

ORIGINAL ARTICLE

Linezolid in the treatment of methicillin-resistant staphylococcal post-neurosurgical meningitis: A series of 17 cases

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Abstract

Background: Linezolid is a bacteriostatic antibiotic with good cerebrospinal fluid penetration. The aim of this study was to evaluate the efficacy of linezolid in methicillin-resistant staphylococcal (methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant coagulase-negative *Staphylococcus* (MRCoNS)) meningitis. **Methods:** We extracted data and outcomes for all adult patients (age > 18 y) with culture-proven MRSA or MRCoNS meningitis treated with linezolid between January 2006 and September 2010 in our hospital. Demographic, clinical, and laboratory data and predisposing factors, as well as information on response to treatment and outcome were obtained by regular visits. **Results:** A total of 17 cases (9 MRCoNS, 7 MRSA, and 1 MRCoNS and MRSA mixed) fulfilled the inclusion criteria. All patients had hospital-acquired meningitis and had undergone neurosurgery. Cumulative microbiological success on day 5 was 88%. There was 1 staphylococcal meningitis-related death. There were no severe adverse events. **Conclusions:** Our experience with linezolid suggests that it can be an alternative for the treatment of MRCoNS- and MRSA-related meningitis.

Keywords: Oxazolidinones, vancomycin, teicoplanin, glycopeptides, daptomycin

Introduction

Staphylococcus aureus and coagulase-negative staphylococci (CoNS) are the major Gram-positive organisms causing nosocomial bacterial meningitis [1–4]. Vancomycin is the mainstay of therapy in both methicillin-resistant *S. aureus* (MRSA) and methicillin-resistant CoNS (MRCoNS) meningitis [1–7]. Linezolid is an oxazolidinone class, mainly bacteriostatic, antibiotic with relatively high cerebrospinal fluid (CSF) penetration and broad anti-Gram-positive activity, including MRSA and MRCoNS. Although linezolid is a bacteriostatic antibiotic, there are several case reports of its use in the management of severe Gram-positive bacterial infection, where antibiotic bactericidal activity might be necessary, such as meningitis and endocarditis [8–14]. The aim of this study was to evaluate the efficacy of linezolid in methicillin-resistant staphylococcal (MRSA or MRCoNS) meningitis.

Methods

This study was performed at an 1811-bed tertiary-care general teaching hospital. The hospital has a 78-bed neurosurgery ward, and 16 of these beds are in an intensive care unit.

We extracted data and outcomes for all adult patients (age > 18 y) with culture-proven methicillin-resistant staphylococcal meningitis (MRSA or MRCoNS) treated with linezolid between January 2006 and September 2010. Demographic, clinical, and laboratory findings and predisposing factors, as well as information on response to treatment and outcome were obtained prospectively.

A definite diagnosis of meningitis was based on the isolation of MRSA in at least 1 CSF culture. Typical CSF findings included a leukocytosis with a predominance of polymorphonuclear cells and classic clinical manifestations of meningitis [1,2,15]. For

MRCoNS meningitis, a definite diagnosis was based on the following 3 criteria (A–C) all being met: (A) positive MRCoNS cultures in at least 2 separate CSF studies; (B) patients with clinical presentations of acute bacterial meningitis, including fever and/or disturbance of consciousness and/or seizures and/or signs of meningeal irritation; (C) a leukocyte count of $> 0.25 \times 10^9/l$ in the CSF, with predominantly polymorphonuclear cells [2].

Nosocomial meningitis was defined as bacterial infection not present when the patient was admitted to the hospital or clinical evidence of infection within a short period of time after discharge from the hospital when the patient had received an invasive procedure. Patients developing meningitis after neurosurgical procedures were defined as having a post-neurosurgical infection [1,15]. Accordingly all cases had nosocomial post-neurosurgical meningitis.

All CSF samples in MRSA meningitis cases and at least 1 CSF sample in MRCoNS meningitis cases were obtained by lumbar puncture or percutaneous aspiration of shunt reservoir. Some of the additional CSF samples in MRCoNS meningitis cases were obtained from lumbar or extraventricular drainage reservoirs.

Samples were routinely centrifuged and the pellet was Gram-stained. *S. aureus* and CoNS isolates were identified using routine microbiological methods. Antibacterial susceptibility tests were performed using the Kirby–Bauer disk diffusion method, as described by the Clinical and Laboratory Standards Institute (CLSI) [16].

Results

A total of 17 patients (11 male and 6 female) fulfilled our inclusion criteria. A further 3 cases received linezolid for staphylococcal meningitis, but did not fulfil the inclusion criteria. The ages and characteristics of cases are shown in Tables I and II.

Clinical presentation and diagnosis

Ten cases had a shunt infection. Their shunts had been infected a mean \pm standard deviation 56.8 ± 39.4 (range 8–128) days after shunt insertion. The reasons for neurosurgical operations in the other patients are shown in Tables I and II.

Data on the presence of fever, disturbances in level of consciousness, neck stiffness, convulsions, nausea and vomiting are summarized in Tables I and II. Eight patients (patients 1, 2, 4, 6, 7, 8, 13 and 15) had leukocytosis. Five cases (patients 3, 5, 10, 15 and 16) did not have leukocytosis, but had polymorphonuclear leukocyte predominance (Tables I and II).

All cases had a CSF pleocytosis (Tables I and II). The CSF mean protein level was 2260 ± 1410 mg/l and glucose level was 210 ± 100 mg/l.

Seven cases (patients 1, 3, 4, 5, 6, 7 and 8) had only MRSA meningitis and 9 cases (patients 9–17) had only MRCoNS meningitis. One case (patient 2) had a mixed MRSA and MRCoNS infection. One case was considered to have concomitant ventriculitis, diagnosed by magnetic resonance imaging findings (patient 6).

All strains were susceptible to vancomycin, teicoplanin, and linezolid according to CLSI criteria [16,17]. Gram stain was negative in all patients except for 1 MRSA meningitis case (patient 2). Vancomycin and teicoplanin minimum inhibitory concentration (MIC) data for the strains were available for only 7 cases (patients 1, 5, 6, 7, 8, 16 and 17) and are shown in Tables I and II.

Treatments prior to staphylococcal meningitis

Before the staphylococcal meningitis episode, all patients had received peri-operative prophylactic ceftizoxime for 3 days. Six cases (patients 2, 5, 9, 10, 12 and 13) had experienced CSF leakage before the onset of meningitis. All but 1 case (patient 5) had received prophylactic ceftriaxone 2 g every 12 h; patient 5 had already developed meningitis at the time of onset of CSF leakage and was started on vancomycin and ceftazidime.

Before acquiring MRSA meningitis, patient 3 had received cefepime and netilmicin due to *Enterobacter cloacae* meningitis, patient 4 had received ceftazidime + amikacin for previous *Pseudomonas aeruginosa* meningitis, patient 6 had received meropenem for previous *Providencia stuartii* meningitis, and patient 8 had received imipenem for previous *Acinetobacter baumannii* pneumonia. In the MRCoNS group patient 16 had received meropenem for previous *A. baumannii* meningitis (Table II). The mean interval between antibiotics and meningitis was 31 ± 17 days.

Meningitis treatment

Patient treatment regimens and the duration of treatment are summarized in Tables I and II. Four cases received additional antibiotics that were not active against MRSA or MRCoNS during the linezolid therapy due to nosocomial pneumonia (Tables I and II).

Seven cases (patients 1, 3, 5, 7, 8, 14 and 15) had microbiological failure with 5 days of vancomycin, and 1 case (patient 4) received 5 days of teicoplanin ($400 \text{ mg} \times 2$) before receiving linezolid. In the remaining 9 cases, linezolid was started as primary therapy during consultation for positive CSF cultures.

Table I. Main demographic characteristics, symptoms, underlying diseases, treatment modalities, and morbidity and mortality findings in MRSA meningitis patients.

| Patient No. | Age, y | Gender | Fever/ convulsions | Disturbances in level of consciousness/ Glasgow coma score | Nausea, vomiting/ neck stiffness | CSF leukocytes; blood leukocytes (blood PML%) | Previous treatment | MIC vancomycin/ MIC teicoplanin, mg/l | Underlying condition | Treatment (IV) and duration | Morbidity | Outcome |
|----------------|--------|--------|-----------------------|--|---|--|--|---|--|---|--|---|
| | | | | | | | | | | | | |
| 1 | 80 | Male | +/- | +/13 | +/- | $>1 \times 10^9/l$; $12.8 \times 10^9/l$ (82.6%) | Ceftizoxime, vancomycin | 2/6 | Operated on due to normal pressure hydrocephalus, VP shunt insertion | Linezolid (600 mg \times 2), 28 days; piperacillin/ tazobactam (4.5 g \times 3) after 5 days of linezolid, lasting 3 weeks | Cranial oedema, decompression surgery, shunt removed, EVD, reoperation for shunt | Microbiologically cured, but died 3 months later due to gastric bleeding |
| 2 ^a | 58 | Male | +/+ | +/11 | -/+ | $>1 \times 10^9/l$; $14.1 \times 10^9/l$ (75.6%) | Ceftizoxime, ceftriaxone | NA | Operation due to intracerebral haematoma | Linezolid (600 mg \times 2), 28 days + imipenem 500 mg \times 4, 14 days for <i>Pseudomonas</i> <i>aeruginosa</i> pneumonia ^b | | Microbiologically cured; survived (GCS 15 ^c) |
| 3 | 49 | Male | -/- | -/15 | +/- | $>1 \times 10^9/l$; $7 \times 10^9/l$ (81.9%) | Ceftizoxime, cefepime, netilmicin, vancomycin | NA | Operation due to meningioma, VP shunt insertion | Linezolid (600 mg \times 2), 10 days | Shunt removal, EVD | Microbiologically cured, but died due to <i>Candida</i> <i>glabrata</i> meningitis on the 10 th day of linezolid |
| 4 | 36 | Male | +/- | +/12 | -/- | $3.2 \times 10^9/l$; $2.04 \times 10^9/l$ (91%) | Ceftizoxime, ceftazidime, amikacin, teicoplanin | NA | Ventriculo-atrial shunt insertion due to hydrocephalus developing after traumatic subarachnoid haemorrhage operation | Linezolid (600 mg \times 2), 12 days | Shunt removal and VP shunt insertion | Microbiologically cured, but died due to sudden cardiac arrest on the 12 th day of linezolid |
| 5 | 72 | Female | +/- | -/15 | +/- | $>1 \times 10^9/l$; $4.78 \times 10^9/l$ (75%) | Ceftizoxime, ceftazidime, vancomycin | 2/6 | Operated on due to degenerative lumbar stenosis | Linezolid (600 mg \times 2), 21 days | Wound revision, lumbar drainage insertion | Microbiologically cured; survived (GCS 15 ^c) |
| 6 | 36 | Male | +/- | +/8 | -/- | $0.25 \times 10^9/l$; $20.5 \times 10^9/l$ (85%) | Ceftizoxime, meropenem | 2/3 | Operated on due to intracerebral haematoma | Linezolid (600 mg \times 2), 21 days | EVD | Microbiologically cured, but died due to intracranial haematoma 2 months later |

(Continued)

Table I. (Continued).

| Patient No. | Age, y | Gender | Fever/convulsions | Disturbances in level of consciousness/ Glasgow coma score | Nausea, vomiting/ neck stiffness | CSF leukocytes; blood leukocytes (blood PML%) | Previous treatment | MIC vancomycin/ teicoplanin, mg/l | Underlying condition | Treatment (IV) and duration | Morbidity | Outcome |
|-------------|--------|--------|-------------------|---|-------------------------------------|---|---|--------------------------------------|--|--|------------------------|--|
| 7 | 69 | Male | +/- | +/12 | -/- | $> 1 \times 10^9/l$; $11.79 \times 10^9/l$ (92%) | Ceftizoxime, vancomycin | 2/4 | Operated on due to intracerebral haematoma, VP shunt insertion | Linezolid (600 mg \times 2), 10 days | Shunt revision and EVD | Microbiological failure; died despite addition of daptomycin on day 6 |
| 8 | 65 | Female | +/- | +/13 | -/- | $0.3 \times 10^9/l$; $14.15 \times 10^9/l$ (67%) | Ceftizoxime, imipenem, vancomycin | 2/6 | Operated on due to aneurysm, VP shunt insertion | Linezolid (600 mg \times 2), 21 days | Shunt revision and EVD | Microbiologically cured, but died 1 month later due to Pseudomonas aeruginosa meningitis |

CSF, cerebrospinal fluid; EVD, extraventricular drainage; GCS, Glasgow coma score; IV, intravenous; MRSA, methicillin-resistant Staphylococcus aureus; MRCoNS, methicillin-resistant coagulase-negative Staphylococcus; NA, not available; PML, polymorphonuclear leukocytes; VP, ventriculo-peritoneal.

^aPatient 2 had both MRSA and MRCoNS meningitis.

^bMeropenem was temporarily unavailable on the market.

^cFinal Glasgow coma score.

Table II. Main demographic characteristics, symptoms, underlying diseases, treatment modalities, and morbidity and mortality findings in MRCoNS meningitis.

| Patient No. | Age, y | Gender | Fever/convulsions | Disturbances in level of consciousness/ Glasgow coma score | Nausea, vomiting/ neck stiffness | CSF leukocytes; blood leukocytes (blood PML%) | Previous treatment | MIC vancomycin/ teicoplanin, mg/l | Underlying condition | Treatment (IV) and duration | Morbidity | Outcome |
|-------------|--------|--------|-------------------|---|-------------------------------------|--|-----------------------------|--------------------------------------|---|--|--------------------|--|
| 9 | 54 | Male | +/- | +/7 | -/- | $> 1 \times 10^9/l$; $7.2 \times 10^9/l$ (83.6%) | Ceftizoxime, ceftriaxone | NA | Meningioma | Linezolid (600 mg \times 2), 28 days | | Microbiologically cured, but died 3 months later due to pan-resistant Pseudomonas aeruginosa pneumonia |
| 10 | 70 | Female | +/- | -/15 | +/+ | $> 1 \times 10^9/l$; $6.8 \times 10^9/l$ (73.7%) | Ceftizoxime, ceftriaxone | NA | Spondylolithesis | Linezolid (600 mg \times 2), 28 days + meropenem (3 \times 1 g), 21 days | | Microbiologically cured; survived (GCS 15 ^a) |
| 11 | 50 | Male | -/- | -/15 | +/- | $0.25 \times 10^9/l$; $5.5 \times 10^9/l$ (73.6%) | Ceftizoxime | NA | Glioblastoma multiforme, VP shunt insertion | Linezolid (600 mg \times 2), 5 days | Shunt removal, EVD | Microbiological failure, treated with vancomycin + rifampin (GCS 15 ^a) |
| 12 | 49 | Female | -/+ | -/15 | +/- | $0.4 \times 10^9/l$; NA | Ceftizoxime, ceftriaxone | NA | Meningioma | Linezolid (600 mg \times 2), 28 days | | Microbiologically cured; survived lived (GCS 15 ^a) |

| | | | | | | | | | | | | |
|----|----|--------|-----|------|-----|--|-----------------------------|-----|---|---|---------------------------------|---|
| 13 | 33 | Male | +/- | -/15 | +/- | $0.5 \times 10^9/l$; $13.4 \times 10^9/l$ (70.1%) | Ceftizoxime, ceftriaxone | NA | Operation due to astrocytoma, VP shunt insertion | Linezolid (600 mg × 2), 28 days + ceftazidime (2 g × 3), 20 days for Enterobacter cloacae pneumonia | Shunt removal, EVD | Microbiologically cured, but died due to Acinetobacter baumannii pneumonia and meningitis |
| 14 | 37 | Female | +/- | -/15 | +/- | $0.25 \times 10^9/l$; $6.24 \times 10^9/l$ (62%) | Ceftizoxime, vancomycin | NA | Operated on due to posterior fossa tumour | Linezolid (600 mg × 2), 21 days | Wound revision | Microbiologically cured; survived (GCS 15 ^a) |
| 15 | 75 | Male | +/- | +/13 | -/- | $0.32 \times 10^9/l$; $10.9 \times 10^9/l$ (83%) | Ceftizoxime, vancomycin | NA | Operated on due to cervical fracture and hydrocephalus developing 3 months after operation, VP shunt insertion | Linezolid (600 mg × 2), 18 days | EVD, VP shunt insertion | Microbiologically cured, but died on the 18th day of therapy due to nosocomial pneumonia |
| 16 | 34 | Female | +/- | +/5 | -/- | $0.7 \times 10^9/l$; $5.2 \times 10^9/l$ (91%) | Ceftizoxime, meropenem | 2/8 | Operated on due to pilocytic astrocytoma and hydrocephalus developing 3 months after, VP shunt insertion | Linezolid (600 mg × 2), 21 days | Shunt removal | Microbiologically cured; survived (GCS 13 ^a) |
| 17 | 28 | Male | +/- | -/15 | +/- | $0.35 \times 10^9/l$; $7.19 \times 10^9/l$ (67%) | Ceftizoxime | 2/3 | Operated on due to hydrocephalus developing after traumatic subarachnoid haemorrhage operation, VP shunt insertion | Linezolid (600 mg × 2), 21 days | Shunt revision and EVD | Microbiologically cured; survived (GCS 15 ^a) |

CSF, cerebrospinal fluid; EVD, extraventricular drainage; GCS, Glasgow coma score; IV, intravenous; MRCoNS, methicillin-resistant coagulase-negative Staphylococcus; NA, not available; PML, polymorphonuclear leukocytes; VP, ventriculo-peritoneal.
^aFinal Glasgow coma score.

Microbiological efficacy

All patients but 2 had clearance of MRSA (patient 7) or MRCoNS (patient 11) from the CSF by day 5 of linezolid. In the MRSA cases, patients 4 and 5 had data for daily CSF cultures. CSF clearance in patients 4 and 5 occurred on days 2 and 5, respectively. In the MRCoNS cases, bacterial clearance data were available for patients 10 and 16. CSF bacterial clearance for these cases occurred on days 3 and 2, respectively.

In the MRSA meningitis case with microbiological failure, daptomycin was added to linezolid. However, the patient died on the 3rd day of linezolid and daptomycin combination. The MRCoNS meningitis case in whom linezolid was not effective on day 5 (patient 11), was treated successfully with vancomycin + rifampin. There was no specific difference in the clinical or CSF findings for these 2 cases compared to the others, however we did not have the blood–CSF barrier abnormality data for any case.

Clinical efficacy

In the MRSA group, 2 of 7 cases (patients 3 and 4) with microbiological efficacy on day 5 of linezolid, died before the end of treatment. Patient 3 died due to *Candida glabrata* meningitis and patient 4 died due to sudden cardiac arrest (Table I). Patient 8 was in a vegetative state at the end of linezolid therapy and died 29 days after linezolid therapy due to *P. aeruginosa* meningitis.

Four cases (patients 1, 2, 5 and 6) in the MRSA group had at least 1 month survival in the post-treatment period, whereas only 2 had at least 6 months survival. Patient 1 died 3 months after treatment due to gastric bleeding. Patient 6 died due to a repeat intracerebral haematoma (Table I). However, none of the cases had relapsing MRSA meningitis during the follow-up.

In the MRCoNS group, 1 of 8 cases (patient 15) with microbiological efficacy on day 5 of linezolid, died before the end of treatment due to nosocomial pneumonia.

Seven cases (patients 9, 10, 12, 13, 14, 16 and 17) had post-treatment survival of at least 1 month, whereas only 5 (patients 10, 12, 14, 16 and 17) had at least 6 months survival. Patients 9 and 13 were in a vegetative state at the end of linezolid therapy. Patient 9 died 3 months after linezolid therapy due to *P. aeruginosa* pneumonia. Patient 13 died 4 months after linezolid therapy due to *A. baumannii* meningitis and pneumonia (Table II). However, none of the cases had relapsing MRCoNS meningitis during the follow-up.

When the efficacy of linezolid was evaluated in terms of mortality, there was 1 staphylococcal

meningitis-related death who did not respond clinically and microbiologically to linezolid and linezolid + daptomycin combination.

Adverse events

There was no severe haematological, nephrological, or hepatological toxicity during linezolid treatment in these cases.

Discussion

Despite developments in intensive care and antibiotic therapy, meningitis is still associated with significant mortality and morbidity. MRSA and MRCoNS may be found in up to 40.9% of all nosocomial meningitis cases [2,4,7–10]. These cases are usually associated with neurosurgical interventions, staphylococcal bacteraemia, or a parameningeal focus. Owing to the methicillin resistance among *Staphylococcus* spp., the treatment of post-neurosurgical infections such as ventriculitis, meningitis, and brain abscesses is challenging [1,2,6–10].

Although there has been no randomized-controlled study controlling its clinical efficacy, vancomycin is the mainstay of therapy in both MRSA and MRCoNS meningitis. The level of evidence for this suggestion is confined to case-series and experimental animal models. Vancomycin does not usually penetrate into the CSF in the absence of inflamed meninges, but when meningitis develops, its penetration can be enhanced to a moderate degree [6]. Several treatment failures have been reported when intravenous vancomycin has been used alone, but there are some reports of successes with intrathecal application [1,7]. In the presented series, intrathecal vancomycin was not used due to possible side effects such as seizures and headache [7]. An additional strategy is combination therapy such as vancomycin + rifampin, which was used in an MRCoNS meningitis patient with microbiological failure with linezolid. Rifampin has excellent activity against *S. aureus* with low MIC values and excellent central nervous system penetration [7].

Teicoplanin may be used as an alternative for the treatment of MRSA meningitis and is as effective as vancomycin in the treatment of MRSA meningitis in the rabbit model [1,18]. However, it was not chosen in the cases for whom linezolid was used as secondary therapy due to the relatively high MIC of the infecting strains. The lowest teicoplanin MIC of the related strains was 3 mg/l and all strains with teicoplanin MIC data could be considered as teicoplanin non-susceptible according to EUCAST criteria [19]. Contrary to the literature, the teicoplanin MIC was

higher than the vancomycin MIC even in *S. aureus* [20,21], probably due to the previously reported higher rates of consumption in our setting [22].

Linezolid is effective in the treatment of MRSA-related pneumonia and complicated skin infections. In addition it has an excellent penetration into CSF (CSF/blood ratio >1) [10]. Viale et al. [14] reported 1 case of MRSA and 2 cases of MRCoNS meningitis unresponsive to vancomycin treated with 28, 14, and 21 days of linezolid. Faella et al. [8] recently used ceftriaxone + linezolid in 7 patients with meningitis due to penicillin non-susceptible pneumococci and reported 1 death, 2 with sequelae, and 4 who made a full recovery. The antibacterial efficacy of linezolid was found non-inferior to vancomycin in the treatment of MRSA meningitis in rabbits [23]. In a recent article, Ntziora and Falagas [10] reviewed the available evidence for the usage of linezolid in central nervous system infections. They described 20 cases of meningitis (4 MRCoNS and 3 MRSA) treated with linezolid up until the end of October 2006. The treatment duration of these cases ranged between 14 and 84 days. In this series, 9 cases received 21 days of treatment and 8 cases received 28 days of linezolid. The fact that all cases treated with a 21-day course of linezolid had microbiological clearance suggests that 21 days may also be successful.

The approach of the CLSI with regard to vancomycin susceptibility testing for *S. aureus* changed several times between January 2006 and September 2010. In the case of the MIC, the vancomycin susceptibility breakpoint decreased to ≤ 2 mg/l from ≤ 4 mg/l [16,17]. According to these criteria, all the cases presented herein who had a vancomycin MIC were susceptible to vancomycin. Until 2010 there were criteria for disk diffusion susceptibility testing for vancomycin, but these criteria were withdrawn in 2010 [17]. All cases treated by the end of 2009 had strains susceptible to vancomycin by disk diffusion test. There were 2 cases in 2010 (patients 8 and 17), and both were susceptible to vancomycin in terms of MIC values.

The vancomycin MIC is closely related to the microbiological eradication rate in *S. aureus* bacteraemia. According to the findings of Moise et al., when MIC values were 0.5, 1, and 2 mg/l, microbiological response rates were 77%, 71%, and 21%, respectively [24]. In our study, vancomycin MICs were 2 mg/l in the 7 cases for whom linezolid was started as secondary therapy after failure with glycopeptides. Strains with a vancomycin MIC of 2 mg/l might also be heterogeneous, intermediate-vancomycin-resistant *Staphylococcus aureus* (hVISA), but we do not have heteroresistance data for those strains. We unfortunately did not have the MIC data for all strains. The linezolid MIC could have resulted in the

failure in the 2 cases with linezolid failure (patients 7 and 11), but we do not have linezolid MIC data for those strains.

Linezolid was started as primary therapy in 9 cases. Recent guidelines for meningitis from the European Federation of Neurological Societies suggest linezolid as the first-line therapeutic option for methicillin-resistant staphylococcal meningitis [25]. As mentioned before, the antibacterial activity of linezolid is not inferior to vancomycin in the treatment of MRSA meningitis in the rabbit model [23]. Another reason to use linezolid as the first-line therapy is to decrease vancomycin consumption following the recent vancomycin-resistant *Enterococcus* (VRE) epidemic in our neurosurgery clinic. We have not experienced any VRE epidemics since that time.

Three cases (patients 3, 8 and 13) died after clearance of staphylococci from the CSF due to additional attacks of nosocomial meningitis. The fact that all 3 were on extraventricular drainage suggests that there might be some problems in the infection control measures.

The major disadvantage of our study is the fact that it comprised a relatively small number of cases and lacked a control group. In addition, although the data were collected prospectively, this was a retrospective cohort study. Another main disadvantage is the heterogeneity of the study group. Despite the fact that all cases had post-neurosurgical nosocomial meningitis, 8 cases had MRSA and 10 had MRCoNS, and 9 received linezolid as the primary therapy and the others received it as secondary therapy. However, as stated above, data on the efficacy of linezolid in staphylococcal meningitis are scarce and confined to series with 1 or only a few cases. This series of 17 cases comprises the largest single-centre experience of the treatment of either MRSA or MRCoNS meningitis with linezolid. In addition, the 2 presented cases with linezolid failure comprise the first reports of treatment failure with linezolid in staphylococcal meningitis.

In conclusion, according to recent textbooks the main therapeutic option in staphylococcal meningitis is vancomycin [4]. However our experience suggests that linezolid may be an alternative, at least in the salvage therapy of MRSA and MRCoNS meningitis, with a cumulative microbiological efficacy rate of 88%. A clinical study comparing vancomycin and linezolid in staphylococcal meningitis may provide an evidence-based approach to the treatment of staphylococcal meningitis.

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