Acta Paediatrica Academiae Scientiarum Hungaricae, Vol. 13 (3), pp. 225—230 (1972)

Sulphenazone Sensitivity of some Pathogens, and its Effect in Diseases of the Upper Respiratory Tract

By

GY. KORÁNYI, ÉVA PESTI, GYÖRGYI SOMOGYI

Section of Paediatrics and Central Laboratory, Péterfy Hospital, Budapest

(Received April 15, 1972)

Sulphenazone sensitivity of 198 different bacterial strains was studied by the serial dilution method. The effect was especially advantageous against *St. aureus*, *Klebsiella* and *Ps. aeruginosa*. The M. I. C. was 625 μg/ml, 850 μg/ml and 750 μg/ml, respectively, for the three microorganisms.

Clinical testing was performed on 75 patients ranging in age from one to three years. Acute diseases of the upper respiratory tract reacted especially well to rectal sulphenazone treatment. No side effects occurred.

The clinical use of sulphenazone is recommended.

The antibiotics synthetized in the last years are often prescribed in cases of mild virus-induced diseases and in infections of the upper respiratory tract, with the natural consequence that the pathogens causing serious clinical conditions (pneumonia, meningitis) had become resistant to these wide spectrum antibiotics. In addition, several of these drugs have proved toxic.

All these gave impetus to a redetection of the sulphonamides. Their general application in paediatric practice was hitherto impeded by three factors. Sulphonamides given in appropriate doses caused gastric complaints and vomiting. Those of lasting effect and applicable in low doses proved to be toxic. Lastly, the application of parenterally administered sulphonamides was impeded by the traditional aversion of the patients and the physicians to injections. Application in early childhood of a rectally introduced reliable sulphonamide preparation seemed therefore to be necessary. We have therefore given a trial to sulphenazone — a drug fast absorbed through the rectal mucosa [4, 5].

Sulphenazone has a potent antipyretic and a good antiphlogistic effect. Its antipyretic effect is similar to that of aminophenazone and its antiphlogistic effect corresponds to that of sulphamethoxypyridazine. Its antibacterial potency is the same as that of sulphamethoxypyridazine. It is well absorbed from the intestines. The blood concentration is high and prolonged.

The LD_{50} of sulphenazone for the rat was 3 g/kg, and a dose of 300 mg/kg daily for 70 days did not cause any toxic effect. Its minimum inhib-

TABLE I

Minimum inhibitory concentrations of sulphenazone

	M. I. C. µg/ml
E. coli	1100
P. mirabilis	1300
St. aureus	625
Ps. aeruginosa	700
P. morganii	900
A. aerogenes	1000
Ps. sp.	700
P. vulgaris	700
Kl. pneumoniae	850

itory concentrations for some organisms is shown in Table I.

EFFECT OF SULPHENAZONE IN VITRO

Prior to clinical testing we established the sensitivity against some standard strains and those obtained from different patients. A total of 198 different strains was examined, distributed as follows:

30 strains of haemolytic Staphylococcus aureus,
40 belonging to the Pseudomonas group,
27 strains of Klebsiella,
46 of E. coli,
31 of Proteus mirabilis
24 of Proteus vulgaris, and
2 Proteus morganii strains.

Apart from St. aureus, this group of bacteria was chosen for the test, because

1. these bacteria are frequently found in our patient material;
2. they are mostly resistant to the usual antibiotics;
3. the antibiotics effective against

TABLE II

Antibiotic sensitivity

Penicillin			Oxacillin			Methicillin			Erythromycin			Oleandromycin			Chloramphenicol			Streptomycin			Tetracyclin		
S	NS	R	S	NS	R	S	NS	R	S	NS	R	S	NS	R	S	NS	R	S	NS	R	S	NS	R
4	2	19	13	3	9	10	6	11	10	6	11	12	2	13	6	3	16	9	3	13	2	2	21
—	—	5	5	—	—	5	—	—	2	3	—	1	2	2	2	1	2	3	—	2	1	1	3
															15	2	2	13	3	3	—	2	17
															4	1	—	4	1	—	—	—	5
															15	5	6	18	5	3	—	2	24
															3	2	—	3	2	—	—	—	5
															2	—	—	2	—	—	—	—	2
															18	—	9	18	3	6	—	5	22
															6	2	2	7	1	2	—	2	8
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	24	4	18	25	6	15	—	—	46
—	—	40	—	—	40	—	—	40	—	—	40	—	—	40	—	—	40	—	—	40	—	—	40

Abbreviations: S, Sensitive; NS, Non-sensitive; R, Resistant.

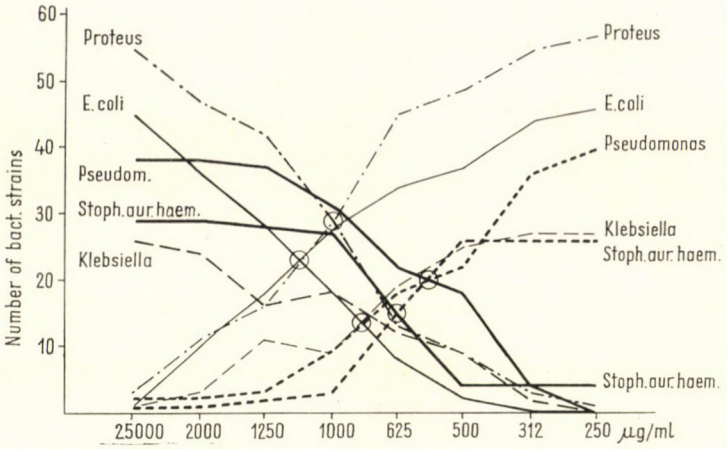

Fig. 1. Optimum sulphenazone concentration

them are partly toxic, partly expensive.

Sensitivity to sulphenazone was examined in serially diluted dextrose or vitamin containing broth in Wassermann tubes. Dilution of sulphenazone was begun below the optimum concentration, with 250 µg/ml and the quantity of the substance was then increased to a concentration of 2500 µg/ml. From the culture medium thus prepared, 1 ml samples were filled into tubes and inoculated with 0.10 ml bacterial suspension. This was prepared by diluting an 18-hour culture, each ml of which contained

with Biotest A method

Neomycin			Furadantin			Polymycin B			Sulphadimidine				
S	NS	R	S	NS	R	S	NS	R	S	NS	R		
17	3	5	—	—	—	3	—	22	—	—	25	St. aureus	25
5	—	—	—	—	—	2	—	3	—	—	5	Haemolytic St. aureus	5
17	—	2	—	—	19	—	1	18	—	—	19	Proteus vulg.	19
4	1	—	—	—	5	—	—	5	—	—	5	St. standard	5
18	6	2	2	5	19	—	3	23	—	5	21	Proteus mir.	26
3	2	—	—	—	5	—	—	5	—	—	5	Proteus standard	5
2	—	—	—	—	2	—	—	2	—	—	2	Proteus morg.	2
18	2	7	7	12	8	18	2	7	2	—	25	Klebsiella	27
10	—	—	6	3	1	10	—	—	—	—	10	E. coli standard	10
39	2	5	27	7	12	39	—	7	4	—	32	E. coli	46
17	3	20	—	—	40	37	3	—	—	—	40	Pseudomonas	40

TABLE III

Quantitative sulphenazone sensitivity of 200 bacterial strains

Sulphenazone concentration

St. aureus			Pseudomonas			Klebsiella			E. coli			Proteus mir.			Proteus vulg.			Proteus morg.			
S	NS	R	S	NS	R	S	NS	R	S	NS	R	S	NS	R	S	NS	R	S	NS	R	
5+24	—	1	37	1	2	26	—	1	39	6	1	29	—	2	23	—	1	4	0	—	2500 μg/ml
	29			*38*			*26*			*45*			*29*			*23*			*2*		
5+24	—	1	36	2	2	18	6	3	30	6	10	23	—	8	20	1	3	2	—	—	2000 μg/ml
	29			*38*			*24*			*36*			*23*			*21*			*2*		
5+21	2	2	35	2	3	10	6	11	23	5	18	17	3	11	18	2	4	1	—	1	1250 μg/ml
	28			*37*			*16*			*28*			*20*			*20*			*1*		
5 12	1	3	25	6	9	9	9	9	10	8	28	5	3	23	16	4	4	—	—	2	1000 μg/ml
	27			*31*			*18*			*18*			*8*			*20*			—		
6	9	15	15	7	18	2	6	19	6	6	34	3	3	25	5	1	18	—	—	2	625 μg/ml
	15			*22*			*8*			*12*			*6*			*6*			—		
4	—	26	10	8	22	2	—	25	5	4	37	2	2	27	1	—	20	—	—	2	500 μg/ml
	4			*18*			*2*			*9*			*4*			*4*			—		
4	—	26	3	1	36	—	—	27	2	0	44	1	—	30	1	0	23	—	—	2	312 μg/ml
	4			*4*			—			*2*			*1*			*1*			—		
2		2	—	—		—	—		—	—		1	—		—	—		—	—		
		26			40			27			46			30			2			2	250 μg/ml
	4			—			—			—			*1*			—			—		

Abbreviations: S, sensitive; NS non-sensitive; R, resistant

TABLE IV

Distribution of patients according to diagnosis

Disease	Number of patients
Acute pharyngitis	29
Follicular tonsillitis	4
Acute pharyngitis and bronchitis	17
Pharyngitis and spastic bronchitis	12
Pyelonephritis	4
Acute otitis	3
Lymphadenitis	2
Subglottic laryngitis	1
Acute mastoiditis	3
Total	75

3×10^5 germs of the strain in question. The series was incubated at 37°C for 24 hours and the minimum inhibitory zone was observed. Results are shown in Fig. 1 and Table II.

As a control, the antibiotic sensitivity of 210 strains was examined with Biotest A disks (Human, Budapest). These results are shown in Table III.

It was remarkable that from the 210 strains only 11 proved sensitive to the sulphadimidine disk marketed by Human; the situation was the same with disks containing 700 and 1400 μg. At the same time, inhibition manifested itself in the appropriate tube dilutions.

SULPHENAZONE TREATMENT OF DISEASES OF THE UPPER RESPIRATORY TRACT

In the last year 75 patients were treated with sulphenazone; 44 were 10—24 months and 29 were 3—6 years, and 2 over six years of age. These age groups were chosen since oral application of tablets is the most difficult and vomiting is the most frequent in such patients. Their distribution according to diagnosis is shown in Table IV.

One suppository contains 0.5 g of sulphenazone; its antibacterial effect corresponds to about 250 mg of sulphamethoxypyridazine, but its therapeutic and clinical effect is better owing to the better rectal absorption [6]. Between the age of 1 and 2 years, $3 \times 1/2$, between 3—6 years 2×1 or 3×1, suppositories were given for 4—5 days on the average. The dosage in the first two days corresponded to 25—30 mg/kg sulphamethoxypyridazone, from the third day to 15—20 mg/kg. Supplementary antipyretic treatment was needed in one third of the patients on the first day.

The patients reacted well to the drug. Their temperature became normal in 24—36 hours in most cases, in 19 patients there was subfebrility for 3—4 further days. All the patients recovered and their findings were normal by the end of the treatment, except for 3 patients suffering from chronic otitis and mastoiditis who recovered only after surgical and further antibiotic treatment. About 10—14 days were needed for the lymphadenitis to disappear.

In conclusion, the clinical application of sulphenazone is recommended, mainly for infants 1—2 years of age.

References

1. Castagna, P., Dall'Acqu, P.: Uso del sulfenazone in affezioni catarrali acute delle vie respiratorie in pediatria. Minerva pediat. **22,** 987 (1970).
2. Keuth, U., Sabbagh, M., Thesen, E.: Therapie bakterieller Infektionen bei Säuglingen und Kindern. (Bericht über 171 Behandlungsfälle mit Trimethopirim-Sulphamethoxazol.) Münch. med. Wschr. **1,** 802 (1970).
3. Korányi, Gy., Pesti, E., Somogyi, Gy.: Pseudomonas aeruginosa and Proteus infections in premature babies and infants. Acta paediat. Acad. Sci. hung. **11,** 141 (1970).
4. Rosini, S.: Antibacterial activity and absorption of sulphenazone. Acta paediat. Acad. Sci. hung. **13,** 230 (1972).
5. Rossolini, A., Panero, C., Puglisi, P., Pindinelli, D.: Curva sulfamidemica in bambini trattati con un nuovo composto sulfamido-pirazolico, per via rettale. Minerva pediat. **19,** 1882 (1967).

Dr. G. Korányi
Péterfy Hospital
Budapest 7, Hungary