

Summary

Penetration of β -lactam antibiotics into cerebrospinal fluid and its relationship to inflammatory markers during invasive bacterial infection

Aim: The penetration of β -lactam antibiotics (ceftriaxone, crystallic penicillin G – potassium salt and cefotaxime) into the cerebrospinal fluid (CSF) was established and the correlation between the penetration and laboratory markers of inflammation was evaluated.

Materials and methods: Levels of β -lactam antibiotics in serum and CSF were determined in 24 patients (76 samples). In all patients ($n = 24$) the CSF/serum ratio for antibiotics was calculated and it was correlated with laboratory markers of inflammation (C-reactive protein, fibrinogen, and CSF numbers of neutrophils). Besides, CSF was examined by a modified bactericidal test in patients ($n = 13$) with positive bacterial culture. In 14 patients (28 samples) levels of serum antibiotic concentration, both before and after its administration, were measured.

Results: Serum levels of ceftriaxone before and after administration ($31.2 \text{ mg/l} \pm \text{SD } 12.29$ and $300.0 \text{ mg/l} \pm \text{SD } 125.9$, respectively) differed with a statistical significance ($p = 0.000156$). Further, a significant difference between value of inflammatory markers and value of CSF/serum ratio ($K_{1/s}$) of ceftriaxone was observed. Patients with ratio values above 0.1 had higher values of CRP ($p = 0.00192$), fibrinogen ($p = 0.0178$) as well as CSF neutrophils ($p = 0.0112$), in comparison with patients with ratio lower than 0.1. However, no inflammatory markers nor their combination could reliably predict the extent of ceftriaxone penetration into CSF. Serum levels of penicillin before and after administration ($14,3 \text{ mg/l} \pm \text{SD } 15,8$ and $110,38 \text{ mg/l} \pm \text{SD } 63,9$) differed with statistical significance as well ($p = 0,216$). CRP values and CSF neutrophil numbers correlated with $K_{1/s}$, tracking the higher penetration. However, no inflammatory markers nor their combination could reliably predict the extent of penicillin penetration into CSF. Cefotaxime was not assessed because of insufficient data.

Conclusion: The higher antibiotic penetration correlated with an intensity of systematic inflammatory response (with one exception for fibrinogen in penicillin). However, no inflammatory markers could reliably predict the extent of antibiotic penetration through the blood-brain barrier. Anyway, the passage of ceftriaxone and penicillin into CSF remains, with a 24-hour dosage mode for ceftriaxone and a 4-hour dosage scheme for penicillin, an efficient therapy.

Keywords: ceftriaxone, penicillin, bacterial meningitis, blood-brain barrier, pharmacokinetics, inflammatory markers