Sir,

We read with great interest the letter by Nix and Matthias regarding pharmacokinetic considerations relating to tigecycline use in urinary tract infections (UTIs). We agree with the authors that tigecycline should not be used for UTIs when other therapies including aminoglycosides, carbapenems and colistin are options; however, in rare situations, tigecycline may be considered. In a recent study, Rodriguez-Bano et al. demonstrated that the susceptibility of all extended-spectrum β-lactamase (ESBL)-producing Escherichia coli to tigecycline was 100%. Since ESBL-producing E. coli is an increasing cause of community-onset bloodstream infections, they suggested that tigecycline might be an alternative in the treatment of non-UTIs. Here, we describe two patients with complicated UTIs caused by ESBL-producing E. coli, who were successfully treated with tigecycline.

The first patient was a 44-year-old renal transplant recipient with end-stage renal disease (ESRD) due to diabetic nephropathy with recurrent renal transplant pyelonephritis with an ESBL E. coli. For the first two UTIs he was treated with meropenem with treatment durations of 2 and 6 weeks, respectively, but within 4 weeks he had a recurrent UTI with systemic symptoms. Urological evaluation did not show any anatomical abnormalities, but because of the recurrent UTIs a chronic prostatitis was suspected. It was decided not to treat him again with a carbapenem, but with tigecycline for 6 weeks, because tetracyclines are lipophilic and reach higher tissue levels in the prostate. The second patient was a 66-year-old female who was on haemodialysis due to ESRD caused by autosomal dominant polycystic kidney disease and who had recurrent UTIs with ESBL E. coli owing to infected renal cysts shown on positron emission tomography CT. Because she had allergies to β-lactam antibiotics and carbapenems, she was treated with tigecycline for 6 weeks. Five (Patient 1) and 4 (Patient 2) months after the end of treatment, both patients had not developed a new UTI.

Tigecycline is a tetracycline derivative and has broad antimicrobial activity, fortunately often also against ESBL-producing microorganisms. Since only 30% of a dose is excreted in urine, it is not licensed for the treatment of UTIs. Furthermore, it is also not licensed for immunocompromised patients. However, with the increase in ESBL-producing microorganisms, sometimes no other treatment possibilities are present.

In summary, we report two patients with complicated UTIs caused by ESBL-producing E. coli with possible foci in prostate and renal cysts, respectively, who were successfully treated with tigecycline. We think that with the worldwide increasing ESBL problem, further research with tigecycline for the treatment of UTIs is warranted.

Sincerely,

[Author]

References

Tobramycin and gentamicin can safely be given by slow push

Mark R. Loewenthal1,2* and Pauline M. Dobson2,3

1School of Medicine and Public Health, University of Newcastle, New South Wales, Australia; 2Immunology and Infectious Diseases Unit, John Hunter Hospital, New Lambton Heights, New South Wales, Australia; 3School of Nursing and Midwifery, University of Newcastle, New South Wales, Australia

*Corresponding author. Immunology and Infectious Diseases Unit, Royal Newcastle Centre, PO Box 664J, Newcastle, NSW 2300, Australia. Tel: +612-4922-3444; Fax: +612-4922-3428; E-mail: mark.loewenthal@hnehealth.nsw.gov.au

Keywords: aminoglycoside, bolus, OPAT, dosing

Sir,

The routine practice of our outpatient intravenous therapy service since 1995 has been to administer tobramycin and gentamicin by slow intravenous injection over 3–5 min. This includes doses up to 920 mg. We report the experience of our first 5593 doses. All doses were administered by either a nurse in our infusion centre, a visiting nurse, or the patient or their carer. In many cases the drugs were administered to patients at home by their parents. For most of our patients, administration by ≥30 min infusion would not be possible in this setting. No acute toxicity was observed.

Demographic and management details for all patients are recorded in real time in a computerized database. This includes a detailed record of all adverse events, and any contact between the patient and our service at any time of day. Patients are contacted by a nurse every day. A doctor is always available.

Funding
This study was carried out as part of our routine work.

Transparency declarations
None to declare.

In summary, we report two patients with complicated UTIs caused by ESBL-producing E. coli with possible foci in prostate and renal cysts, respectively, who were successfully treated with tigecycline. We think that with the worldwide increasing ESBL problem, further research with tigecycline for the treatment of UTIs is warranted.
should the patient require further assessment. Otherwise, the patients are seen by a doctor at least once every week.

All doses <800 mg are diluted to 20 mL with normal saline. Larger doses are given as the neat 40 mg/mL solution supplied in the manufacturers’ vials.

In the period between November 1995 and October 2009, we documented the administration of 5593 doses (3652 of tobramycin and 1941 of gentamicin). The drugs were administered in 361 courses (244 of tobramycin and 117 of gentamicin) to 132 patients. Sixty-seven of these patients had cystic fibrosis and received multiple courses. Twelve of the remaining 65 had bronchiectasis and also received more than one course. The other remaining patients were treated for a variety of diagnoses, typically requiring only one course. One hundred and forty-five courses were administered to children and 216 to adults. The ages of the patients ranged from 3 to 84 years. The median dose was 360 mg of tobramycin and 320 mg of gentamicin in cystic fibrosis, and 240 mg of tobramycin and 170 mg of gentamicin in those without cystic fibrosis. The median course duration was between 15 and 18 days across the same groups.

One patient, a middle-aged female with complex medical problems, developed vestibular toxicity and some hearing loss 16 h after her last dose of 320 mg of tobramycin. There has never been the suggestion of neuromuscular toxicity or hearing loss at the time of injection.

Current recommendations are that tobramycin and gentamicin be given by infusion over ≥30 min. We have shown that tobramycin and gentamicin can be safely administered by slow push over 3–5 min. We recommend that consideration be given to the use of this simple method as the standard of care.

Funding
This study was carried out as part of our routine work.

Transparency declarations
None to declare.

Reference

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Rapid HIV-RNA decline following addition of raltegravir and tenofovir to ongoing highly active antiretroviral therapy in a woman presenting with high-level HIV viraemia at week 38 of pregnancy

Carmela Pinnetti1*, Silvia Bononcelli2, Paola Villani2, Massimo Fantoni3, Valerio Tozzi2, Andrea De Luca1,5, Roberto Caudo2, Gianfranco Anzidei4, Maria Cusato3, Mario Regazzi3, Marco Floridia2 and Enrica Tamburrini1

1Department of Infectious Diseases, Catholic University, Rome, Italy; 2Department of Therapeutic Research and Medicines Evaluation, Istituto Superiore di Sanità, Rome, Italy; 3Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; 4INMI L. Spallanzani, Rome, Italy; 5Infectious Diseases UOC2, Azienda Ospedaliera Universitaria, Siena, Italy

*Corresponding author. Tel: +39-06-3015-4945; Fax: +39-06-305-4519; E-mail: carmenpinnetti@yahoo.it

Keywords: mother to child transmission, drug plasma levels, HAART

Sir,
A maximal suppression of HIV-1 replication before delivery is a main objective of anti-HIV treatment in pregnancy.1 Although there is limited information on the use of the integrase inhibitor raltegravir in pregnancy, this drug has been shown to induce a rapid HIV-RNA decline in other studies2 and could therefore be considered in cases characterized by limited time available for intervention.

A woman co-infected with HIV-1/HCV was referred to our Department of Infectious Diseases at 38 weeks of pregnancy. She presented with sustained HIV replication, despite ongoing treatment with zidovudine, lamivudine and darunavir/ritonavir (600/100 mg twice daily). During her antiretroviral treatment history, the patient had received several drugs, including zidovudine, lamivudine, emtricitabine, tenofovir, stavudine, nevirapine, lopinavir and atazanavir (with low-dose ritonavir), with several episodes of drug interruptions due to intolerance and poor adherence. A previous genotypic resistance test showed changes in the reverse transcriptase (K103R) and protease (A71V/I77V/I93L) regions. She had an unplanned pregnancy while on therapy with tenofovir/emtricitabine (in a fixed-dose combination) plus raltegravir (400 mg twice daily). At the diagnosis of pregnancy, CD4 T cell count was 543 cells/mm3 and HIV-RNA was <50 copies/mL, with good medication adherence.

In order to use drugs with a favourable safety and tolerability profile in pregnancy, the nucleoside backbone was changed from tenofovir plus emtricitabine to zidovudine plus lamivudine. Given the limited information available on raltegravir use in pregnancy, raltegravir was also discontinued, and in order to maintain HIV suppression with potent antiretroviral drugs, darunavir plus ritonavir were prescribed (in combination with zidovudine plus lamivudine) at 8 weeks of pregnancy. The patient reported poor adherence with this new regimen, due to nausea and vomiting, and, as a probable consequence of incomplete adherence, at 25 weeks HIV plasma levels rebounded to 189 copies/mL. At 38 weeks of pregnancy, she presented to our clinic with a CD4 cell count of 350 cells/mm3 and a plasma viral load of 75 584 copies/mL (Figure 1). Despite the absence of obstetric complications, the woman was hospitalized, in order to allow close obstetric monitoring. After a case discussion within a multi-disciplinary team and a careful counselling session with the woman, it was decided to avoid the use of nevirapine, given the