

Neurosurgical Gram-Negative Bacillary Ventriculitis and Meningitis: A Retrospective Study Evaluating the Efficacy of Intraventricular Gentamicin Therapy in 31 Consecutive Cases

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Background. Gram-negative bacillary (GNB) ventriculitis and meningitis are rare but serious complications after neurosurgery. Prospective studies on antibiotic treatment for these infections are lacking, and retrospective reports are sparse. At our hospital in Uppsala, Sweden, meropenem has been recommended as empirical therapy since 1996, with the addition of intraventricular gentamicin in cases that do not respond satisfactorily to treatment. In this study, we retrospectively compare the efficacy of combination treatment with intraventricular gentamicin to that of systemic antibiotics alone. In addition, we report our experience of meropenem for the treatment of GNB ventriculomeningitis.

Methods. Adult consecutive patients with gram-negative bacteria isolated from cerebrospinal fluid during a 10-year period and with postneurosurgical GNB ventriculitis or meningitis were included retrospectively. Data were abstracted from the medical records.

Results. Thirty-one patients with neurosurgical GNB ventriculitis or meningitis and follow-up for 3 months were identified. The main intravenous therapies were meropenem ($n = 24$), cefotaxime ($n = 3$), ceftazidime ($n = 2$), imipenem ($n = 1$), and trimethoprim-sulfamethoxazole ($n = 1$). Thirteen patients were given combination treatment with appropriate intraventricular gentamicin. These patients had a higher cure rate and a lower relapse rate than did those treated with intravenous antibiotics alone ($P = .03$). Relapse occurred in 0 of 13 patients treated intraventricularly and in 6 of 18 patients treated with systemic antibiotics alone. The mortality rate was 19%; 3 patients in each group died, but in no case was death considered to be attributable to meningitis.

Conclusions. Our results support combination treatment with intraventricular gentamicin for postneurosurgical GNB ventriculomeningitis. Meropenem seems to be an effective and safe alternative for the systemic antibiotic treatment of these neurointensive care infections.

Bacterial ventriculitis or meningitis is a relatively rare but serious complication after neurosurgery. Clinically, the diagnosis is often difficult to establish because of its sometimes insidious onset and atypical symptoms [1].

In addition, the underlying trauma or neurosurgery may result in a meningeal inflammatory response that will consequently affect cerebrospinal fluid (CSF) parameters [2]. Postneurosurgical ventriculomeningitis is typically caused by *Staphylococcus aureus* or coagulase-negative staphylococci [3, 4]. Gram-negative etiology is associated with severe underlying disease and a worse prognosis [4]. The overall mortality rate among patients with neurosurgical gram-negative bacillary (GNB) ventriculitis or meningitis has been reported to be 8%–70%, with the highest rates being reported before the introduction of third-generation cephalosporins [1, 4–8]. In recent studies, mortality attributable to meningitis has been reported to be 3%–12% [5, 9, 10].

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Since the early 1980s, third-generation cephalosporins have been used for the treatment of GNB meningitis [7, 11]. Following increased rates of resistance to these antibiotics in gram-negative bacteria [12, 13], carbapenems have been suggested as empirical treatment [5, 9]. In previous clinical reports, combination therapy with aminoglycosides has been used in treating all or some of the patients [1, 5, 6, 8–10, 14]. In these studies, aminoglycosides have been administered intravenously, intraventricularly, intralumbarily, or in combinations of these administration routes.

Since 1996, written institutional guidelines at our hospital have recommended cefotaxime plus vancomycin for the empirical treatment of neurosurgical meningitis or ventriculitis. If gram-negative bacteria were isolated or suspected, it was recommended that cefotaxime be replaced by meropenem. In cases in which the patient did not respond satisfactorily to intravenous antibiotics alone, the addition of gentamicin was proposed. Because penetration of intravenous aminoglycosides to CSF has been reported to be limited [15, 16], the intraventricular route was recommended.

To date, reports on the clinical efficacy of intraventricularly administered gentamicin for the treatment of neurosurgical ventriculomeningitis in adults are limited [16, 17], and no comparative study has been published. Therefore, the principal aim of the present study was to retrospectively compare the efficacy of intraventricularly administered gentamicin in combination with intravenous antibiotics with the efficacy of intravenous antibiotics alone. Because data on treatment with meropenem are relatively sparse, a secondary aim was to report our experience of meropenem for the treatment of GNB ventriculitis and meningitis in neuro-intensive care.

METHODS

Study Population and Criteria for Neurosurgical Gram-Negative Ventriculitis and Meningitis

Consecutive patients who were at least 15 years of age; who had been treated at the Department of Neurosurgery, Uppsala University Hospital (Uppsala, Sweden); and who had gram-negative bacilli isolated from CSF between 1 January 1998 and 31 December 2007 were identified retrospectively.

Detailed data about patient characteristics, CSF findings, antibiotic treatment, and outcome were abstracted from each patient's medical record. Day 0 was defined as the day on which the first CSF sample that subsequently grew gram-negative bacilli was collected. In patients with an external ventricular drain (EVD) in place at the onset of symptoms, ventricular CSF was used for diagnosis. Routine removal or change of external drains was not part of the institutional recommendations.

A case of definite postneurosurgical GNB ventriculitis or meningitis was defined on the basis of all of the following criteria: (1) isolation of gram-negative bacilli from the CSF, (2) CSF neutrophil count of $>10 \times 10^6$ cells/L, (3) clinical features of bacterial CNS infection (≥ 1 of temperature $>37.5^\circ\text{C}$, headache, or neck stiffness), (4) a diagnosis of ventriculitis or meningitis by the infectious diseases consultant, and (5) neurosurgery within the preceding 2 months. Patients lacking either clinical signs or an increase in CSF neutrophil count were defined as having a possible GNB CSF infection. These definitions were based on those used by Parodi et al [9] and Briggs et al [5]. Positive CSF cultures from patients who presented with no other clinical or laboratory signs of meningitis were regarded as attributable to contamination. A patient with an EVD at the onset of CNS infection was considered to have an EVD-related ventriculitis.

Criteria for Outcome and Antibiotic Treatment

The criteria for cure proposed by Briggs et al [5] were slightly modified, with cure defined as resolution of clinical and laboratory signs of meningitis, negative CSF culture results (if performed), and no relapse within 3 months after withdrawal of antibiotics. Treatment failure was defined as death attributable to meningitis or relapse within 3 months. Death was considered not to be attributable to meningitis if all of the following criteria were met: (1) ≥ 2 negative CSF culture results before death (if performed), (2) resolving inflammatory parameters, (3) resolution of clinical signs of meningitis, and (4) a cause other than meningitis was found to be more probable according to the treating physician. In cases where follow-up CSF cultures were not obtained, death was assessed as not attributable to meningitis if all of the following could be shown: (1) resolving inflammatory parameters, (2) resolution of clinical signs of meningitis, (3) some other preexisting serious illness than meningitis was determined to be a more probable cause according to the treating physician, and (4) completion of antibiotic treatment before death as modified by the criteria proposed by Durand et al [18]. Relapse was defined as isolation of the same organism from CSF or from a CNS lesion after completion of antibiotic treatment or the development of presumed meningitis as characterized by all of the following: (1) CSF neutrophil count $>250 \times 10^6$ cells/L, (2) $>50\%$ neutrophils, and (3) CSF/blood glucose ratio <0.4 [19].

Intravenous antibiotic treatment was classified as appropriate if the bacteria isolated were susceptible in vitro and if the antibiotics chosen were prescribed in recommended dosages [3]. Intraventricular treatment with gentamicin was classified as appropriate if the infecting organism was susceptible to aminoglycosides in vitro.

CSF Cultures

Conventional microbiological methods were used to culture and identify gram-negative bacilli. Antibiotic susceptibility testing was performed using the disc diffusion technique on Iso-Sensitest agar (Oxoid) and interpreted using breakpoints defined by the Swedish Reference Group for Antibiotics.

Statistical Analysis

For statistical evaluations, Fisher's exact test (2-tailed) and the Mann-Whitney *U* test were used.

RESULTS

During the 10-year study period, 44 adult patients had gram-negative bacilli isolated from CSF cultures. Five CSF samples were contaminated, and 2 patients with gram-negative ventriculoperitoneal shunt infections had not undergone recent neurosurgery. Four patients met the criteria for possible neurosurgical GNB ventriculomeningitis. All of them presented with fever but with no other clinical signs of meningitis, and there was no increase in CSF neutrophil count. According to the medical records, the infectious diseases physician consultant suspected ongoing infections other than meningitis. Because of the uncertainty of the diagnosis, these patients were excluded. Of the 33 patients who received a diagnosis of definite neurosurgical GNB CSF infection, 2 were excluded because of insufficient follow-up, leaving 31 patients in the final analysis.

Nineteen patients were given standard empirical antibiotic treatment with intravenous cefotaxime and vancomycin. In 9 cases, the result of Gram staining or isolation of a gram-negative organism from CSF was available, and the patients initiated meropenem at a dosage of 2 g every 8 h. Three patients were prescribed meropenem as empirical treatment without prior isolation of gram-negative bacteria. Regimen changes were made in 18 of the patients who initiated cefotaxime after the results of Gram staining or culture: 17 patients had therapy switched to meropenem, and 1 patient had therapy switched to trimethoprim-sulfamethoxazole. In 2 patients who initiated meropenem therapy, the antibiotic regimen was changed to ceftazidime after isolation of carbapenem-resistant *Xanthomonas maltophilia*. Subsequent changes of therapy from meropenem to cefotaxime were made in 2 cases because of rash and elevated liver enzymes, and therapy was changed to imipenem in 1 case because of the lower minimum inhibitory concentration of the *Pseudomonas* strain isolated. The main intravenous therapies were meropenem ($n = 24$), cefotaxime ($n = 3$), ceftazidime ($n = 2$), imipenem ($n = 1$), and trimethoprim-sulfamethoxazole ($n = 1$). No drug-related seizures were reported. Three patients also had gram-positive bacteria isolated from CSF, including *Staphylococcus epidermidis* ($n = 1$),

Enterococcus faecium ($n = 1$), and *Bacillus cereus* ($n = 1$), and they received combination treatment with vancomycin intravenously.

Fifteen patients were additionally treated with intraventricular gentamicin at a dosage of 4–8 mg once daily. In 2 patients, the gram-negative bacilli isolated were resistant to aminoglycosides in vitro. In the additional analysis, these 2 patients are combined with the 16 patients who were treated with intravenous antibiotics alone (group A). Thirteen patients received appropriate intraventricular gentamicin (group B). The median duration of intraventricular treatment was 8 days (range, 1–23 days). One patient received intraventricular gentamicin from the start of antibiotic treatment, and 5 patients received treatment after 2–3 days, following isolation of gram-negative bacteria. In the remaining seven patients, gentamicin was added after a median interval of 10 days (range, 4–19 days) because of persistent unsterile CSF cultures ($n = 4$), persistent CSF parameters consistent with meningitis ($n = 2$), or clinical failure ($n = 1$).

Neurosurgery performed before the onset of GNB ventriculomeningitis is listed in Table 1, whereas age and underlying diagnoses are given in Table 2. Traumatic head injuries were recorded in 6 patients, all of whom had undergone neurosurgical procedures within 24 h after the injury. A median of 1 neurosurgical procedure (range, 1–3 procedures) was performed before the episode of meningitis. Postoperative or posttraumatic CSF leaks before the onset of GNB ventriculomeningitis were reported in 16 cases (52%). The median interval between the last neurosurgery and first positive CSF culture was 10 days (range, 1–40 days). There were no significant differences in age or underlying diagnoses between groups A and B. Nine patients (50%) in group A and 10 patients (77%) in group B had an EVD at the onset of meningitis and were considered to have an EVD-related ventriculitis.

Causative bacteria are shown in Table 2. Three patients (10%) had polymicrobial gram-negative meningitis. Two patients were double-infected with *Enterobacter cloacae* and *Acinetobacter baumannii* or *Pseudomonas* species, and 1 patient was double-infected with *Klebsiella pneumoniae* and *Pseudomonas* species. Two of the patients with polymicrobial GNB meningitis were treated with appropriate intraventricular gentamicin. Nineteen patients (61%) were infected with *Enterobacter* species, 9 of whom (47%) had strains that were resistant in vitro to third-generation cephalosporins. None of the isolates was reported to produce extended-spectrum β -lactamases. Details regarding antibiotic treatment and CSF drains are shown in Table 3. In all patients, the main intravenous antibiotic treatment was appropriate.

There was a higher cure rate and a lower treatment failure rate in patients treated with appropriate intraventricular gentamicin ($P = .03$). There was no mortality attributable to

Table 1. Neurosurgical Procedures Performed on 31 Patients Before Onset of Gram-Negative Bacillary Meningitis

Neurosurgical procedure	No. (%) of patients		
	Group A: IV antibiotics alone or IV antibiotics and inappropriate ^a intraventricular gentamicin (n = 18)	Group B: IV antibiotics and appropriate ^a intraventricular gentamicin (n = 13)	Total (n = 31)
Insertion of EVD	14 (78)	10 (77)	24 (77)
Extirpation of intracranial tumor	8 (44)	2 (15)	10 (32)
Evacuation of hemorrhage ^b	2 (11)	5 (38)	7 (23)
Evacuation of expansive infarction	3 (17)	2 (15)	5 (16)
Clipping of aneurysm	1 (6)	4 (31)	5 (16)
Insertion of lumbar CSF drain	4 (22)	...	4 (13)
Postoperative CSF leak repair	1 (6)	1 (8)	2 (6)
Evacuation of postoperative hematoma	1 (6)	...	1 (3)
Decompression of the posterior fossa	1 (6)	...	1 (3)

NOTE. CSF, cerebrospinal fluid; EVD, external ventricular drain; IV, intravenous.

^a Intraventricular treatment with gentamicin was classified as appropriate if the infecting organism was susceptible to aminoglycosides in vitro.

^b Aneurysmal subarachnoid hemorrhage and intracerebral hematoma (n = 4), spontaneous intracerebral hematoma (n = 1), traumatic subarachnoid hemorrhage (n = 1), and traumatic epidural hematoma (n = 1).

meningitis in either of the groups. Relapse occurred in 6 patients in group A who were given appropriate intravenous treatment for a median of 17 days (range, 9–23 days). Four of these 6 patients presented with recurrent clinical features of meningitis and had a positive CSF sample obtained at a median interval of 3 days after completion of antibiotic therapy (range, 2–13 days). One patient had a more insidious relapse with development of a brain abscess diagnosed after 8 weeks. In all of these cases, the same bacterial species was isolated from CSF at the time of relapse as was isolated at the first episode, and the isolates had similar susceptibility patterns. Infecting organisms were *E. cloacae* (n = 3), *Xanthomonas maltophilia* (n = 1) and *Pseudomonas aeruginosa* (n = 1). One patient with *P. aeruginosa* meningitis experienced clinical relapse with meningitis after 56 days. CSF analyses displayed marked leukocytosis and glucose consumption consistent with bacterial meningitis, and

Table 2. Age, Underlying Diagnoses, and Gram-Negative Bacteria Recovered From Cerebrospinal Fluid

Variable	Group A: IV antibiotics alone or IV antibiotics and inappropriate intraventricular gentamicin (n = 18)	Group B: IV antibiotics and appropriate intraventricular gentamicin (n = 13)	Total (n = 31)
Age, median years (range)	54 (35–75)	49 (16–69)	54 (16–75)
Underlying diagnoses			
Spontaneous hemorrhage	5 (28)	7 (54)	12 (39)
Intracranial tumor	8 (44)	2 (15)	10 (32)
Traumatic brain injury	3 (17)	3 (23)	6 (19)
Brain infarction	2 (11)	1 (8)	3 (10)
Bacteria isolated (patients with polymicrobial gram-negative meningitis not included)			
<i>Enterobacter</i> species	8 (44)	9 (69)	17 (55)
<i>Pseudomonas</i> species	3 (17)	2 (15)	5 (16)
<i>Klebsiella pneumoniae</i>	3 (17)	...	3 (10)
<i>Xanthomonas maltophilia</i>	2 (11)	...	2 (6)
<i>Escherichia coli</i>	1 (6)	...	1 (3)
Bacteria isolated (patients with polymicrobial gram-negative meningitis)			
<i>Enterobacter</i> species	...	2	2
<i>Pseudomonas</i> species	1	1	2
<i>K. pneumoniae</i>	1	...	1
<i>Acinetobacter baumannii</i>	...	1	1

NOTE. Data are numbers (%) of patients, unless otherwise indicated. IV, intravenous.

the patient improved with meropenem treatment. However, the patient's CSF cultures were negative. All patients who experienced relapse eventually recovered with prolonged intravenous antibiotic treatment (n = 4) or combination treatment with intraventricular gentamicin (n = 2). Three of the relapsing patients had an EVD-related ventriculitis. There were no significant differences regarding neurosurgical procedures, underlying diagnoses, antibiotics, or drains in patients who experienced relapse in relation to patients who did not.

Table 3. Antibiotic Treatment and Cerebrospinal Fluid (CSF) Drainage in Relation to Treatment Groups and Outcome

Parameter	Group A: IV antibiotics alone or IV antibiotics and inappropriate intraventricular gentamicin			Group B: IV antibiotics and appropriate intraventricular gentamicin (all cured) (<i>n</i> = 13)	Total of group A and B (<i>n</i> = 31)	<i>P</i>
	Total (<i>n</i> = 18)	Cure (<i>n</i> = 12)	Treatment failure (<i>n</i> = 6)			
IV antibiotic treatment						
Appropriate IV treatment from start of therapy	11 (61)	8	3	7 (54)	18 (58)	>.30 ^a
Initiation of appropriate IV treatment after first positive CSF culture, median days (range)	0 (0–7)	0 (0–7)	0.5 (0–3)	0 (0–2)	0 (0–7)	>.30 ^b
Duration of appropriate IV treatment, median days (range)	20.5 (9–35)	22 (13–35)	17 (9–23)	26 (14–64)	22 (9–64)	.13 ^b
Meropenem treatment	13 (72)	9	4	11 (85)	24 (77)	>.30 ^a
Cefotaxime treatment	2 (11)	2	...	1 (8)	3 (10)	>.30 ^a
Ceftazidime treatment	2 (11)	1	1	...	2 (6)	>.30 ^a
Imipenem treatment	1 (8)	1 (3)	>.30 ^a
Trimethoprim-sulfamethoxazole treatment	1 (6)	...	1	...	1 (3)	>.30 ^a
CSF drains						
EVD or lumbar drain at the onset of ventriculomeningitis	13 (72)	9	4	10 (77)	23 (74)	1.0 ^a
EVD at the onset of ventriculomeningitis	9 (50)	6	3	10 (77)	19 (61)	.16 ^a
Lumbar drain at the onset of ventriculomeningitis	4 (22)	3	1	...	4 (13)	.12 ^a
Persistent EVD or lumbar drain after first positive CSF culture	10 (56)	6	4	13 (100)	23 (74)	.01 ^a
Removal of last EVD or lumbar drain after first positive CSF culture ^c , median days (range)	11.5 (3–39)	13 (3–39)	9 (3–15)	15 (5–56)	12 (3–56)	.28 ^b

NOTE. Data are numbers (%) of patients, unless otherwise indicated. CSF, cerebrospinal fluid; EVD, external ventricular drain; IV, intravenous.

^a Fisher's exact test (2-tailed) was used for the comparison between groups A and B.

^b The Mann-Whitney *U* test was used for the comparison between groups A and B.

^c EVDs or lumbar drains were changed in 3 patients in group A (at days 3, 8, and 18) and 4 patients in group B (at days 2, 5, 8, and repeatedly in one patient at days 2, 19, 30, and 54).

Details about antibiotic treatment and CSF drains in patients with relapse are shown in Table 3.

Three patients in each group died at a median interval of 49.5 days after onset of GNB ventriculomeningitis (range, 22–90 days). None of the patients demonstrated persisting clinical or laboratory signs of bacterial meningitis. Death was referred to causes other than meningitis: postoperative or posttraumatic brain edema (*n* = 4), cardiac arrhythmia (*n* = 1), and candidemia (*n* = 1). In 4 cases, several consecutive CSF cultures obtained after onset of treatment were sterile, and inflammatory parameters had resolved. The remaining 2 patients received no antibiotic treatment and displayed no clinical or laboratory signs of ventriculomeningitis or other bacterial infection during the last month preceding the time of death.

DISCUSSION

Because of the low incidence of the disease, there are no prospective randomized clinical trials evaluating the efficacy of different antibiotic regimens for GNB ventriculomeningitis in adults. Because of the lack of prospective trials, this study is an attempt to retrospectively study the effect of intraventricular administration of gentamicin in addition to systemic antibiotics in a comparative way that, to our knowledge, has not been done before. The retrospective nature of the study, the low number of patients involved, and the absence of random allocation constitute limitations of this study. However, a special strength of the study is the existence of written institutional guidelines that were not changed during the study period and the fairly

good adherence to them. In addition, criteria for the diagnosis of GNB ventriculitis and meningitis, appropriateness of treatment, possible confounding factors, and outcome were prospectively defined.

In our study, the cure rate was significantly higher among patients with postneurosurgical GNB ventriculomeningitis treated with intraventricular gentamicin (group B) than it was among patients given intravenous antibiotics alone (group A). No relapse occurred in group B, whereas 6 of 18 patients in group A experienced relapse. All patients had isolates that were susceptible to the systemic antibiotic given, and there were no significant differences between the groups with respect to age, underlying diagnoses, frequency of drains prior to the onset of meningitis, or causative bacteria. There was a nonsignificant trend toward shorter duration of intravenous antibiotic treatment in group A. However, the median treatment duration in group A was 3 weeks, which is in agreement with general recommendations [20], and there was little difference in treatment duration between patients who experienced relapse and those who did not. Furthermore, if treatment duration in group B is calculated from the start of intraventricular treatment in the 4 patients with persistently positive culture results, there was no difference in treatment duration. Thus, the difference in duration of intravenous antibiotic treatment in group B is an unlikely explanation for the difference in relapse rate.

There was a somewhat higher frequency of EVD-related ventriculitis in group B than in group A. It may be argued that EVD-related infections may not have a prognosis similar to that of other types of postoperative or posttraumatic meningitis and, thus, that the differences in EVD-related infections might have affected the outcome. However, the difference is small, and an additional number of patients in group A might, in fact, have had an EVD-related infection, because their EVD was removed just a few days before onset of symptoms, making this difference even smaller. In all patients with EVD-related infections, with the exception of possibly 1 or 2 patients with tumors, there was communication between the ventricles and the subarachnoid space, and in these patients, bacteria were probably transported by the CSF flow to the subarachnoid space, with the gradual development of meningitis as a consequence. Furthermore, in group A, the patients who experienced relapse had the same proportion of EVD-related infections as did those who were cured, indicating that the difference in EVD-related infections did not affect the outcome.

In contrast, there were more persistent drains in group B, a circumstance that might have slowed down the sterilization rate. Moreover, 7 patients in group B were included as having experienced treatment failure, suggesting that group B might represent a subpopulation of patients with a worse prognosis. Thus, we have not found confounding factors that might explain the results, indicating that there may be a beneficial effect

associated with the addition of gentamicin in neurointensive care patients with GNB ventriculomeningitis, at least in those patients who do not rapidly respond to systemic antibiotics. The results of the present study are in contrast with the findings of McCracken et al [21], which demonstrated a worse outcome and increased mortality in children with GNB meningitis treated with intraventricular gentamicin in addition to systemic antibiotics. However, the results from that study are not transferable to adult neurointensive care patients with an EVD in place. In the study by McCracken et al [21], published 3 decades ago, most children were ≤ 30 days old, and gentamicin was administered by repeated intraventricular punctures.

The favorable outcome after the addition of intraventricular gentamicin might be explained by its pharmacodynamic properties. When measured, gentamicin CSF concentrations were in the magnitude of those previously reported [16, 17], with peak concentrations of 20–50 mg/L and trough values in the range of 5–20 mg/L after administration of intraventricular gentamicin in doses of 4–8 mg once daily (data not shown). Aminoglycosides have a rapidly bactericidal effect on many gram-negative bacteria, and their rate of bacterial killing escalates as the antibiotic concentration increases, regardless of the inoculum [16, 22, 23]. Against some gram-negative strains, even synergistic effects with β -lactam antibiotics have been demonstrated [24, 25]. Consequently, high intraventricular concentrations might have resulted in a faster sterilization rate in patients treated with gentamicin.

Meropenem has been shown to be an effective treatment of community-acquired meningitis in children [26]. Although it has been proposed as an alternative for the treatment of neurosurgical meningitis, data are limited [5, 9], with the exception of pharmacokinetic data demonstrating that meropenem reaches bactericidal concentrations in CSF [27]. In the present study, 24 patients were treated with meropenem. To our knowledge, this is the largest study to report the results of meropenem for the treatment of neurosurgical GNB ventriculomeningitis. There was no mortality attributable to meningitis, which is low when compared with the results reported by others [5, 9, 10]. Despite a treatment duration that was in accordance with general recommendations, the overall rate of relapse in our study was 19%, and the rate of relapse among those treated with meropenem was 17%. This is somewhat higher than the rate of 12% reported in a recent study on GNB ventriculomeningitis, in which the majority of patients were treated with third-generation cephalosporins, often in combination with aminoglycosides administered intravenously [10]. In the present study, there was no relapse in patients given combination treatment with meropenem and intraventricular gentamicin.

In summary, and taking into consideration the limitations of the retrospective nature of the study and the low number of patients, our results support the addition of intraventricular

gentamicin to systemic antibiotics in the treatment of post-neurosurgical GNB ventriculomeningitis. Furthermore, meropenem seems to be an effective and safe alternative for the systemic antibiotic treatment of these severe neurointensive care infections.

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