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Some Pharmacokinetic Parameters of Amoxycyline (Amoxycyline — a Preparation at the Stage of Preproductive Examinations)

Niektóre parametry farmakokinetyczne amoksycyliny
(amoksycylina — preparat w fazie badań przedprodukcyjnych)

Некоторые фармакокинетические параметры амоксициллина
(амоксицилин — препарат в допроизводственной стадии)

Modern medicine has more and more frequently made use of pharmacokinetic parameters in planning pharmacotherapy, and especially in therapy with antibiotics. Therefore, it is so important to determine these parameters for individual antibiotics. Basis of the study are determinations of concentrations or quantities of the unaltered therapeutic substance or its metabolites in body fluids.

The study aimed at determining some pharmacokinetic parameters of amoxycyline produced in Tarchomin Pharmaceutic Works "Polfa" in the form of tablets containing 250 mg of active substance each (examination series no. 141277).

MATERIALS AND METHODS

Calculations of pharmacokinetic parameters were performed on the basis of an unicompartmental open model of kinetics according to the authors' recommendations (1, 2, 3, 4,). Calculations were performed on the basis of concentration parameters of the assessed antibiotic in blood serum in 11 healthy men — probands selected according to generally accepted principles, after administration on empty stomach, adorally a single 250 mg dose of the antibiotic. Blood samples were taken

at the so-called O-hour and after 30 and 45 min., and also 1, 2, 3, 4, 5, 6, 8, 10, 12 hours after administration of the drug. Amoxycyline concentration in blood serum was determined by the diffusion method in agar by means of an adequate standard strain.

On the basis of the results obtained in that way there were calculated:

(a) — constant velocity of resorption (K_a),
(b) — constant velocity of elimination (K),
(c) — biologic period of half duration ($t_{0,5}$),
(d) — distriibution volume (V_d),
(e) — time after which maximum concentration in blood serum is obtained (t_p),
(f) — maximum concentration in blood serum (C_{max}),
(g) — retardation of absorption (T_o),
(h) — area below the curve of drug concentration changes in the blood (AUC).

For each calculated parameter there were given: value range (from — to), mean value, standard deviation.

RESULTS AND DISCUSSION

The obtained results of amoxycyline concentrations in blood serum of individual probands after a single adoral administration of the drug at the examined time intervals are presented in Table 1.

A graphic comparison of the obtained concentration values is presented in Fig. 1 by plotting separate curves for each examined person.

Using accepted systems of mathematic formulas (1) individual pharmacokinetic parameters for the examined antibiotic were calculated, which were set up in Table 2.

Table 1. Measurements of concentrations of the examined antibiotic-amoxycyline in blood serum of a selected group of probands, after a single adoral administration of 250 mg of the antibiotic

No. of proband	Concentration in blood serum /μg/ml/											
	Minutes			Hours								
	0	30	45	1	2	3	4	5	6	8	10	12
1	0	0.62	2.5	4.20	3.00	1.30	0.63	0.30	0	0	0	0
2	0	0	0.4	2.20	6.25	1.86	0.78	0.30	0	0	0	0
3	0	2.10	2.5	4.20	2.20	1.60	0.63	0.40	0.36	0.3	0	0
4	0	2.10	3.3	5.00	2.50	1.10	0.40	0	0	0	0	0
5	0	0	2.5	3.60	5.00	1.90	0.95	0.45	0.30	0	0	0
6	0	1.25	2.5	4.00	4.50	4.00	1.50	0	0	0	0	0
7	0	0	0	0.62	3.50	4.00	2.00	1.25	0.62	0	0	0
8	0	2.25	3.3	5.00	4.50	3.00	1.25	0.62	0	0	0	0
9	0	8.34	10.0	9.20	6.25	5.00	2.50	0.46	0	0	0	0
10	0	2.50	6.6	7.50	7.00	5.00	1.90	0	0	0	0	0
11	0	5.00	6.2	7.50	7.30	6.50	3.75	0.46	0	0	0	0

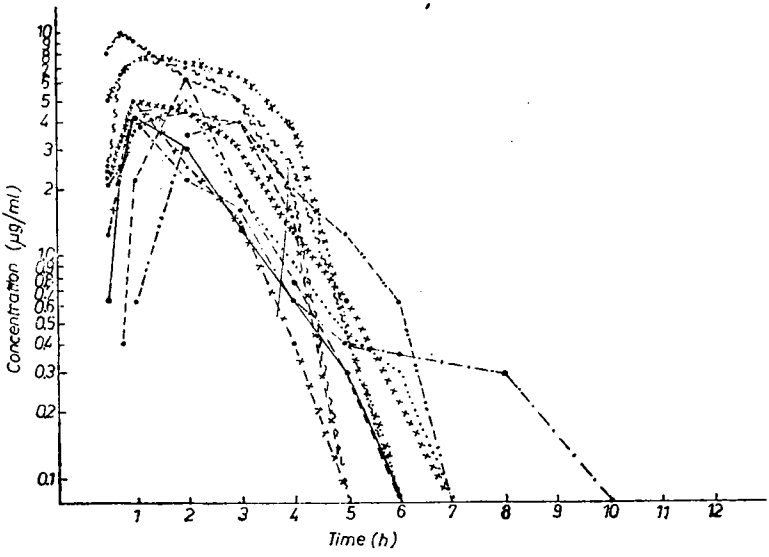

Fig. 1. Amoxycyline concentration in blood serum of probands

The obtained examination results determining magnitude of amoxycyline pharmacokinetic parameters let, among others, determine an adequate dosage diagram of this antibiotic; determine magnitude of an adequate therapeutic dose and also time interval between administration of consecutive doses ensuring a desirable concentration level of this drug

Table 2. Pharmacokinetic parameters of amoxycyline

Assessed parameter	Range of values /min.-max/	Mean value	Standard deviation
Constant velocity of resorption /K_a/	1.313-3,657 /h^{-1}/	2.016 /h^{-1}/	0.697
Constant velocity of elimination /K/	0.305-0,981 /h^{-1}/	0.631 /h^{-1}/	0.259
Biologic period of half-duration /$t_{0.5}$/	0.112-2.272 /h/	1.079 /h/	0.614
Distribution volume /V_d/	3.305-20.047 /l/	13.724 /l/	5.191
Time after which maximum concentration in blood serum is reached /t_p/	0.334-1.110 /h/	0.769 /h/	0.222
Value of maximum concentration in blood serum /$C_{max.}$/	4.2-10.0 /µg/ml/	5.740 /µg/ml/	1.407
Retardation of absorption /T_o/	0.061-0.924 /h/	0.436 /h/	0.252
Area below the curve of drug concentration changes in the blood /AUC/	17.057-77.184 /µg/ml·h/	34.856 /µg/ml·h/	17.427

in blood serum. This is conditioned, among others, by clinical condition of patient as well as by sensitivity (MIC) of the pathogenic bacterial strain to the administered antibiotic.

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STRESZCZENIE

Przedstawiono metodykę i wyniki oznaczeń niektórych parametrów farmakokinetycznych antybiotyku amoksycyliny. Badania przeprowadzono w grupie odpowiednio dobranych probantów, po jednorazowym doustnym podaniu 250 mg antybiotyku. Oznaczenia wykonano w kolejnych przedziałach czasowych od 0 do 12 godz.

РЕЗЮМЕ

В данной работе представлено методику и результаты определений некоторых фармакокинетических параметорв антибиотика амоксициллина. Исследования проводились в группе соответственно подобранных пробандов. Производилось однократное пероральное введение 250 мг антибиотика. Определения проводились в очередных промежутках времени от 0 до 12 часов.