Journal of Microbiology, Immunology and Infection (2014) 47, 204–210

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.e-jmii.com

ORIGINAL ARTICLE

Intraventricular antimicrobial therapy in postneurosurgical Gram-negative bacillary meningitis or ventriculitis: A hospital-based retrospective study

Jui-Hsing Wang [a], Po-Chang Lin [a], Chia-Hui Chou [a], Cheng-Mao Ho [a], Kuo-Hsi Lin [a], Chia-Ta Tsai [a], Jen-Hsien Wang [a,b], Chih-Yu Chi [a,b,*], Mao-Wang Ho [a,b,*]

[a] *Division of Infectious Diseases, Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan*
[b] *Department of Medicine, China Medical University, Taichung, Taiwan*

Received 30 April 2012; received in revised form 20 August 2012; accepted 28 August 2012
Available online 30 November 2012

KEYWORDS
Gram-negative bacilli;
Intraventricular;
Meningitis;
Ventriculitis;
Postneurosurgical

Background: Postneurosurgical Gram-negative bacillary meningitis (GNBM) or ventriculitis is a serious issue. Intraventricular (IVT) therapy has been applied; however, its effectiveness remains controversial, and the adverse drug effects are considerable.
Methods: The demographic data, treatment strategies, and clinical outcomes of patients with postneurosurgical GNBM or ventriculitis were recorded.
Results: From 2003 to 2011, data on 127 episodes of infection in 109 patients were collected, and 15 episodes in 14 patients were treated using a sequential combination of intravenous antibiotics and IVT therapy; others received intravenous antibiotics alone. The average age of patients who received a sequential combination with IVT therapy was 48.9 years, and 71.4% of the patients were men. The regimens used for IVT therapies included gentamicin ($n = 4$), amikacin ($n = 7$), and colistin ($n = 4$). After meningitis had been diagnosed, the average period that elapsed before initiation of IVT therapy was 25.4 days, and the average duration of IVT therapy was 13.3 days. The most frequently isolated pathogen from cerebrospinal fluid (CSF) was *Acinetobacter baumannii*, followed by *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Serratia marcescens*. The cure rate was 73.3%.

* Corresponding authors. Division of Infectious Diseases, Department of Internal Medicine, China Medical University Hospital, 2 Yu-Der Road, Taichung 40447, Taiwan.
E-mail addresses: D12129@mail.cmuh.org.tw (C.-Y. Chi), u702026@gmail.com (M.-W. Ho).

http://dx.doi.org/10.1016/j.jmii.2012.08.028

Of note, the mean period to sterilize the CSF after appropriate IVT antibiotic treatment was 6.6 days. There were no incidents of seizure or chemical ventriculitis during this IVT therapy. *Conclusion:* The findings of this study suggest that IVT antibiotic therapy is a useful option in the treatment of postneurosurgical GNBM or ventriculitis, especially for those with a treatment-refractory state.

Introduction

Nosocomial postneurosurgical meningitis is a serious medical issue, particularly in patients with Gram-negative bacillary infection.[1] There is an increasing incidence of postneurosurgical meningitis; this has risen from 12% to 27% of all cases of bacterial meningitis,[2] and the overall mortality for Gram-negative bacillary meningitis (GNBM) has been reported to be high.[1,3] Furthermore, the treatment strategies for GNBM or ventriculitis have become more complex. Multiple bacteria with reduced sensitivity to antibiotics have been emerging[4,5]; moreover, there are limitations to antimicrobial concentrations at the sites of infection.[6] Thus, a combination of intravenous (IV) and intraventricular (IVT) antibiotic administration may be one choice to ensure sterilization of the cerebrospinal fluid (CSF) while minimizing adverse drug effects.[7]

The use of IVT antimicrobial agents remains a challenging intervention due to limited evidence for the efficacy and safety of this treatment. McCracken et al demonstrated a threefold increased relative risk for mortality.[8] Conversely, some studies have reported an overall cure rate of 80% with IVT polymyxins[9] and 100% for those with IVT gentamicin.[10,11] In terms of the controversial option of employing IVT therapy for GNBM, there have been few well-designed studies and clinical trials to verify IVT therapy among adult populations.

In this study, we report our experience with IVT antibiotic therapy in 15 episodes of postneurosurgical GNBM or ventriculitis, and we also made a comparison of the clinical and laboratory data and therapeutic results between patients receiving IVT therapy and those with IV antibiotic treatment alone.

Methods

Patients and setting

From January 2003 to October 2011, we enrolled patients who experienced complications including GNBM and ventriculitis following neurosurgical procedures at the China Medical University Hospital, a 2000-bed medical center in Taiwan. Patients were included when all of the following criteria were met: (1) isolation of Gram-negative bacilli from the CSF, (2) a CSF neutrophil count of >10 cells/μL, (3) clinical features of bacterial central nervous system (CNS) infection (at least one episode of temperature $>37.5^{\circ}$C, headache, or neck stiffness), and (4) neurosurgery within the preceding 2 months.[10] A second episode of meningitis was considered a recurrence if it was due to a organism different from the one causing the initial episode or if it was due to the same organism occurring more than 3 weeks after completion of treatment for the initial episode.[12]

All patients were treated empirically with IV antibiotics, and antibiotic treatment was later adjusted according to the culture report. The CSF analysis and culture were repeated once or twice every week until the CSF culture was negative or until the patient was discharged. Revision or removal of intracranial devices such as external ventricular drainage, a ventriculoperitoneal shunt, or an Ommaya reservoir was decided by the doctor in charge.[7] For patients with persistent bacterial growth in CSF cultures or clinical failure, sequential combination with IVT therapy was undertaken according to procedures outlined in previous studies[7,10,11,15,19] and the practice guidelines of the Infectious Diseases Society of America.[13] All patients were followed up for more than 3 months after completion of antimicrobial treatment. Medical charts were thoroughly reviewed, and any event of IVT therapy-related adverse drug effects was recorded.

Definitions

Mixed infection was defined as a patient having two or more bacterial organisms isolated from the initial CSF cultures.[14] Co-infection was defined as a patient having GNBM or ventriculitis with a simultaneous additional infection.

Efficacy was evaluated by both clinical and bacteriologic responses to therapy. In the treatment period, clinical failure was considered to be presentation with deteriorating clinical and laboratory signs of meningitis during appropriate antimicrobial therapy. For the clinical outcome, treatment failure was defined as death due to meningitis, or relapse.[10] Death was considered to be not due to meningitis if all of the following criteria were met: (1) resolving inflammatory parameters; (2) resolution of the clinical signs of meningitis; (3) a serious illness other than meningitis determined to be a more probable cause according to the treating physician; (4) completion of the antibiotic treatment before death; and (5) two negative CSF culture results (if performed) before death as modified by the criteria proposed by Durand et al.[12] Relapse was defined as isolation of the same organism from the CSF or from a CNS lesion within 3 weeks of completing therapy for the initial episode.[12] The criteria for cure proposed by Briggs et al.[3] were modified as follows: resolution of clinical and laboratory signs of meningitis; negative CSF culture results (if performed); and no relapse after withdrawal of