Shimane J. Med. Sci. Vol. 4, pp. 56—60, 1980

Studies of Administration of Disodium-α-Sulfobenzylpenicillin under Surgical Conditions of Extracorporeal Circulation

(extracorporeal circulation/prophylaxis/disodium-α-sulfobenzylpenicillin)

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(Received December 28, 1979)

Administration of antibiotics in cases of open heart surgery under conditions of extracorporeal circulation requires careful management with regard to prophylaxis against infection as well as possible renal failure. In this study, the dose of semi-synthetic penicillin SB-PC was calculated from the sum of the assessed circulating blood volume, based on body weight and the priming volume. As a result of a study on the concentration in the circulating blood, the antibiotics was administered via drip infusion, at a constant rate throughout the operation, under extracorporeal circulation, in order to obtain a stable concentration.

Progress in cardiac surgery is to a great extent attributed to improvement in operative technics, extracorporeal circulation and postoperative care. Antibiotics of a wide spectrum have also played an important role.

In open heart surgery, the blood in the circulatory system is exposed to the atmosphere, oxygen and anesthetics and artificial valves, patch materials, artificial blood vessels and homogenous or heterogenous tissues are used. Thus, the opportunistic infection is often greater as compared with general surgery, and adequate prophylactic measures against infection are required.

In previous work, cefazolin and cephalothin for prophylaxis were discussed (1). In this paper we report our findings on the prophylactic use of disodium-α-sulfobenzylpenicillin (SB-PC) (Fig. 1).

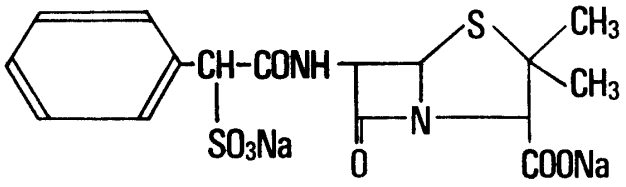

Fig. 1. Chemical structure of disodium-α-sulfobenzylpenicillin.

MATERIALS AND METHODS

During open heart surgery in the 2nd Department of Surgery at Kyoto University in 1977, SB-PC was administered in various doses and the concentration in the blood was studied (Table I). Total circulating blood volume

TABLE I. *Administration of SB-PC in Open Heart Surgery*

Patient	Age	Sex	Body weight (kg)	Disease	Initial dose into E.C.C.	Drip infusion	E.C.C.time (min)
1	27	M	56.2	ASD	1.0 g/*l*		106
2	35	F	55.8	AS+MS	1.0 g/*l*		135
3	4	M	15.0	VSD	1.0 g/*l*		33
4	14	F	27.0	PS	1.0 g/*l*		61
5	35	M	44.4	MSI+TI	0.5 g/*l*		60
6	13	F	13.0	TOF	0.5 g/*l*		77
7	4	M	18.5	ASD	0.5 g/*l*		27
8	30	F	61.5	MS	0.5 g/*l*		44
9	3	F	14.5	AS	0.5 g/*l*		35
10	1	M	9.7	TOF	0.5 g/*l*		86
11	9	M	22.5	TOF	0.5 g/*l*		117
12	24	F	42.5	MS+PH	0.25g/*l*	0.25 g/*l*/hr	92
13	9	M	26.6	ASD	0.25g/*l*	0.25 g/*l*/hr	45
14	9	M	20.0	TOF	$0.5\times\frac{1}{3}$g/*l*	0.5 g$\times\frac{2}{3}$/*l*/hr	62
15	31	F	42.0	MS	0.25g/*l*	0.25 g/*l*/hr	89

Abbreviations :

ABS……atrial septal defect
AS……aortic stenosis
MS……mitral stenosis
VSD……ventricular septal defect
MSI……mitral stenosis & insufficiency
TI……tricuspid insufficiency
TOF……tetralogy of Fallot
PH……pulmonary hypertension
PS……pulmonary stenosis

During open heart surgery, disodium α-sulfobenzylpenicillin was administered by various doses and methods.

was calculated as the sum of the assessed circulating blood volume, i. e. body weight $\times\frac{1}{13}$, and the priming volume in the heart-lung machine. The initial, single dose of SB-PC was administered either 1.0 g/*l* or 0.5 g/*l* in proportion to the total circulating blood volume. Based on the results, the initial single administration of 0.25 g/*l* with successive drip infusion at the rate of 0.25 g/*l*/hr, or initial administration of 0.5 g$\times\frac{1}{3}$/*l* with successive drip infusion at the rate of 0.5 g$\times\frac{2}{3}$/*l*/hr was given and the results were studied. Drip infusion was continued at a constant rate immediately following the initial administration. Blood samples were drawn at regular intervals from the circuit of the heart-lung machine and the concentration of the antibiotics was obtained, following the cup method (2), using Pseudomonas aeruginosa NCTC 10490* as a test organism.

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RESULTS

1) The group given a single initial administration of SB-PC in 1.0 g/*l*: As shown in Fig. 2, all of the initial concentrations of the antibiotics in blood were high (> 700 μg/m*l*), the decrease was rapid and a concentration was over 200 μg/m*l* even one hour after the start of extracorporeal circulation (E. C. C.).

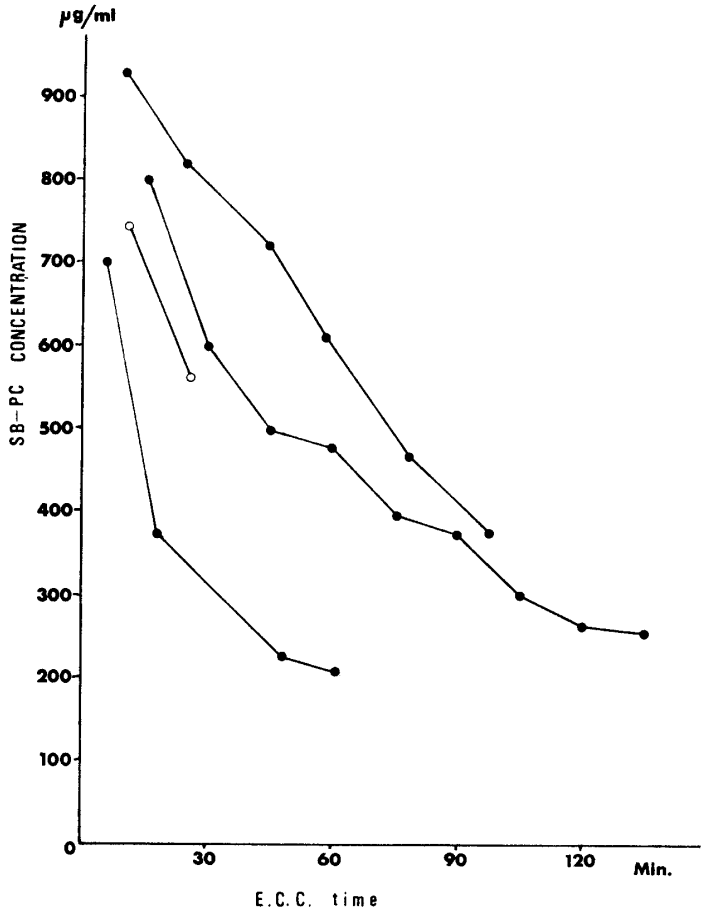

Fig. 2. Blood concentration of SB-PC 1.0 g/*l* after a single initial administration during E. C. C.

2) The group given a single initial dose of SB-PC in 0.5 g/*l*: At the start of E. C. C., the concentrations of the antibiotics in blood were 150~400 μg/m*l*, and after 40~50 min over 100 μg/m*l* (Fig. 3).

3) Based on the results of 1) and 2), an appropriate dose of SB-PC during E. C. C. was calculated as 0.5 g/*l* in the total circulatory blood volume. To maintain a constant concentration, SB-PC of 0.25 g/*l*/hr was continuously administered by drip infusion after an initial single administration of SB-PC 0.25 g/*l*. As shown in Fig. 4, the blood concentration remained at fairly constant levels during the first 90 minutes of E. C. C.

4) In this group, the dose of SB-PC was 0.5 g/*l*/hr of the total circulating blood volume. The initial single injection was $\frac{1}{3}$ of 0.5 g/*l* and $\frac{2}{3}$ of 0.5

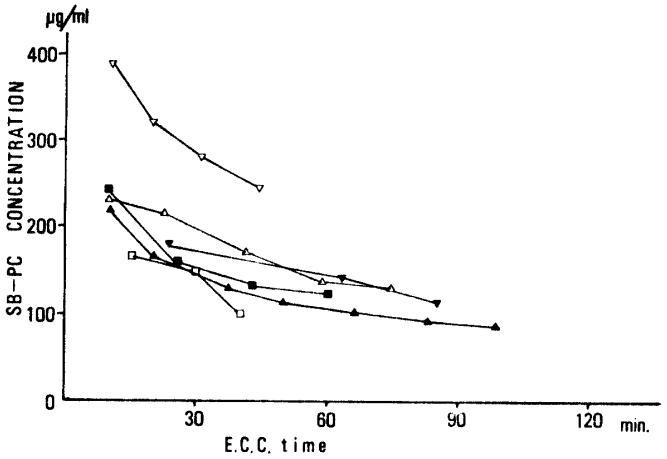

Fig. 3. Blood concentration of SB-PC 0.5 g/*l* after a single initial administration during E. C. C.

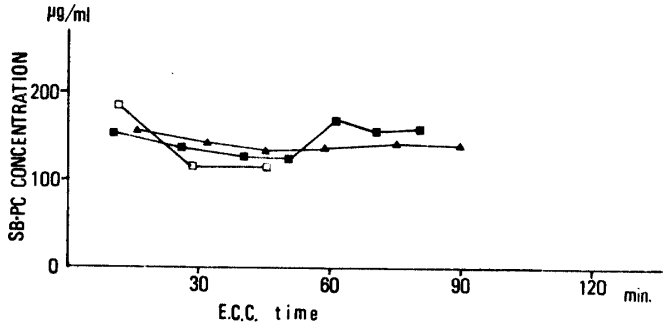

Fig. 4. Blood concentration of initial SB-PC 0.25 g/*l* and following drip administration of SB-PC by 0.25 g/*l*/hr.

g/*l* an hour was followed by continuous drip infusion. Since the blood concentration at the early stage of E. C. C. was already lower than 100 μg/m*l*, and the blood concentration remained low during E. C. C., this method was not used again (Fig. 5).

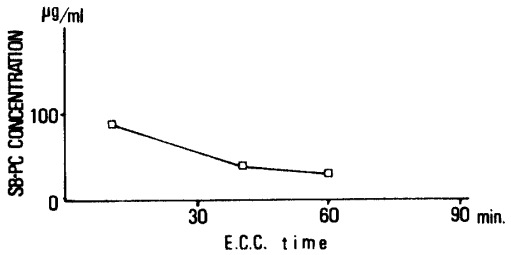

Fig. 5. Blood concentration of initial SB-PC 0.5 g×1/3 /*l* and following drip administration of SB-PC by 0.5 g×2/3 /*l*/ hr.

DISCUSSION

The method of administration and dose of antibiotics are usually determined

by past experiences of the cardiac surgeons, particularly in cases of open heart surgery. Prophylaxis against infection during this surgery has become increasingly important due to introduction of artificial materials such as prosthetic valves. Acute renal failure due to untoward effect of antibiotics also requires due attention.

In our previous study using cephalosporins, namely cefazolin and cephalothin, the dose of the antibiotics were determined based on body weight only. As a result, the blood concentration of the drugs showed a wide variation, depending on the priming volume of the extracorporeal circuit, and the volume of artifical lung employed. In the present work, the dose was calculated based on the assessed circulatory blood volume plus the priming volume and the blood concentration of SB-PC could be maintained within a minimum variation. The minimum blood concentration of SB-PC was assumed to be over 100 μg/ml, based on minimum inhibitory concentrations observed for various pathologic microorganisms (3).

Although the incidence of renal injury and myocardial damage due to SB-PC is relatively low (4) (5), nevertheless a lower blood concentration would be ideal. Conventionally, an initial single administration tends to result in an excessively high blood concentration, and as experiment 1) and 2) shows, the following decline in the blood concentration of these drugs is more rapid.

The initial single administration of 0.5 g$\times\frac{1}{2}/l$ SB-PC followed by 0.5 g $\times\frac{1}{2}/l$/hr drip infusion was sufficient to maintain a constant blood concentration of 100$\sim$200 μg/ml, as shown in experiment 3). with this dose and method, the blood concentration can be maintained constant so as to avoid an increase and a resulting renal and/or myocardial damage. In all our patients, so-treated infection as well as acute renal or myocardial failure have been avoided.

In conclusion, the administration of antibiotics should be in the smallest dose feasible and the method of parenthetical infusion maintained constant. To attain this purpose, SB-PC of 0.5 g$\times\frac{1}{2}/l$ should be administered in a single dose followed by the same dose/hr by drip infusion during E. C. C.

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