L. monocytogenes by ~50%, and glatiramer did not modify this effect. When infected cells were exposed to ampicillin for 24 h after phagocytosis, the bacterial load was reduced by ~1.7 log compared with the original, post-phagocytosis inoculum. Glatiramer, IFN-γ, or the combination of glatiramer and IFN-γ did not significantly modify this effect of ampicillin. In the next series of experiments, we examined the activity of moxifloxacin (4 mg/L) using the 5 h model. We observed a decrease in the post-phagocytosis inoculum of 1.34 ± 0.03, 1.26 ± 0.16, 1.31 ± 0.07 and 1.32 ± 0.07 log10 units for cells treated with moxifloxacin alone, glatiramer and moxifloxacin, IFN-γ and moxifloxacin, and the combination of glatiramer, IFN-γ and moxifloxacin, respectively. In parallel experiments, we examined the influence of glatiramer on the accumulation of moxifloxacin and no effect was seen [apparent cellular to extracellular drug concentration ratios at 2 h of 9.6 ± 2.0 in controls versus 9.4 ± 1.1 in cells exposed to glatiramer (20 mg/L) during the uptake period; similar values were found for cells pre-exposed to glatiramer (20 mg/L) for 24 h]. Glatiramer did not influence the accumulation of three other quinolones (ciprofloxacin, levofloxacin and garenoxacin).

Our data, therefore, show that the production of TNF-α is not critical in IFN-γ-stimulated THP-1 cells for anti-L. monocytogenes activity. The model used has been validated to analyse the behaviour of intracellular L. monocytogenes with respect to the action of cytokines and to the influence of antibiotics. THP-1 cells display functional receptors for TNF-α and their presence in the cell line used here has been confirmed (J. Zanon, unpublished data). TNF-α may be a more potent inhibitor of IFN-γ than a true effector for the control of L. monocytogenes growth in THP-1 cells. Because intracellular multiplication of L. monocytogenes is an important determinant in the persistence and the spread of the infection, our results suggest that glatiramer (i) may not increase this risk, and (ii) may not adversely affect ampicillin or quinolone-based antibiotic treatments should the necessity arise. This will need to be confirmed by in vivo studies.

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Serotonin syndrome due to co-administration of linezolid and venlafaxine

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Keywords: oxazolidinones, interactions, selective serotonin reuptake inhibitors

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Sir,

Linezolid is an oxazolidinone antibiotic with non-selective, reversible monoamine oxidase inhibitor (MAOI) action. It has been reported to interact with selective serotonin reuptake inhibitors (SSRIs) and other sympathomimetic drugs resulting in serotonin syndrome. We report the first published case of serotonin syndrome due to interaction of linezolid and venlafaxine.

An 85-year-old man was referred for management of a chronically infected total hip joint prosthesis. He had a past history of Parkinson’s disease, ischaemic heart disease, atrial fibrillation, diabetes, previous stroke and a permanent pacemaker. The hip prosthesis was removed and surgical specimens isolated Pseudomonas aeruginosa, methicillin-susceptible Staphylococcus aureus and methicillin-resistant Staphylococcus epidermidis. Intravenous antibiotics were given for 6 weeks. Following closure of the wound, oral therapy was commenced with ciprofloxacin 750 mg twice daily, rifampicin 300 mg twice daily
and linezolid 600 mg twice daily. At that time the patient was also receiving venlafaxine 150 mg nocte for depression.

Twenty days after commencing the oral antibiotic regimen the patient was noted to be confused and disorientated, with disturbance of his sleep–wake cycle, and was intermittently aggres-

The diagnosis is based on clinical signs and symptoms and an appropriate drug history.1

Treatment is symptomatic, although the use of serotonin-receptor antagonists may speed resolution. Cyproheptadine is a drug with 5HT-1a and 5HT-2 receptor blocking activity, and may be used.1

Linezolid is the first member of the synthetic oxazolidinone family of antimicrobials to be used in clinical practice. This group of drugs was originally developed as monoamine-oxidase inhibitors for the treatment of depression, but was subsequently noted to have antimicrobial properties against Gram-positive organisms and was further developed for this purpose.2 As an antimicrobial, linezolid inhibits bacterial ribosomal protein synthesis, preventing formation of the 70S initiation complex. This unique process precludes cross-resistance to other agents.2

Linezolid is active against major Gram-positive pathogens, Neisseria spp., Nocardia spp. and possibly Mycobacteria spp. It has 100% bioavailability, does not require dosage adjustment for renal or hepatic disease and comes in oral and intravenous forms. Other than reversible marrow suppression, the drug has a very favourable side-effect profile and is tolerable to patients.2

These factors all make linezolid a very attractive option for the treatment of complicated Gram-positive infections on an outpati-ent basis.

A Phase III study of linezolid included 52 patients receiving concomitant linezolid and an SSRI with no reports of serotonin syndrome. Given the limited treatment experience with these agents in combination, physicians were alerted to be aware of the potential for interaction.3

Serotonin syndrome has been reported in a patient receiving low-dose venlafaxine (a serotonin noradrenergic reuptake inhibitor) alone; however, it is most commonly caused by drug inter-

The syndrome has been now been described as being the result of interaction between linezolid and citalopram, and linezolid and paroxetine.5,6

Linezolid is a useful antimicrobial that has a role in treating difficult Gram-positive infections. There is an increasing body of reports of clinically important interactions between linezolid and serotoninergic antidepressant drugs. Physicians need to be continually aware of the potential for significant interactions, particularly in these groups of patients with complex infections, in whom depression is common.

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References


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Successful treatment of Acinetobacter meningitis with intrathecal polymyxin E

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Keywords: post-neurosurgical infections, polymyxins, meningitis

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