Hemodialysis with Polysulfone Membrane for Vancomycin Overdose in a Child with Acute Renal Failure Already on Acute Peritoneal Dialysis

Akut Böbrek Yetmezliği Nedeni ile Akut Periton Diyalizi Uygulanan bir Çocuk Olguda Vankomisin Doz Aşımında Polisülfon Membran ile Hemodiyaliz

ABSTRACT

A 26-month-old girl who had acute renal failure after a major cardiac operation received an accidental 4-fold vancomycin dose. She was already on peritoneal dialysis when the error in vancomycin dose and high serum vancomycin levels were first noticed. Optimal venovenous hemodiafiltration filter or high-flux membrane could not be provided for her, but she benefited from hemodialysis with a conventional polysulfone membrane. We presented this case to emphasize that conventional hemodialysis may be beneficial for vancomycin overdose when optimal treatment modalities cannot be attained, contrary to what has been thought before,.

KEY WORDS: Acute renal failure, Vancomycin overdose, Nephrotoxicity, Hemodialysis

ÖZ

Majör bir kardiyak operasyonu takiben akut böbrek yetmezliği gelişen ve kaza ile alması gerekenin 4 katı dozunda vankomisin alan 26 aylık kız hastaya, vankomisin dozunda hata olduğu ve serum vankomisin düzeyleri yüksek tespit edildiği sırada periton diyalizi uygulanmakta idi. Hasta için uygun venovenöz hemodiyafiltrasyon filtresi ya da yüksek akımlı membran temin edilemedi, ancak konvansiyonel polisülfon membran ile yapılan diyalizden fayda gördü. Hasta, daha önce düşünülenin aksine, vankomisin doz aşımında sayılan uygun tedavi yöntemlerine ulaşılamadığında konvansiyonel membran ile de iyi sonuç alınabileceğini vurgulamak amacı ile sunulmuştur.

ANAHTAR SÖZCÜKLER: Akut böbrek yetmezliği, Vankomisin doz aşımı, Nefrotoksisite, Hemodiyaliz

Alper SOYLU
Belde KASAP
Mehmet TÜRKMEN
Salih KAVUKÇU

Dokuz Eylül University
Faculty of Medicine,
Child Health and Diseases,
İnciraltı, İzmir, Turkey

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INTRODUCTION

Vancomycin (VNC) is one of the most commonly used antibiotics and its plasma concentrations should be monitored carefully. In addition to its adverse effects including fever, rash, phlebitis, neutropenia and the "red man syndrome", it may cause reversible ototoxicity and may be nephrotoxic especially when combined with aminoglycosides (1-4). Although treatment of VNC overdose is not necessary in patients with normal renal function, VNC accumulates and causes severe toxicity in patients with pre-existing renal failure (5). Charcoal hemoperfusion, hemodialysis (HD) with high-flux membrane and hemodiafiltration have been successfully used in patients with renal failure and VNC overdose (1,4,6). However, neither HD with conventional membranes nor peritoneal dialysis (PD) was found to be effective for VNC removal in such patients (4). Standard HD with cuprophane and cellulose acetate membranes has a limited capacity to remove substances larger than 500 Da. VNC has a molecular weight of approximately 1500 Da and it is therefore only marginally removed by standard HD or PD (7). We reported a child receiving PD due to acute renal failure who benefited from additional HD with a conventional polysulfone membrane for VNC overdose.

Correspondence Address:
Salih KAVUKÇU
Mithatpasa Cad. No: 665/4 35280
Küçükyalı, İzmir, Turkey
Fax : +90 232 231 26 10
E-mail : s.kavukcu@deu.edu.tr

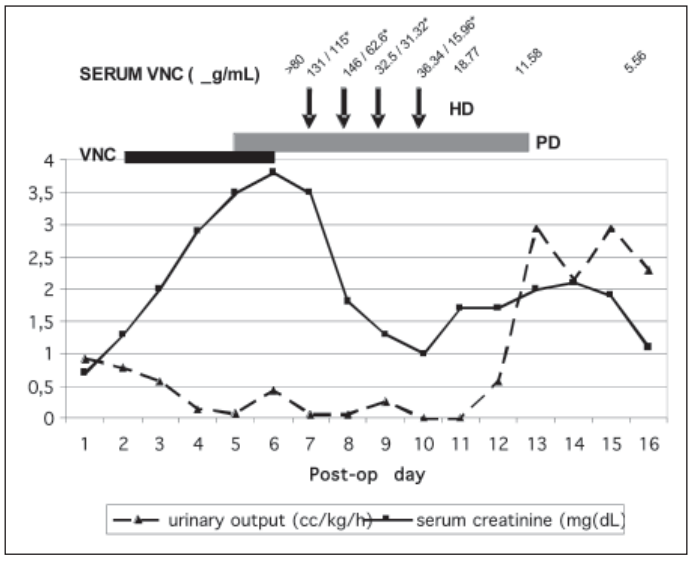

Figure 1: *Serum (free) vancomycin, serum creatinine, urinary output levels and administration of vancomycin, hemodialysis and peritoneal dialysis in post-operative days.* ***VNC:*** *vancomycin,* ***HD:*** *Hemodialysis,* ***PD:*** *Peritoneal dialysis. *: serum vancomycin levels before and after hemodialysis.*

Case report

A 26-month-old girl had a major cardiac operation for total correction of Fallot tetralogy and she was prescribed VNC, adjusted for her decreased GFR (serum creatinine 1.37 mg/dL, estimated GFR by Schwartz formula 31.7 mL/min/1.73 m^2), for infiltrative lung lesions on the second post-operative day. Two days later, her clinical condition deteriorated with a pulse of 169/min, blood pressure of 82/49 mmHg, decreased urine output, blood urine nitrogen (BUN) 106 mg/dL, serum creatinine (Scr) 2.9 mg/dL, ALT 1167 U/L, white blood cell count 19,700/mm^3, thrombocyte 49,000/mm^3, prothrombin time 23.4 sec, and activated partial thromboplastin time 31.11 sec. She was intubated and PD was initiated with manual exchanges of small volumes (10cc/kg) of 1.36% glucose solutions with a 10-min filling period, 30-min dwell period, and 20-min emptying period. We used PD solutions including lactate and added 500 U/L heparin. Potassium was added according to the serum potassium levels as 0, 2 and 4 mmol/L for serum [K] >6, 4-6, and <4 mmol/L, respectively. Dwell volumes were gradually increased up to 30 cc/kg in a few days.

While on PD, the serum free VNC level of the patient was realized to be significantly high (80 μg/mL) on the fourth day of treatment. An error was noticed in the ordered adjusted VNC dose as 40 mg/kg/18 hours, which was nearly 4-fold high. At that time, her BUN was 97 mg/dL and Scr was 3.8 mg/dL. Her body weight was 10 kg and neither a venovenous hemodiafiltration filter nor an appropriate high-flux HD membrane could be provided. Thus, she received HD with a 0.4 m^2 polysulfone membrane along with PD. Vascular access was performed via a 7F dual lumen femoral venous catheter. On the first session, HD was stopped at the end of 2 hours due to hypotension, but it was performed for 6 hours in each of the following three days. Despite some fluctuations, VNC levels gradually decreased to 15.96 μg/mL. Thus, HD was stopped and she was treated only with PD (Figure1). Although she was oliguric during the VNC treatment, urine output decreased further and the patient became even anuric after institution of HD (Figure1). After another four days, PD was also stopped since her urine output was adequate and renal function tests returned to normal levels. Her Scr levels decreased to appropriate levels for her age at the post-operative 18th day and she was discharged from the intensive care unit at the post-operative 21st day. We performed an audiogram which was normal. After a few days, she was discharged from the hospital and followed up as an outpatient with an uneventful course.

DISCUSSION

VNC is a commonly prescribed glycopeptide antibiotic in critically ill children. It is primarily eliminated via the renal route. The nephrotoxic potential of VNC is reported to be around 5% and it also potentiates the nephrotoxicity of aminoglycosides 3-4 fold (3). Preexisting renal disease or sepsis may also contribute to the renal injury (7). The decreased renal functions and urinary output along with VNC treatment and improved renal functions following drug removal support VNC nephrotoxicity in our patient. Underlying sepsis and preexisting renal dysfunction probably contributed to the deterioration of renal functions during VNC treatment.

Our patient, who had acute renal failure and VNC overdose, benefited from HD with a conventional membrane. In fact, neither HD nor PD is thought to be effective for rapid removal of VNC, since it has a molecular weight of ~1500 Da and binds to the proteins with a range of 10-50% (3,6). Despite this high rate of protein binding, the effect of plasma exchange on VNC blood levels in therapeutic doses has been controversial **(8,9)**. Furthermore, this technique has not been used in overdose situations. More recently, charcoal hemoperfusion, high-flux membranes, and continuous renal replacement modalities have been found to be efficient in VNC toxicity (1,4,6). Although we planned to institute high-flux membrane dialysis or hemodiafiltration, we could not obtain membranes of appropriate sizes. Meanwhile, her serum free VNC levels increased from 80 to131 μg/mL despite continuous PD, highlighting that PD was ineffective in clearing VNC. On the other hand, it has been reported that intradialytic clearance of VNC was higher (73 vs 15 mL/min) and elimination half-life was shorter (60 vs 86 h) with polysulfone membranes compared to cuprophane membranes in conventional HD (10,11). Thus, we performed HD with a conventional polysulfone membrane. Since Scr and free VNC levels decreased after institution of HD along with diminished urinary output decreasing the chance of renal elimination of

VNC, we concluded that VNC was cleared by HD. Although PD and HD were used concomitantly, failure to decrease serum VNC levels during PD only and significant decrease of serum VNC levels during HD sessions signify that HD was the main source of VNC removal in this patient. Nevertheless, administration of PD along with HD might have helped the improvement of renal functions by the removal of renal toxins.

The target therapeutic peak and trough ranges of VNC are 30-40 μg/mL and 5-10 μg/mL, respectively (3). In previous reports of VNC overdose in children with concomitant or pre-existing renal failure, serum VNC levels decreased to normal ranges after two or three HD sessions (4 hours each) with high-flux membranes (1,7,12) and after 41 hours with continuous venovenous hemodiafiltration (4). Serum VNC levels decreased to <40 μg/mL after the third HD cycle in our patient. However, we performed a fourth HD cycle to be on the safe side for the risk of VNC rebound which is an expected situation due to VNC redistribution from the tissue compartment to the plasma (1,4).

We performed an audiogram before we discharged the patient, since deafness resulting from transient or permanent ototoxicity might develop in excessive VNC doses. This is especially seen in serum VNC concentrations >80 μg/mL for more than several days (13). Although it is a well-defined adverse effect, the overall incidence of VNC ototoxicity is rare (14). In the literature, a 14-month-old girl with chronic renal insufficiency who received a high dose of VNC and had serum free VNC concentrations higher than 80μg/mL for five days has been reported to experience high-frequency deafness, but it improved in a few months (6). We do not know how long our patient was exposed to a VNC level over 80μg/mL, since serum VNC level was first checked on the third day of administration, but fortunately she had no hearing loss at all.

This case represents a beneficial experience about the institution of HD with a conventional polysulfone membrane in VNC overdose in a patient with preexisting renal failure when ideal treatment modalities cannot be provided due to technical limitations.

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