL)	292	187,1	85,5	179,0	41,0	630,0
Creatinine (mg/dL)	292	7,9	2,9	7,7	1,9	18,3
Sodium (mEq/L)	292	136,8	6,7	138,0	106,0	154,0
Potassium (mEq/L)	292	5,3	1,1	5,3	3,2	8,7
Total Calcium (mEq/L)	292	4,7	0,7	4,6	3,0	7,7
AST (SGOT) (U/L)	292	69,8	270,5	21,0	6,0	2605,0
ALT (SGPT) (U/L)	292	81,9	349,9	15,0	3,0	3275,0
Alk. Phosphatase (U/L)	292	198,3	119,2	165,0	21,0	654,0
Total Protein (g/L)	292	6,7	0,9	6,7	4,4	9,6
Albumin (g/L)	292	3,4	0,7	3,4	1,9	7,1

Table 1: Data from the 7 months prospective evaluation. The various hematological and biochemical estimations are from pre-dialysis blood sampling

Two types of hollow-fiber, wet dialyzers have been randomly used (ethylene-vinyl-alcohol and polyethylene glycol coated membranes) with membrane surface 0,8 to 1,0 m^2 and ultrafiltration coefficient 4,5 to 5,5 ml/hr/mmHg. Blood lines of standard configuration with air-bubble traps on both the arterial and the venous line are used. Dialysis machines were Gambro AK-10 or Fresenius 2008/4008 with bicarbonate dialysate (500 ml/min). Ionic concentration of the dialysate was: Na^+ 135 mMol/L, K^+ 1,9 mMol/L, Ca^{++} 1,66 mMol/L (3,32 mEq/L), Mg^{++} 0,47 mMol/L (0,95 mEq/L), Cl^- 104,04 mMol/l, HCO_3^- 36,28 mMol/L, CH_3COO^- 2,85 mMol/L.

The duration of the dialysis session is limited to 3 hours. Blood, plasma or platelets transfusions were not avoided during treatment and were instituted through the arterial blood line, or preferably, through a peripheral vein of the patient. Fluid removal was performed with stable ultrafiltration rate during treatment. Isolated ultrafiltration was also applied whenever necessary.

The priming protocol for anticoagulation free hemodialysis. One liter of normal saline is prepared with 5000 IU of unfractionated heparin. The priming port of the arterial line is connected to the saline that is let flow by gravity to the arterial patient connector and to the arterial dialyzer connector, the blood line is then connected to the dialyzer. The extremely low priming flow is essential at this point, since, the slow smooth unbiased flow of the fluid aids removal of all air from the lines. During this procedure the air-bubble trap of the arterial line must be completely filled with the priming solution. The venous blood line is then connected to the dialyzer and priming is continued preferably by gravity or with very slow blood pump. All lines are continuously inspected to ensure that all air is removed, particularly from the pump segment, and that all internal surfaces of the circuit are adequately wetted. After approximately 1 liter of heparinized saline has passed through the circuit and careful inspection for removal of all air, the line is clamped and the circuit is connected to the patient. To avoid blood oversunction, which may introduce air bubbles in the circuit, gradual and not abrupt increase of the blood pump is used. The heparinized saline is completely discarded as the blood flows into the extracorporeal circuit. Also, the low blood flow used during priming does not produce a turbulent flow which may cause excessive mixing of blood with the heparinised saline. Although blood flow of at least 250 ml/min is desirable optimal blood delivery is reached at the point where the highest uninterrupted flow is achieved. Total time of priming of the circuit does not exceed 20 minutes. After initiation of the treatment, except for hourly rinsing with 50 ml normal saline to inspect the circuit (i.e. 100 ml for a three hours session), no other special nursing attendance is applied and in essence the dialysis is considered as "another everyday treatment".

Statistical analysis

Results are reported as mean±1SD, median and minimum, maximum for each parameter. Comparison of observed failures with an expected frequency was done as described by Armitage and Berry [Armitage and Berry 1991]. Level of statistical significance is 95% ($p \leq 0,05$).

Results

In the analysis of the data we regard as failures those cases

a) Necessitating termination of the session due to clotting of any part of the extracorporeal circuit.
b) Whenever the bloodlines were clotted and had to be changed in order to continue the session.
c) Whenever the dialyzer was clotted and had to be changed in order to continue the session.

Cases where, clot formation in any part of the bloodlines or clotting of the peripheral fibers of the dialyzer occurred but did not impede the completion of the session were not regarded as failures.

The prevalence of failures for the 7 years retrospective data was 762/15730 (4,84%) which is not significantly different (p=0,38) than the 5% expected failure [Hertel 2001] [2].

During the 7 months prospective evaluation, 1224 sessions were performed in 266 (159 males, 107 females) patients (1 to 35 sessions/patient) aged 58,1±15,4 years (16 to 97 years, median: 59 years). Internal arterio-venous access was used in 426 (34,8%) and external double lumen catheter in 798 (65,2%) sessions. Isolated ultrafiltration sessions were 42/1224 with duration of 1,5±0,4 hrs (1,0 to 2,25 hrs). Reasons for avoidance of systemic anticoagulation were: Insertion of blood access catheter 131, renal transplantation 39, autologous AV fistula creation or correction 30, major abdomen or urological surgery 20, heart catheterization 9, gastrointestinal bleeding 6, liver biopsy 5, pericarditis 4, other 22. Incidence of failure was 45/1224 (3,68%), probably reflecting the acquired experience of the utilization of this method compared to the previous 7 years. Cumulative failure for all data is 807/16954 (4,76%) which is not different (p=0,16) than 5%. Blood flow was 100-149 ml/min in 2 sessions, 150-199 in 34, 200-249 in 483, 250-299 in 696 and more than 300 ml/min in 9 sessions. In total, 517/1224 (42.2%) sessions were performed with blood flow less than 250 ml/min. Transfusion of 64 blood, 21 plasma and 9 platelet units were instituted to 39 patients during 67 sessions. Table 1 shows the results for the various parameters that were evaluated. A logistic regression analysis performed for

the observed failures with independent predictors: the duration of the session, type of dialysis (usual vs isolated ultrafiltration), ultrafiltration rate, hematocrit, number of platelets, serum total protein, transfusions, blood flow and type of access (internal vs external), showed a statistically significant impact only of the blood flow parameter (coefficientB=-0,041, exp(B)=0,96, p=0,04), which indicates that the probability of failure decreases as the blood flow increases and vice versa. Post/pre urea ratio was calculated in 151 sessions (0,50±0,12, min=0,24, max=0,83, median=0,49).

No complications due to clotting of the extracorporeal circuit with anticoagulation free dialysis were noted.

Discussion

Replacement of renal function with hemodialysis requires the use of an extracorporeal blood circuit. Contact of the blood with the various parts of the circuit may initiate the process of blood clotting, thus necessitating some form of anticoagulation. This is usually achieved with the use of unfractionated or low molecular weight heparin [Vigano 1996] [Hertel 2001] [1,2]. In clinical practice it is not unusual to have to perform hemodialysis for patients with active bleeding or at risk for bleeding, a setting where systemic anticoagulation with heparin is contraindicated. In this case, several other ways of prevention of blood clotting are proposed. These are dialysis with the use of minimal dose of heparin (tight heparinization), regional heparinization with protamine reversal, regional anticoagulation with citrate or prostacyclin, use of newer anticlotting agents (prostanoids, protease inhibitors) and anticoagulant-free hemodialysis with or without periodic saline infusion [Vigano 1996] [Hertel 2001] [1,2]. Tight heparinization is not recommended for patients with active or at high risk for bleeding and requires frequent monitoring of clotting parameters [Hertel 2001] [2]. Regional heparinization with protamine reversal is a complex procedure with potential rebound anticoagulation and protamine side effects and is largely abandoned. The use of citrate is limited by the need for additional equipment, potential risk for electrolyte and acid-base equilibrium deterioration and need for clotting time evaluations [Vigano 1996] [Hertel 2001] [1,2]. Prostacyclin is costly and requires close hemodynamic monitoring and other anti-clotting agents need to have their utility and safety more extensively assessed in clinical situations [Vigano 1996] [Hertel 2001] [1,2]. Anticoagulant-free (heparin-free) hemodialysis is probably the method of choice in patients with active or at high risk for bleeding, but has the disadvantages of need for close one-to-one nursing, it is not recommended in patients with catheters as blood access, requires frequent washouts of the extracorporeal circuit with substantial volume (250-300 ml/flush) of saline infusions, high blood flows (250-300 ml/min) and blood transfusions increase the risk of clotting [Vigano 1996] [Hertel 2001] [1,2]. The expected risk of complete clotting of the dialyzer with heparin-free hemodialysis is approximately 5% [Hertel 2001] [2].

A comparative analysis between dialysis with heparin and anticoagulation free mode without saline flushes reported a 9,6% frequency of dialyzer clotting for the anticoagulation free treatment [Glaser 1979] [3]. In two studies with heparin-free dialysis, with high blood flows (280-300 ml/min) and frequent saline infusions, total clotting of the dialyzer or parts of the extracorporeal circuit approximately occurred in 5-10% and partial clotting in 6-20% of the sessions [Casati 1984] [Sanders 1985] [4,5]. In the prospective trial by Schwab et al [Schwab 1987] [6] in patients with contraindication for anticoagulation, of whom 92% were in intensive care units, with the use of parallel plate dialyzers, saline flushing of the circuit every 15 min, one-to-one nursing and blood flows not less than 230 ml/min, 9% of the anticoagulation free sessions were reported to have failed. Raja et al reported 70 dialysis sessions without heparin infusion, in both stable chronic and patients with active bleeding or potential bleeding problems, which were all successfully completed. Nevertheless, although the method included use of a small amount of heparin by means of infusion of part of the heparinized priming solution, heavy fiber clotting was observed in 7% of the dialyzers [Raja 1980] [7]. Two studies indicate that heparin free dialysis can be performed with reasonably high blood flows (250-300 ml/min) without saline flushing [Caruana 1987] [Romao 1997] [8,9]. Severe clotting of the dialyzers was 7% in one of these two studies [Caruana 1987] [8], while the second study reports no failures but it was conducted with stable, not at risk of bleeding patients and for a total of 10 dialysis sessions (one session per patient) [Romao 1997] [9]. Neither of these two studies reports how tight nursing attendance was.

In all the above studies the maximum number of anticoagulation free dialyses is 520 [Glaser 1979] [3]. Our study includes 16954 sessions without systemic anticoagulation, of which, in 1224 treatments, data were prospectively collected. To the best of our knowledge no such sample has been reported. Our results compare favorably to those of the aforementioned studies and are quite acceptable, since failure prevalence is in essence equal to the 5% expected.

Priming of the extracorporeal circuit for hemodialysis treatment always involves a procedure for air removal to avoid embolization of the patient, but small, clinically insignificant amounts of air (microbubbles) are not always removed. Since air-blood interfaces are known to initiate clotting process [Hertel 2001]

[Polaschegg and Levin 1996] [2,10], the modified method of preparation of the extracorporeal circuit for hemodialysis without systemic anticoagulation which we use, focuses on careful, almost total removal of air from the extracorporeal circuit. This is done with very slow priming, which produces uniform flow without turbulence and the use of wet type dialyzers. Although we have used only two types of membranes it is very probable that other membranes with low thrombogenicity may also be used [Cazenave 1988] [Leanza 1991] [Naito 1988] [Kuriyama 1992] [11-14]. The analysis of collected data showed that, of the predictor parameters used (duration of the session, type of dialysis, ultrafiltration rate, hematocrit, number of platelets, serum total protein, transfusions, blood flow and type of access) only blood flow affected significantly the outcome of treatment without anti-coagulation. Nevertheless, between increased suction at the access site, which may introduce microbubbles of air in the efferent limb of the circuit, and lower blood flows, the latter is preferable. In fact, 42,4% of the dialyses during the prospective evaluation were performed with blood flow less than 250 ml/min. The duration of the dialysis session is limited to 3 hours in agreement with others [Raja 1980] [Caruana 1987] [7,8] and inspection of the circuit with only 50 ml/hr normal saline flushing obviates the need for excessive fluid removal during treatment. This allows for use of dialyzers with low ultrafiltration coefficient, low transmembrane pressure during treatment and low ultrafiltration rate. Adequacy of treatment is also quite acceptable as also reported by others [Schwab 1987] [Romao 1997] [Cazenave and Mulvihill 1988] [6,9,11] and indicates that this mode of dialysis is sufficient to deal with the limited time requirements for these "acute" cases. Furthermore, the easiness and safety of the procedure allows for daily dialyses and isolated ultrafiltration without systemic anticoagulation whenever necessary. Blood, plasma or platelet transfusions may also be given during treatment. Nursing attendance was as usual in the hemodialysis unit, without the need for one-to-one nursing due to the procedure per se. In fact, the staff usually deals with various other medical and nursing problems and not the anticoagulantion free session(s) [15].

Conclusion

In conclusion, the results of our study show that, in patients with active bleeding or at risk for bleeding, adequate hemodialysis without systemic anticoagulation can be safely performed even in patients with temporary vascular access, with reasonably low blood flows without avoidance of blood transfusions and with conservation of nursing attendance, facilitating thus a potentially difficult hemodialysis procedure.

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