DOI:10.1111/j.1365-2125.2007.02897.x

Letter to the Editors

Severe local vancomycin induced skin necrosis

Dianne W. M. Hoelen,[1] David H. T. Tjan,[1] Roel van Vugt,[1] Y. Geert van der Meer[2] & Arthur R. H. van Zanten[1]
[1]Department of Intensive Care and [2]Department of Clinical Pharmacy, Gelderse Vallei Hospital, Ede, the Netherlands

Vancomycin is a glycopeptide antibiotic with activity against gram-positive bacteria, used in the treatment of endocarditis, as an alternative to penicillin in the case of allergy and is the drug of choice for the treatment of infections due to methicillin-resistant staphylococci (MRSA). With the increase of MRSA infections, the use of vancomycin is on the rise. Vancomycin use is estimated at 3.5/100 admissions in the Netherlands [1].

Vancomycin has been documented to cause a variety of adverse reactions that can be roughly divided into two groups. The first is related to an acute release of histamine and is also called vancomycin pseudo-allergic reaction [2]. A well-known example is the Red Men Syndrome (RMS) with an incidence 1–10%. Clinical signs are erythematous or maculopapular rash on face, upper body and extremities, in some cases accompanied by hypotension [3, 4]. The causative mechanism is related to a direct release of histamine by vancomycin or coproducts. This reaction is not IgE mediated. RMS is often associated with the speed of the infusion. Antihistamines, epinephrine and corticosteroids can reduce this reaction. Desensitization is an option for these pseudo-allergic reactions like RMS, IgA dermatosis and Stevens–Johnson syndrome if no other therapy is available [5, 6]. The second group of adverse reactions is related to a hypersensitivity reaction caused by IgE mediated histamine release and can occur in up to 5% of patients [6, 7]. The third group of adverse reactions consists of a heterogeneous mix which include ototoxicity, nephrotoxicity, drug-induced fever, neurological, haematological, gastrointestinal and various dermatological reactions [8]. The mechanism of these reactions is not clear but some may be due to impurities in the vancomycin.

We would like to describe a new adverse effect of vancomycin.

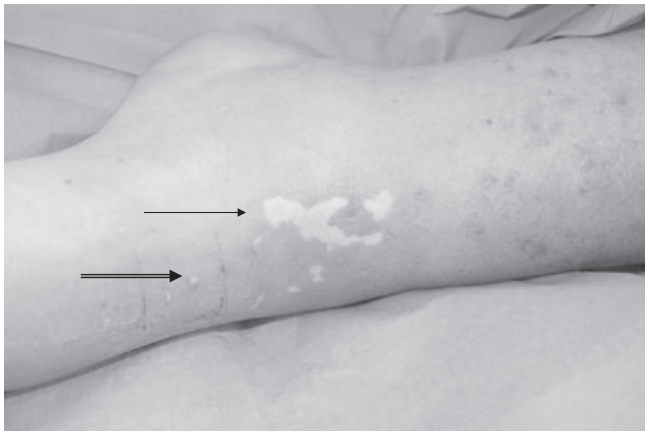

Figure 1
Left foot with ischaemic lesions after vancomycin infusion in the flow area of the vein. Double arrow venous access point

A 63 year old woman was admitted to the ICU after an emergency laparotomy for an anastomotic leakage after hemicolectomy. Peritoneal cultures became positive for *Enterococcus faecium* for which intravenous vancomycin therapy was started, using an IV line in the dorsum of the left foot due to difficulty in obtaining peripheral venous access. After 48 h, a progressive skin lesion was noted in the regional vascular bed of the IV line and the left leg was swollen and red (Figure 1). An ischaemic lesion developed after 72 h. The line was tested for patency, working appropriately and not running subcutaneously. No other drugs were given over the IV line and a 0.9% saline drip was running. After discontinuation of the vancomycin and removal of the IV line the lesions regressed and recovered gradually over several weeks. Four weeks later vancomycin administered through a subclavian central venous catheter did not cause any adverse effects.

Phlebitis can occur in up to 3–13% in patients with a peripheral venous line. Vancomycin is an irritating drug most likely because of its low pH (2.8–4.5), which has a direct irritant effect on the vascular wall [9]. Therefore, the most likely cause of the skin necrosis was a leakage

of the i.v. line or capillary leakage, with drug extravasation causing necrosis. An allergic or generalized reaction did not occur after rechallenge of vancomycin. This adds to the likelihood of a local irritant aetiology. In addition, although drug-induced bullous dermatosis and more generalized toxic epidermal necrolysis have been related to vancomycin use, local nonbullous vancomycin-induced skin necrosis as encountered in our patient has not been reported before [10, 11].

If vancomycin is administered via a peripheral line, regular checks for phlebitis and skin necrosis are advised.

We are grateful to A.J. van 't Veen, MD, Dermatologist, for his advice.

References

1 SWAB. Nethmap 2006. Consumption of antimicrobial agents and antimicrobial resistance among medically important bacteria in the Netherlands, eds. Verbrugh HA, Neeling de AJ., 2006. Publishing Department RIVM, Bilthoven, The Netherlands (www.swab.nl).

2 Levy JH, Marty AT. Vancomycin and adverse drug reactions. Crit Care Med 1993; 21: 1107.

3 Wallace MR, Mascola JR, Oldfield EC 3rd. Red man syndrome: incidence, etiology, and prophylaxis. J Infect Dis 1991; 164: 1180–5.

4 Garrelts JC, Peterie JD. Vancomycin and the 'red man's syndrome'. N Engl J Med 1985; 312: 245.

5 Anne S, Middleton E, Reisman RE. Vancomycin anaphylaxis and successful desensitization. Ann Allergy 1994; 73: 402.

6 Neughebauer BI, Negron G, Pelton S, Plunkett RW, Beutner EH, Magnussen R. Bullous skin disease: an unusual allergic reaction to vancomycin. Am J Med Sci 2002; 323: 273–8.

7 Polk RE. Anaphylactoid reactions to glycopeptide antibiotics. J Antimicrob Chemother 1991; 27(Suppl B): 17–29.

8 Garrelts JC, Smith DF Jr, Ast D, LaRocca J, Peterie JD. Phlebitis associated with vancomycin therapy. Clin Pharm 1988; 7: 720–1.

9 Hadaway L, Chamallas SN. Vancomycin: new perspectives on an old drug. J Infus Nurse 2003; 26: 278–84.

10 Hughes AP, Callen JP. Drug induced linear IgA bullous dermatosis mimicking toxic epidermal necrolysis. Dermatology 2001; 202: 138–9.

11 Craycraft ME, Arunakul VL, Humeniuk JM. Probable vancomycin-associated toxic epidermal necroslysis. Pharmacotherapy 2005; 25: 308–12.

Received
8 August 2006
Accepted
8 January 2007
Published *OnlineEarly*
10 April 2007

Correspondence
Arthur R. H. van Zanten, MD, Department of Intensive Care, Gelderse Vallei Hospital, PO Box 9025, 6710 HN Ede, the Netherlands. E-mail: zantena@zgv.nl