Efficacy of pre-operative cephalosporin prophylaxis in controlling pathogenic oral bacteria growth in comatose patients

Saliva contains many bacteria, and bad oral hygiene and periodontal diseases lead to the proliferation of pathogenic bacteria that can cause aspiration pneumonia (Finegold, 1991; Scannapieco, 1999; Japanese Respiratory Society, 2004). The aetiological role of pathogenic flora in aspiration pneumonia is of special concern for neurosurgical patients, because the likelihood of long-term post-operative endotracheal intubation and immobilization are additional risk factors for infectious complications involving the lungs (Erman *et al.*, 2005; Korinek *et al.*, 2005).

Administration of cephalosporins to patients as prophylaxis for high-risk surgical procedures at the time of induction of general anaesthesia is routinely carried out in many institutes. In this study the efficacy of pre-operative cefazolin, cefuroxime and cefamandole in controlling the growth of pathogenic aerobic oral flora in comatose patients undergoing neurosurgical procedures was investigated.

At the time of induction of general anaesthesia for neurosurgical procedure, 10, 11 and 9 comatose patients (Glasgow coma scale <7) received 1 g cefazolin, 1.5 g cefuroxime or 2 g cefamandole intravenously, respectively. Clinical data are detailed in Table 1. At the completion of the surgical procedure, saliva samples were obtained from above the cuff of the endotracheal tube and residual serum samples from routine blood testing were simultaneously collected by procedures

that were approved by the Ethical Committee of the University of Debrecen. The actual antibiotic concentrations in the serum and saliva samples were determined by capillary electrophoresis (CE) as described previously (Andrasi *et al.*, 2007). The bacteria from the saliva were isolated, and the MICs of the cephalosporins against the specific bacteria were evaluated by the standard broth microdilution method according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI, 2005).

Twenty-one bacteria were isolated from the saliva of patients who received 1 g cefazolin prior to surgery. The MIC values of only 3 bacteria (*Acinetobacter baumannii*, *Citrobacter freundii* and *Pseudomonas aeruginosa*) were higher than the mean drug concentrations in the serum ($68.4 \pm 14.4 \text{ mg l}^{-1}$), but the MIC values of 16 bacteria exceeded the level of cefazolin in the saliva ($<0.5 \text{ mg l}^{-1}$). The concentration of antibiotic is given as the mean $\pm$ SD.

Twenty bacterial species were isolated from the saliva of patients who received 1.5 g cefuroxime prophylactically. Two bacteria (*C. freundii* and *P. aeruginosa*) had higher MIC values than the mean antibiotic level in the serum ($50.3 \pm 18.2 \text{ mg l}^{-1}$). The concentration of cefuroxime in the saliva ($<0.5 \text{ mg l}^{-1}$) remained less than the MIC values of 15 bacteria.

Twenty-four bacteria were isolated from the saliva of patients who received 2 g cefamandole. Four bacteria (*A. baumannii*,

C. freundii, *Enterobacter cloacae* and *P. aeruginosa*) had higher MIC values than the mean drug level in the serum ($42.4 \pm 9.9 \text{ mg l}^{-1}$). The MIC values of 18 bacteria exceeded the levels of cefamandole in the saliva ($<0.5 \text{ mg l}^{-1}$).

Aspiration of oral bacteria is one of the main aetiological factors in developing pneumonia in hospitals. During lengthy surgical procedures, saliva accumulates in the pharynx above the cuff of the tube used for endotracheal anaesthesia. Such secretions are periodically suctioned out, but this procedure cannot always be executed completely. The risk for post-operative aspiration is especially high in comatose patients because of the impaired function of the lower cranial nerves, resulting in impaired pharyngeal and coughing reflexes that also increase the chance of developing pneumonia (Morgan & Mackay, 1999; Rosenstock *et al.*, 2001).

Since aspiration of pathogenic oral flora increases the incidence of pneumonia, administration of prophylactic antibiotics in high-risk patients is of enormous clinical importance (Kraus *et al.*, 2005). In this study, the efficacy of prophylactic cefazolin, cefuroxime and cefamandole in controlling the growth of oral pathogenic bacteria was evaluated by monitoring the actual concentrations of antibiotics in the serum and saliva. The detected drug levels in the serum proved to have a significant effect against bacteria isolated from the saliva, but the concentrations of every cephalosporin tested were very low in the saliva; cefazolin, cefuroxime and cefamandole did not reach the MIC values of 76.2, 75 and 75 % of the bacteria, respectively, and therefore had only a very moderate effect on the oral flora, and thus the potential prevention of aspiration pneumonia.

Direct monitoring of the effectiveness of antibiotics is not yet included in any clinical practice, although many previous analyses have called attention to very

Table 1. Clinical parameters of patients

	Cefazolin	Cefuroxime	Cefamandole
No. of cases	10	11	9
Age (years)	53.5 ± 12.3	49.2 ± 11.5	46.9 ± 11.5
Gender (female/male)	5/5	4/7	5/4
Body weight (kg)	72.0 ± 15.2	71.1 ± 12.0	69.3 ± 12.7
Duration of surgery (min)	133.5 ± 19.5	125.5 ± 23.7	120.4 ± 24.3

different penetration rates of antibiotics in different secretions. These observations are particularly important for patients in whom bacterial diseases can develop by means of a secretion. During recent investigations CE has been applied and shown to be an inexpensive, simple and effective method that requires very small samples, and offers the opportunity for clinicians to evaluate the actual efficacy of antibiotics thus promoting the optimization of individual antibiotic therapies.

In the case of patients at high risk for the aspiration of pathogenic oral flora, e.g. comatose patients, in place of cefazolin, cefuroxime and cefamandole, a prophylactic antibiotic should be administered that is able to reach the MIC values of the majority of pathogenic bacteria in the saliva. Determination of the MIC values of the bacteria isolated from the saliva collected during the surgical procedure can facilitate specific antibiotic therapy in the case of post-operative aspiration pneumonia.

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