TISSUE CONCENTRATIONS OF CEFUROXIME DURING PREOPERATIVE ANTIBIOTIC PROPHYLAXIS IN ABDOMINAL SURGERY

Poster No.: P0786

V. Pleshkov, L. Stratchounski, A. Muckonin, N. Sudilovskaya, N. Lebedeva
Departments of General Surgery, Clinical Pharmacology and Antimicrobial Chemotherapy
Smolensk State Medical Academy, Smolensk, Russia

Tel.: +7 0812 553401, 553630
Fax: +7 0812 552327
E-mail: hirurg@admin.smolensk.ru
str@cliph.keytown.com

INTRODUCTION AND OBJECTIVES

For effective antibiotic prophylaxis of surgical site infections (SSI) is necessary to maintain the stable bactericidal concentrations of the antibiotics in the serum and the surrounding incision tissues (Trilla A., 1993). β-lactams exhibit the primarily time-dependent killing of bacteria (Craig W., 1996). The time (t) during which the antibiotic concentration in the surgical site (SS) exeeds the MICs of major pathogens of the wound infection is the main pharmacodynamic parameter for this class of antibacterials. The concentration of β -lactams should be at least in 4 times higher than MICs of major pathogens. The standard drug for the AP is Cefuroxime (CEF).

The data on cefuroxime tissue concentrations during the preoperative antibiotic prophylaxis are extremely limited.

The objectives of the study:

- To determine the concentration of CEF in the serum, subcutaneous adipose tissue (SAT) and preperitoneal fat (PF) during the operation.
- To determine the time of administrating the additional dose of CEF for adequate antimicrobial protection of the operative wound.

MATERIALS AND METHODS

There have been examined 12 patients (3 men and 9 women).

The average age was 57±13 years, the weight was 81±19 kg.

All patients undergone the elective cholecystectomy through the laparotomy (9) and mini-laparotomy (3). The average duration of operation was 73±20 minutes.

All patients were administred CEF by intravenous bolus injection at dose of 1.5 g 40 minutes before the incision.

Venous blood were sampled every 10-15 minutes after CEF bolus injection through the 120 minutes period.

The tissue samples were taken from upper corner of the operation wound every 15 minutes after the beginning of the operation through the 60 minutes period.

The CEF concentration in the serum, SAT and PF were determined by disk-diffusion method with strain *E. coli* ATCC 3804 as the test-culture.

The concentrations were compared with the MIC_{90s} of CEF against *S.aureus* (2 mg/L), *S.epidermidis* (2 mg/L), *E.coli* (4 mg/L) (data from different publications).

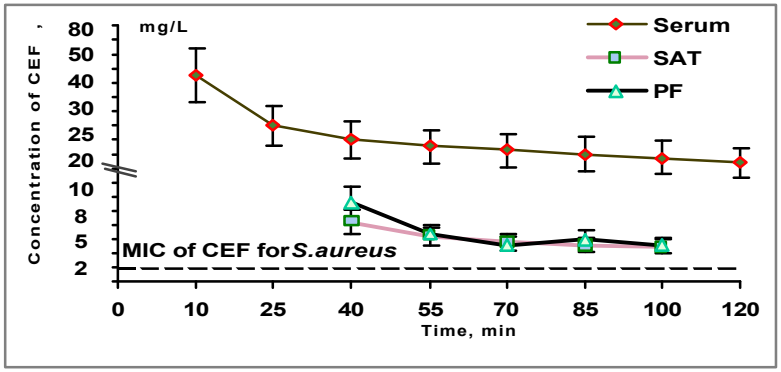
RESULTS

The mean concentrations of CEF in subcutaneous adipose tissue, preperitoneal fat and serum are represented in the Table and Figure.

Table. The mean concentrations of CEF in the serum and tissues.

t, min	10	25	40	55	70	85	100	120
	Concentration, mg/L (M+SD)							
Serum	77,3+10,7	56.5±11.9	41±11.9	38.8±9.8	32.8±12.6	28.3±7.8	25.2±6.4	22.7±6.5
SAT	-	-	8.4±4.6	6.4±1.7	5.6±0.6	5.2±0.6	4.9±0.6	
PF	-	-	11.2±6.7	6.7±1.7	5.3±0.9	5.9±1.5	5.1±0.5	

Figure. Concentrations of CEF in serum and tissues.



DISCUSSION

Intravenous bolus injection of CEF 1,5 g 40 min before the operative incision for pre-operative antibiotics prophylaxis achieved the serum concentrations of antibiotic 14 times higher than MICs of *S.aureus* and *S.epidermidis* and 7 times higher than MIC of *E.coli*.

The CEF concentrations in tissues to the end of operation 100 min after antibiotic administration became only 2 times higher than MICs of *S.aureus* and *S.epidermidis* and 1,3 times higher than MIC of *E.coli*.

If the general principle of AP in surgery to maintain adequate levels of prophylactic antibiotic throughout the operation (Sanderson J., 1993), then the single-dose regimen of 1.5 g CEF for AP do not provide the CEF levels above 4xMIC for the common bacteria.

CONCLUSIONS

- Intravenous bolus injection of CEF (1.5 g) for antibiotic prophytlaxis failes to maintain adequate concentrations (4-5 times higher than MIC) of the antibacterial in surrounding incision tissues.
- The tendency to the decrease of CEF concentration in SS to the end of operation require already in 60 min after preoperative AP of administrating the additional dose of CEF.
- These data stimulate the future investigations of dosing regimen of AP.