Abstract

A 17-year-old anuric female patient with end-stage renal failure received a massive overdose of vancomycin and was treated with high-flux hemodiafiltration, as described in this report. The hemodiafiltration procedure with a polysulfone membrane was performed 3 times. The vancomycin concentration was decreased from 101 mg/l to 16.59 mg/l at the end of the procedure. No adverse effects were noted from either vancomycin or hemodiafiltration. Hemodiafiltration with a high-flux polysulfone membrane is a novel and safe treatment modality for vancomycin overdose in pediatric patients.

Keywords

Vancomycin · Anuric renal failure · Overdose · Hemodiafiltration

Introduction

Treatment of vancomycin overdose is not necessary in patients with normal renal function because of rapid clearance by the kidney [1]. However, vancomycin dose adjustment is important in patients with renal failure, and vancomycin toxicity is considered a serious problem in these patients. For this reason, vancomycin given every 7 days is an adequate and safe treatment in anuric adult patients with renal failure. However, authors of various studies in adults do not agree with the recommended dose [2–4]. Plasma vancomycin concentrations should be monitored during the vancomycin treatment even if the patient has normal renal functions. Peak vancomycin level should not exceed 30 mg/l, and trough level should not exceed 10 mg/l. Acute adverse effects of vancomycin are fever, phlebitis, hypotension and shock (with rapid infusion), muscle spasms, nausea, anaphylaxis, rash, and the “red man syndrome.” Chronic adverse effects are neutropenia, agranulocytosis, thrombocytopenia, ototoxicity and nephrotoxicity [5].

Charcoal hemoperfusion and continuous venovenous hemodiafiltration (HDF) with high-flux membrane have been documented in two children with chronic renal failure and vancomycin overdose [6, 7]. We report the use of hemodiafiltration with high-flux membrane to accelerate vancomycin removal in an anuric patient with end-stage renal failure.

Case report

A 17-year-old female patient with end-stage renal failure for 5 years secondary to chronic pyelonephritis was admitted to the Pediatric Nephrology Department, Ege University, for the treatment of resistant peritonitis. She had been on continuous ambulatory peritoneal dialysis for 4 years. Her height was 148 cm, and her weight was 38 kg (under the 3rd percentile). Her blood pressure was 110/70 mmHg, and her abdomen was sensitive on palpation. Serum creatinine level was 5.47 mg/dl and urea was 52 mg/dl. Initial antibiotic therapy included cephazoline (500 mg/l) and amikacin (4 mg/l) followed by ceftazidime (500 mg/l followed by 125 mg/l) and vancomycin (single dose, 1 g vancomycin) intraperitoneally. Peritoneal dialysis was ended due to severe abdominal pain, and hemodialysis was started. Vancomycin treatment continued intravenously 1 week after intraperitoneal road. An error in the vancomycin dose was noticed on the 8th day. She had received 40 mg/kg/day vancomycin for 8 days (320 mg/kg cumulative dose). Hemodiafiltration treatment was started for 3 days to accelerate vancomycin removal, and the treatment was successful in decreasing vancomycin levels.

An audiogram on the 8th day and a second one 3 months later showed no loss of hearing. Living donor kidney transplantation (from her father) was done 10 months later. The patient is healthy and graft functions are normal at this time.

Materials and methods

Access for hemodialysis consisted of an 8F double-lumen catheter placed in the right subclavian vein. A pediatric hemodialysis machine (Fresenius Medical Care 4008B) was used for arteriovenous HDF with a high-flux polysulfone dialyser (Fresenius 50S). The effective surface area was 1 m². The priming volume was 63 ml of
the dialyser. The dialysate flow rate was 30 l/h. The dialysate contained 140 mmol/l sodium, 111 mmol/l chloride, 2 mmol/l calcium, 1 mmol/l magnesium, 35 mmol/l acetate and no potassium and glucose.

Serum electrolytes and complete blood counts were measured before and after the procedure. Her complete blood count and electrolytes, measured before the first HDF section were: hemoglobin level 9.2 g/dl, hematocrit 27%, platelet 162,000/mm³, white blood cells 11,000/mm³, sodium 140 mEq/l, potassium 5.3 mEq/l, calcium 8.2 mg/dl, and phosphorus 6.3 mg/dl. After three procedures, levels were as follows: hemoglobin level 8.9 g/dl, hematocrit 26%, white blood cells 8900/mm³, platelets 148,000/mm³, sodium 138 mEq/l, potassium 4.3 mEq/l, calcium 9.2 mg/dl and phosphorus 3.2 mg/dl. Three sessions of treatment were applied (2 h, 4 h, and 4 h) on consecutive days. It was the first time we applied this method and the first section lasted 2 h because we were cautious about the side effects of HDF. The serum vancomycin level was determined by an enzyme-multiplied immunoassay technique [6]. Half-lives were calculated according to the formulas: \( t_{1/2} = \frac{0.693}{K_e} \) and \( K_e = \frac{\ln C_1 - \ln C_2}{(t_2 - t_1)} \). \( K_e \) is the elimination constant, \( C \) is vancomycin concentration, and \( t \) is time [6].

**Results**

The first serum vancomycin level obtained 12 h after the eighth dose was 101 mg/l in the patient. We performed 2 h HDF (first procedure) and the level of vancomycin decreased to 98 mg/l. Vancomycin level was checked every 24 h after the start of the HDF procedure. Vancomycin levels were measured before the HDF procedure because the patient was anuric. We thought that there might be a negligible difference in the determination of the vancomycin clearance. Twenty-four hours later, vancomycin level decreased to 78 mg/l after the second section (4-h HDF) and 48 h later to 16.59 mg/l after the third procedure (4-h HDF). The calculated vancomycin \( t_{1/2} \) was 231 h after the first procedure, and then it decreased to 92.4 h and 11.5 h on consecutive days. Twenty-four hours later, with no further HDF, the vancomycin level was 9.75 mg/l and 5 mg/l on consecutive days, and the vancomycin \( t_{1/2} \) was calculated subsequently to be 31.5 h and 25.6 h (Fig. 1).

**Discussion**

In this patient, the decision to perform HDF was made because of her kidney failure, which resulted in decreasing endogenous vancomycin clearance and ototoxicity. The half-life of vancomycin is 4–6 h in patients with normal renal function; renal and plasma clearance decrease and half-life increases to as much as 7.5 days in patients with renal failure. Its pharmacokinetics in critically ill young children and children with renal failure are quite variable [7]. Because of the high molecular weight (1500 kDa) and high protein binding (55%) of vancomycin, neither hemodialysis nor peritoneal dialysis is effective for its removal [8, 9].

Continuous arteriovenous HDF has been used with success to treat an adult patient with vancomycin overdose and acute renal failure [10]. Vancomycin removal in a 6-day-old patient with solitary hypodysplastic kid-

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**Fig. 1** Serum vancomycin concentration profile before and after hemodiafiltration treatments

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Kay and anuric renal failure has been attempted using continuous venovenous HDF with high-flux membrane. Accidentally, vancomycin was given to the patient at the dose of 100 mg/kg instead of 10 mg/kg. His serum vancomycin level decreased from 240 mg/l to 30.7 mg/l with 41-h continuous venovenous HDF [7]. A 14-month-old girl with chronic renal insufficiency and vancomycin overdose was treated with charcoal hemoperfusion, but the patient did not regain her previous level of renal function. Bunchman et al. reported two children with vancomycin intoxication successfully treated with high-efficiency dialysis membranes [11].

The case presents one of the first patients in Turkey to whom HDF with high-flux membrane was applied. The procedure was successful; rapid removal of vancomycin and therapeutic range were obtained in 3 days. No adverse effects of vancomycin were seen in spite of the anuric end-stage renal disease. Alwakeel et al. reported that polysulfone membranes are better than polyacrylonitrile and cuprophan membranes for vancomycin clearance. The intradialytic clearances of vancomycin were reported to be 73, 54 and 15 ml/min, respectively [12].

As a conclusion, HDF with high-flux polysulfone membrane is a novel and safe treatment modality for vancomycin overdose in pediatric patients.

**References**