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BRIEF REPORT

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Treatment of vancomycin overdose using high-efficiency dialysis membranes

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Abstract Two children underwent acute hemodialysis using high-efficiency dialysis membranes for vancomycin intoxication (plasma levels 238 µg/ml and 182 µg/ml). During a 3-h treatment, plasma vancomycin removal was on average 60%, with a calculated vancomycin half-life ($t_{1/2}$) of 2 h. This is in contrast to a recent report using charcoal hemoperfusion for vancomycin intoxication (plasma level of 137 µg/ml), which resulted in a 40% relative plasma clearance and a calculated vancomycin $t_{1/2}$ of 12.5 h for a 4-h treatment. The choice of optimal modality for clearing a toxin should take into account the availability of equipment, protein or lipid binding of the toxin, and inherent risks of charcoal hemofiltration (large extracorporeal circuit, reversible hypocalcemia, heat loss, reversible coagulation defects) versus risks of high-efficiency hemodialysis (large extracorporeal circuit).

Key words High-efficiency dialysis membranes · Vancomycin intoxication

Introduction

Vancomycin, a commonly prescribed antibiotic in severely ill children, is primarily excreted by the kidney and can accumulate in a child with deteriorating renal function. Vancomycin can be associated with ototoxicity but, when combined with aminoglycosides, can be nephrotoxic [1].

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Historically, vancomycin overdose was treated by forced diuresis, due to its limited toxicity and limited ways of removing the drug. The recent report by Panzarino et al. [2] suggested the use of charcoal hemoperfusion for vancomycin overdose. Although charcoal hemoperfusion is effective, it adds the increased risks associated with a large extracorporeal circuit volume, namely associated heat loss, hypocalcemia, and possible predisposition to a coagulative state [3].

The advent of high-efficiency dialysis membranes, has resulted in improved vancomycin removal, with a need for an increase in dosing frequency compared with standard dialysis membranes [4, 5]. We recently had experience using high-efficiency dialysis membranes for vancomycin overdose in two separate children. We report this experience suggesting that it offers an alternative method to charcoal hemoperfusion.

Case reports

Case 1

Patient 1 is a 22-kg female with a liver transplant who was admitted to hospital for central indwelling venous line sepsis and was treated with vancomycin. Her renal function deteriorated due to the sepsis, resulting in a vancomycin level of 345 µg/ml (normal <40 µg/ml), oliguria, and a serum creatinine of 3.2 mg/dl; 36 h later, the Nephrology Service was consulted, and dialysis was instituted at a vancomycin level of 238 µg/ml. For comparison purposes, the calculated vancomycin half-life ($t_{1/2}$) was 67.2 h using the method described by Panzarino et al. [2]. Access was obtained via a femoral 9.0-Fr MedComp dual-lumen amless. A Baxter 550 hemodialysis machine was used with a high-efficiency cellulose triacetate dialysis membrane (CT 110 Travenol-Baxter Healthcare, Deerfield, Ill., USA) and pediatric lines giving an extracorporeal blood volume of 165 ml [6]. Blood flow was 5 ml/kg per min; duration of treatment was 3 h and the potassium, phosphorus, and calcium baths were adjusted according to the needs of the patient. The post-run (3 h later) vancomycin level was 78 µg/ml, demonstrating greater then 67% removal of the intravascular content of vancomycin, or a calculated vancomycin $t_{1/2}$ of 1.9 h. In the next 24 h, despite no further drug being given, the vancomycin level had rebounded to 123 µg/ml, which is expected due to normal kinetics and pools of vancomycin [6]. A second dialysis treatment decreased the vancomycin level to 54 µg/ml (calculated vancomy-

cin $t_{1/2}$ of 2.5 h). The next day, the vancomycin had rebounded to 74 µg/ml and a third hemodialysis treatment resulted in a post-run level of 28 µg/ml (calculated vancomycin $t_{1/2}$ of 2.2 h).

Case 2

Patient 2 is a 5.6-kg boy with obstructive uropathy and renal dysplasia who had urosepsis and was treated at an outside hospital with vancomycin and gentamicin. Whereas the gentamicin was adjusted, the vancomycin level was found to be 313 µg/ml with a serum creatinine of 1.0 mg/dl and a calculated creatinine clearance of 45 ml/min per 1.73 m^2 by the Schwartz method [7]. He was transferred with the request for charcoal hemoperfusion. Due to his underlying renal dysplasia, he never had oliguria, and his creatinine improved with hydration. Access was obtained via a femoral 7.0-Fr Cook (Bunchman coaxial) dual-lumen amless. A Baxter 550 hemodialysis machine was used with a high-efficiency dialysis membrane (CT 110 Travenol-Baxter Healthcare) and pediatric lines giving an extracorporeal blood volume of 165 ml. Blood flow was 12 ml/kg per min; duration of treatment was 3 h and the potassium, phosphorus, and calcium baths were adjusted according to the needs of the patient. The pre-run vancomycin level was 182 µg/ml (calculated vancomycin $t_{1/2}$ of 31 h using his admission vancomycin level) and the post-run level (3 h later) was 73 µg/ml, suggesting greater then 60% removal of the intravascular content of vancomycin, or a calculated vancomycin $t_{1/2}$ of 2.3 h. A second dialysis treatment decreased the vancomycin level from 63 µg/ml to 37 µg/ml over 2 h (calculated vancomycin $t_{1/2}$ of 3.9 h).

Discussion

Both of these patients demonstrated adequate removal of vancomycin using a high-efficiency dialysis membrane. The smallest high-efficiency dialysis membrane requires an 80 ml blood volume, which requires blood priming in the small pediatric patient. However in these two cases, both children were blood primed. The patient with an intravascular blood volume of 1,400 ml, was blood primed due to hemodynamic instability. The second child was 5.4 kg, and required blood priming of the circuit due to the large extracorporeal blood volume [8]. Although the dialysate rate is often increased from the standard 500 ml/min to as high as 800 ml/min in true high-flux dialysis, normal (500 ml/min) dialysate flow rates were used in both of these patients.

Similar to charcoal hemoperfusion, both circuits in this study had the added disadvantage of large extracorporeal blood volume requiring blood transfusions during the time of therapy. In contrast to charcoal hemoperfusion, the use of a high-efficiency dialysis membrane does not have the added disadvantage or risk of removing calcium, inducing hypothermia, or thrombocytopenia [3]. Although these risks associated with charcoal hemoperfusion are all predictable and preventable, these side effects will not occur using a high-efficiency dialyzer.

The charcoal hemoperfusion circuit is classically placed in line prior to the hemodialysis membrane in order to normalize calcium and warm the blood prior to returning the blood to the patient. Because the blood flow is often increased in order to maximize toxin removal, this higher rate of blood flow may not allow for complete normalization of these potential complications of charcoal hemoperfusion.

Panzarino et al. [2] identified a 40% relative removal of vancomycin from the intravascular content during the initial run. This is compared with our findings of 67% and 60% removal during both initial treatments using a high-efficiency dialysis membrane with treatment times 1 h shorter. Panzarino et al. [2] reported an initial $t_{1/2}$ of 12.5 h for a 4-h treatment with an initial vancomycin level of 137 µg/ml. We found a $t_{1/2}$ of 1.9 h for an initial level of 238 µg/ml and 2.3 for an initial level of 182 µg/ml, each of these treatments being over 3 h. Therefore, the removal of vancomycin is effective with high-efficiency dialysis membranes or charcoal hemoperfusion, but different techniques and flow rates do not allow for a direct comparison of efficacy. The decision of optimal modality may be influenced by whether or not the drug is bound (e.g., lipid or protein) or free in plasma [5].

Data to date do not adequately compare high-efficiency dialysis membranes with continuous hemofiltration for the treatment of intoxication [9]. Continuous hemofiltration has been found to effectively clear vancomycin, but this depends upon blood flow rate, dialysate flow, and the surface area and charge of the hemofilter membrane. In conclusion, when approaching a child with a drug overdose, one should consider high-efficiency dialysis membranes as a primary therapy for clearing medications.

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