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### The safety of accelerated infusion versus standard rate infusion of low-molecular-weight iron dextran in patients with chronic kidney disease

Sir,

Low-molecular-weight iron dextran (cosmoFer<sup>®</sup> (marketed as INFed<sup>®</sup> in the USA), Pharmacosmos, Denmark) is available as a total dose infusion (TDI) in the United Kingdom (UK). The use of TDI regimen enables patients to receive their iron dose in one visit as opposed to numerous visits required with other preparations. However, the TDI can take up to 8 h and it would be preferable if the infusion could be safely administered over a shorter duration. The aim of this audit was to evaluate the safety of adopting an accelerated regimen of administering TDI low-molecular-weight iron dextran in comparison to standard rate infusion of the same product.

### Methods

We conducted a retrospective audit of stage 3–5 CKD patients who had undergone intravenous low-molecular-weight iron dextran TDI at Salford Royal Foundation Trust Hospital (Salford RH) and Sunderland Royal Hospital (Sunderland RH) between 2002 and 2008. Approval for the accelerated rate TDI low-molecular-weight iron dextran protocol was reviewed and granted by the local renal and pharmacy departments.

For TDI, the SmPC states that low-molecular-weight iron dextran should be infused over 4–6 h and so the use of accelerated rate infusion was consequently unlicensed. The decision to receive an accelerated or standard protocol low-molecular-weight iron dextran infusion was made by the patient's consultant.

Sunderland RH patients prescribed 1 g low-molecular-weight iron dextran TDI received this over a period of 1 h 40 min; the total infusion and observation period was 3 h 40 min. The patients at Salford RH received either standard

rate infusion or accelerated rate infusion. The standard rate involved 1 g infusion over 4 h with total infusion and observation period of 6 h 15 min, whereas accelerated rate patients received 1 g low-molecular-weight iron dextran over 1 h 40 min, total infusion and observation period being 3 h 55 min.

Adverse event rates were recorded. Fisher's exact test was used to evaluate statistically significant difference in adverse events.

### Results

Accelerated low-molecular-weight iron dextran infusion was administered to 791 patients at Sunderland RH and Salford RH. This was compared with 188 standard rate infusions at Salford RH.

There were three adverse events associated with the accelerated rate regimen (3/791, 0.4%) and none in patients with standard rate infusions. One patient developed diarrhoea post-infusion that persisted for 48 h. The second patient felt unwell and cold during the infusion with blood pressure rising from a baseline of 116/69 to 136/95, but was afebrile. Paracetamol was administered and the infusion was continued safely at a slower rate of 120 ml/h. The third patient, who was previously IV iron naïve, had urticaria and associated erythema within 1 min of commencement of the test dose. The infusion was stopped, and chlorpheniramine and hydrocortisone were administered immediately. Iron infusion was deferred and the patient subsequently received an alternative IV iron (venofer<sup>®</sup>) with no adverse events. There was no statistical difference between adverse events in the two groups (Fisher's exact test;  $P = 1.000$ ).

### Discussion

This is the first study to compare the effects of administering TDI low-molecular-weight iron dextran at accelerated and standard infusion rates in a CKD population. Results suggest that an accelerated rate of low-molecular-weight iron dextran infusion, which is currently an off-licence rate of delivery for this TDI, is as safe as standard rate infusion, and this is of major clinical significance. In particular, it has positive implications for health care resource utilization in the management of renal patients. In a recent editorial, Auerbach *et al.* also commented on the benefit of infusing low-molecular-weight iron dextran at doses ranging from 1000 to 2250 mg over 90 min in ~150 patients with no adverse events; however, most of their experience was in patients with haematological conditions [1]. The cost benefits of adopting a low-molecular-weight iron dextran TDI protocol (at standard infusion rate) for repleting iron stores in CKD patients has been reported [2,3]. Adoption of an accelerated rate protocol would enable all CKD patients to complete TDI in less than 4 h, which in turn would enable a greater number of patients to undergo iron infusion in any given period. In addition, the benefits of convenience for patients cannot be overstated.

**Conflict of interest statement.** Dr PA Kalra has received an educational grant from Pharmacosmos and has given educational lectures on behalf of Pharmacosmos in the past.

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### Catheter-related *Chryseobacterium meningosepticum* bacteraemia in a haemodialysis patient

Sir,

*Chryseobacterium meningosepticum* (*C. meningosepticum*), an unusual opportunistic pathogen resistant to multiple antimicrobial agents, was rarely reported to be a cause of bacteraemia in haemodialysis patients.

A 77-year-old female with end-stage renal disease was admitted with fever, chills and tenderness on the insertion site of the femoral double-lumen catheter 2 weeks after the start of haemodialysis. Her body temperature was 38.4°C. Erythema and swelling were present around the exit site of the double-lumen catheter. Laboratory evaluation revealed a haemoglobin of 7.6 g/dL and a C-reactive protein of 7.3 mg/dL. A provisional diagnosis of catheter-related bacteraemia was made. The double-lumen vein catheter was removed along with empiric antimicrobial agents with intravenous vancomycin (2 g/week) plus oral rifampin (450 mg/day). Blood cultures grew *C. meningosepticum* that was resistant to gentamicin, amikacin and all cephalosporins, but only susceptible to ciprofloxacin and vancomycin. Cultures of the exit site and the tip of catheter also grew *C. meningosepticum*. Despite 1-week antibiotic therapy, blood cultures still grew the same pathogen. At this time, an echocardiogram was normal. The addition of oral ciprofloxacin (250 mg q12 h) to vancomycin for another 2 weeks achieved uneventful recovery without subsequent growth of this organism. Cultures for tap water and dialysate were also negative for this pathogen.

*Chryseobacterium* spp. are of low virulence but give rise to severe infections in neonate and immunocompromised hosts. *C. meningosepticum* was the most common species of human pathogens. In neonates, *C. meningosepticum* meningitis is the most common infection, whereas pneumonia and sepsis were the most common infections in adults with impaired immunity [1]. Patients with uraemia are at a risk for *C. meningosepticum* infection due to their compromised T- and B-cell immunity. To date, there were only few reports regarding *C. meningosepticum* infections in uraemic patients on dialysis (Table 1) [2–5]. Among 42 episodes in 41 dialysis patients, a majority (37/42, 88%) of episodes were related to peritoneal dialysis (PD) catheter peritonitis and a minority (5/42, 12%) of episodes had bacteraemia in patients on haemodialysis. Initial antibiotics to eradicate *C. meningosepticum* infections were usually inappropriate, leading to the necessity of removal of the catheter in most patients. Four (4/41, 10%) patients died from *C. meningosepticum* infection. In *C. meningosepticum* bacteraemia, the exact port of entry was unknown in three episodes. *C. meningosepticum* was isolated from sink water in only one episode. Although *C. meningosepticum* was not identified in tap, tank and dialysis water, in our patient it was also isolated from the exit site and the tip of the double-lumen catheter, suggesting that the port of entry be the disruption of skin integrity by internal placement of the catheter. Our case is the first report of *C. meningosepticum* bacteraemia associated with catheter-related infection in a haemodialysis patient.

Although vancomycin has been previously recommended as the drug of choice for *C. meningosepticum* infection, recent reports and our case revealed that *C. meningosepticum* infection failed to respond to vancomycin administration alone [6]. Vancomycin should not be used alone to treat *C. meningosepticum* infections, especially associated with bacteraemia [6], as shown in the patient.

In conclusion, *C. meningosepticum* should be considered as a causative pathogen of gram-negative bacilli catheter-related bacteremia in haemodialysis patients. Early recognition of this pathogen with appropriate antimicrobial agent administration will avoid the loss of the catheter and even mortality.

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