Linezolid in Neurosurgery

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- Bacteriological Profile of Patients With Stroke-Associated Pneumonia and Antimicrobial Susceptibility of Pathogens: A Cross-Sectional Study

Evidence for the effectiveness of linezolid in neurosurgical infections (NSIs) is growing. The comfortable oral dosage and tolerance of linezolid open the possibility for sequential antimicrobial treatment (SAT) in stable patients after a period of intravenous treatment [1].

Reviews

Relevant studies were identified through searches of the PubMed, Current Contents, and Cochrane databases (publications archived until October 2006).

Case reports, case series, prospective and retrospective studies, and randomized controlled trials were eligible for inclusion in our review if they evaluated the effectiveness and safety of linezolid for the treatment of patients with CNS infections.

In 18 (42.9%) of the 42 relevant cases identified, patients had undergone neurosurgical operations and/or had prosthetic devices. Meningitis was the most common CNS infection, accounting for 20 (47.6%) cases. Other CNS infections included brain abscesses (14; 33.3%), ventriculitis (5; 11.9%), and ventriculo-peritoneal shunt infection (3; 7.1%). In the 39 patients in whom the responsible pathogen was isolated, those predominantly responsible for the CNS infections were: penicillin-nonsusceptible Streptococcus pneumoniae (7; 17.9%), vancomycin-resistant enterococci (6; 15.4%), Nocardia spp. (5; 12.8%), methicillin-resistant Staphylococcus epidermidis (4; 10.3%), and methicillin-resistant Staphylococcus aureus (3; 7.7%). Of the 42 patients who received linezolid for the treatment of CNS infections, 38 (90.5%) were either cured or showed clinical improvement of the infection. The mean duration of follow-up was 7.2 months; no recurrent CNS infection was reported.

The limited published data suggest that linezolid may be considered for the treatment of patients with CNS infections in cases of failure of previously administered treatment or limited available options [2].

Case series

To evaluate the efficacy and safety of SAT with oral linezolid in patients with NSI and to analyse the cost implications, an observational, non-comparative, prospective cohort study was conducted on clinically stable consecutive adult patients at the Neurosurgical Service. Following intravenous treatment, patients were discharged with SAT with oral linezolid.

A total of 77 patients were included. The most common NSIs were: 41 surgical wound infections, 20 subdural empyemas, 18 epidural abscesses, and 16 brain abscesses. Forty-four percent of patients presented two or more concomitant NSIs. Aetiological agents commonly isolated were: Propionibacterium acnes (36 %), Staphylococcus aureus (23 %), Staphylococcus epidermidis (21 %) and Streptococcus spp. (13 %). The median duration of the SAT was 15 days (range, 3-42). The SAT was interrupted in five cases due to adverse events. The remainder of the patients were cured at the end of the SAT. A total of 1,163 days of hospitalisation were saved. An overall cost reduction of €516,188 was attributed to the SAT. Eight patients with device infections did not require removal of the device, with an additional cost reduction of €190,595. The mean cost saving per patient was €9,179.

SAT with linezolid was safe and effective for the treatment of NSI. SAT reduces hospitalisation times, which means significant savings of health and economic resources [3].

Seventeen patients were included in the study. The main comorbidities among these patients included one or more of the following: subarachnoidal or intraventricular hemorrhage (n=8), solid neurological cancer (n=7), corticosteroids(n=9), and hydrocephalus (n=6). Eight patients underwent a craniotomy and fourteen patients had external ventricular drainage (EVD) as a predisposing factor for infection. Meningitis was the most common infection (11; 64.7%), followed by ventriculitis (4; 23.5%) and brain abscesses (2;11.8%). The main causative organisms were coagulase-negative Staphylococcus spp. (13; 76.5%). Linezolid was used as the initial therapy in 8 episodes, after therapy failure in 6, and for other reasons in 3. The oral route was used in 9 (52.9%) episodes; linezolid was initiated orally in 2 cases. The mean duration of treatment was 26.5 days (range 15-58). No adverse events were reported. Sixteen (94.1%) patients were considered cured. There was one recurrence. The mean length of hospital stay was 45.6 (range 15-112) days and the mean duration of follow-up was 7.2 (range 0.4-32) months. No related deaths occurred during active episodes.

Linezolid was mainly indicated in post-neurosurgical EVD-associated infections due to coagulase-negative Staphylococcus spp. It was used as initial therapy in most cases. A high rate of clinical cure was observed and no related adverse events were reported. More than half of the patients benefited from the advantages of the oral route of administration [4].

In order to study the penetration of this antimicrobial into the cerebrospinal fluid (CSF) of such patients, the disposition of linezolid in serum and CSF was studied in 14 neurosurgical patients given linezolid at 600 mg twice daily (1-h intravenous infusion) for the treatment of CNS infections caused by gram-positive pathogens or for prophylactic chemotherapy. Serum and CSF linezolid steady-state concentrations were analyzed by high-pressure liquid chromatography, and the concentration-time profiles obtained were analyzed to estimate pharmacokinetic parameters. The mean +/- standard deviation (SD) linezolid maximum and minimum measured concentrations were 18.6 +/- 9.6

microg/ml and 5.6 +/- 5.0 microg/ml, respectively, in serum and 10.8 +/- 5.7 microg/ml and 6.1 +/- 4.2 microg/ml, respectively, in CSF. The mean +/- SD areas under the concentration-time curves (AUCs) were 128.7 +/- 83.9 microg x h/ml for serum and 101.6 +/- 59.6 microg x h/ml for CSF, with a mean penetration ratio for the AUC for CSF to the AUC for serum of 0.66. The mean elimination half-life of linezolid in CSF was longer than that in serum (19.1 +/- 19.0 h and 6.5 +/- 3.6 h, respectively). The serum and CSF linezolid concentrations exceeded the pharmacodynamic breakpoint of 4 microg/ml for susceptible target pathogens for the entire dosing interval in the majority of patients. These findings suggest that linezolid may achieve adequate concentrations in the CSF of patients requiring antibiotics for the management or prophylaxis of CNS infections caused by gram-positive pathogens [5].

References

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