

patients. The literature of the last few years offers convincing information that supports this opinion, both in patients with normal kidney function [1] and in haemodialysis patients [2].

So we were not surprised to learn that a second treatment course with a higher RBV dose in one of the two patients that failed a sustained viral response in our pilot study was as yet effective.

At the time that the guidelines for our pilot study were settled and placed on the website of the Dutch Federation of Nephrology (NFN) only scarce information was available concerning the use of RBV in renal insufficiency. It was even considered to be contraindicated. Partly based on earlier experience [3] we were convinced that RBV could be used in a safe and possibly effective way if the dosage could be guided by plasma trough level determinations aiming at a so-called therapeutic range (1.5–2.5 µg/ml). This range was defined on the available experimental information at that moment but there was no firm proof of the clinical efficacy. To start a pilot study we had to be very careful and made a choice for a relative low dose.

To prevent serious haemolytic anaemia—the most important complication of RBV—a high dose of erythropoietin (Epo) is necessary in the treatment of dialysis patients. A dose of 30 000–40 000 IU/week was permitted in the studies of Rendina [2] and Bruchfeld [4] and also in our study, but the mean dose remained limited to 19 000 IU/week in the last one.

During the first 12 weeks of our study the RBV plasma level was often low despite small increases of the dose. Based on this experience we will advocate now a higher starting dose of 300 mg/day, preceded by a much more generous use of Epo.

Plasma level monitoring of RBV promotes safety and helps to guide the dosing of RBV.

Future results will possibly help to define an optimal therapeutic range. A higher RBV dose is necessary to achieve still better results and this needs further exploration.

We believe that our pilot study has contributed to the effective treatment of hepatitis C-infected vulnerable dialysis patients.

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New recommendations in the treatment of Gram-positive bacteraemia in dialysis patients

Sir,

Professor Ponticelli timely reviewed a wealth of important, new information on the prevention and treatment of Gram-positive bacteraemia in dialysis patients. Surprisingly, despite the title of his paper [1], he does not discuss a point of major clinical relevance, i.e. the optimal empirical antibiotic regimen in haemodialysis patients with suspected bacteraemia. It should be based on local epidemiology (country, unit) and characteristics of the individual patient (history of MRSA carriage, recent hospitalization in a high MRSA risk setting such as an ICU). The incidence of MRSA bacteraemia in our chronic haemodialysis patients was very low in 2007 (0.063 per 1000 patient-days) and the previous 5 years (L. Labriola, unpublished data), and such episodes were only observed in patients with a history of recent ICU stay. Therefore, whenever bacteraemia is suspected, we still use cefazolin alone at the end of each HD session as a first-line empirical therapeutic option. This simple, inexpensive regimen has proved both safe and effective against methicillin-sensitive *Staphylococcus aureus* (MSSA) in dialyzed patients, in our hands and that of others [2]. Only a history of recent hospitalization, particularly in the ICU, or recent infection by another agent than MSSA, triggers the empirical choice of vancomycin, alone or with a third-generation cephalosporin or aminoglycoside. We acknowledge that the local epidemiology of *S. aureus* strains may differ greatly from country to country [3] or unit to unit but emphasize that our approach has the major advantage not to favour the indiscriminate use of last-resort anti-MRSA antibiotics, be it vancomycin or the newer, more expensive drugs reviewed by Ponticelli.

Professor Ponticelli further cited a single study of an antibiotic-lock solution as an effective method to reduce catheter-related bacteraemia (CRB) [1]. As showed by our recent meta-analysis of eight randomized controlled trials, the use of antimicrobial lock solutions (ALS) reduced the incidence of CRB by about a factor 3 [4]. However, the incidence of CRB with an ALS was similar to rates in units not using ALS but with a low CRB incidence. Moreover, two included studies with a low baseline incidence of CRB did not show a significant reduction of CRB by the ALS [4]. On the other hand, some trials revealed a dramatic reduction of CRB simply after reinforcing hygienic precautions in catheter care (discussed in [4]). In our unit, the incidence of CRB in 2007 was 0.23 per 1000 catheter-days, without using ALS.

Finally, the author did not mention thrombocytopenia as a side effect of vancomycin [1]. Recently, Von Drygalski *et al.* reported thrombocytopenia due to vancomycin-dependent antiplatelet antibodies in 34 patients. [5]. Thus thrombocytopenia should be considered as a potential side effect of vancomycin, like cutaneous reactions, neutropenia and hepatotoxicity.

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Reply

Sir,

In response to the kind letter of Dr Labriola *et al.*, I would like to specify the following points:

- (a) The aim of my editorial was to illustrate the *new* recommendations for Gram-positive bacteraemia. This is why I did not review the wide literature devoted to the empiric antibiotic administration. On the other hand, it should be pointed out that such therapy remains *empiric* by definition and the choice of broad spectrum antibiotics widely ranges among different countries.
- (b) Dr Labriola *et al.* attribute the low incidence of MRSA bacteraemia observed in their dialysis unit to the use of cefazolin. Actually, cephalosporins proved to be effective in preventing Gram-positive infection. The problem is that in the last 20 years many strains of *Enterococci* and *Staphylococci* acquired resistance to these antimicrobial agents [1]. Thus, the good results obtained in Louvain cannot necessarily be repeated in other dialysis units.

(c) As pointed out in my editorial, I fully agree with the importance of hygienic preventive measures. However, whether antibiotic lock therapy may be helpful for preventing catheter infection is still disputed. Even the meta-analysis of Dr Labriola *et al.*, unfortunately available at present only in the form of abstract [2], does not seem to allow firm conclusions. In their analysis, the authors could not find differences in catheter infection between patients assigned to antibiotic lock therapy and untreated controls. However, they reported that gentamycin-containing lock solutions significantly reduced the risk of catheter-related bacteraemia. Thus, the choice of the antibiotic can influence the efficacy of antibiotic lock therapy. At any rate, I recommended a word of caution with antibiotic lock therapy as this preventive treatment may theoretically favour resistance.

(d) I have not reported an uncommon side effect of vancomycin, namely thrombocytopenia. Cases of thrombocytopenia have been described and it has been shown that they may be related to anti-platelets antibodies by Von Drygalski *et al.* [3]. It should be noted, however, that during a period of 5 years only 34 serum samples from patients in several parts of the United States in whom vancomycin-induced thrombocytopenia was suspected were referred to the Platelet and Neutrophil Immunology Laboratory at the Blood Center of Wisconsin (Milwaukee) to be tested for vancomycin-dependent antibodies. It was out of the scope of the editorial to describe the many side effects that may occur with vancomycin (other adverse events were also not mentioned, i.e. rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue; bloody stools; chest pain; decrease in the frequency of urination or in the amount of urine; fever, chills, or sore throat; flushing; irritation, pain, or swelling at the injection site; numbness of an arm or leg; red, swollen, or blistered skin; severe diarrhoea; severe stomach pain; sudden leg pain; sudden severe dizziness, nausea, headache, or vomiting; sudden shortness of breath; unusual bruising or bleeding and wheezing). I simply intended to outline the most frequent and severe side effects, which may render difficult the use of this important antibiotic in dialysis patients.

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