ORIGINAL ARTICLE

Treatment of Acute Urinary Tract Infection in Children with Pipemidic Acid

by

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Abstract

Urinary tract infection in children is still an important problem in uronephrology. The disease tends to develop recurrently and results in chronic progressive renal disease in the future.

Pipemidic acid is a bactericidal quinolone derivate, with a wide spectrum against gram positive and negative bacteria. Compared with nalidixic acid, pipemidic acid proves to be more effective against Pseudomonas, E. coli, Alkaligenes and Salmonella.

Thirty one cases with acute urinary tract infection had been studied descriptively. The etiology revealed as follows: E. coli (45,2%), Alkaligenes (16,2%), Enterobacter (9.6%), Staphylococcus (9,6%), Pseudomonas (9,6%), Paracolon (6,5%), and Proteus (3.3%).

Pipemidic acid was administered orally to these patients, 15-20 mg/kg/day divided in 2 equal doses for 10 days. Bacteriological examinations was repeated on the 6th day and 11th day treatment. The result revealed that on the 6th day of treatment, in 27 patients (87,09%) there was no bacteriuria while on the 11th day the urine of 29 patients (93,54%) were sterile.

In conclusion, a 5 day treatment of acute urinary tract infection in children with pipemidic acid is quite effective.

Introduction

Urinary tract infection in children is still an important problem in uronephrology. The disease tends to develop recurrently and results in chronic progressive renal disease in the future (Alatas, 1984; Chantler, 1985; Tune et al., 1984).

Many authors had discussed urinary tract infection with its problems, especially the urinary tract infection caused by microorganisms resistant to antimicrobial treatment (Faieley et al., 1980; Gan et al., 1980; Kempe et al., 1982).

The most common causative agent of urinary tract infection in children was E. coli. The other causes were Staphylococcus, Proteus, Klebsiella, Enterobacter and

Pseudomonas (Gauthier et al., 1982: Peter et al., 1986, Sidor and Resnick, 1983).

Pipemidic acid (Ethyl-8-oxo-5 (piperazynil-1) 2-dihydro-5-8 pyrido- ABS (2,3,-d) -pyrimidine-6-carboxylic acid) had a broad antibacterial spectrum, covering not only the gram negative germs, but also the gram-positive ones, more frequently found in urinary tract infections (Senda et al., 1975).

The purpose of this study is to measure the effectiveness of pipemidic acid in the treatment of urinary tract infection in the Child Health Department, Medical Faculty of Diponegoro University/Dr. Kariadi Hospital in Semarang.

Materials and Methods

The study was carried out discriptively to patients with acute urinary tract infection at the Child Health Department, Medical Faculty of Diponegoro University/Dr. Kariadi Hospital Semarang, since October 1986 - August 1987. There were 16 boys and 15 girls, their age range from 2 to 14 years.

Acute urinary tract infection was considered as a first episode or simple infection, provided no earlier urinary tract infection had been documented or appreciated (Cicmanec and Evans, 1980).

Physical and laboratory examinations performed included routine examination.

renal function tests (ureum, creatinine) and urine bacteriological cultures. Diagnosis of urinary tract infection is based on a significant bacteriuria i.e. more than 100.000 single bacteria per ml urine (mid streamclean catch urine) (Vaughan, 1981; Moffet, 1981; Ongkie, 1983).

Pipemidic acid is administered orally 15 - 20 mg/kg/day, devided in 2 equal doses for 10 days. Urine was against bacteriologically cultured on the 6th and 11th day of the treatment. Successful treatment was considered if the repeated bacteriological urine culture revealed no bacterial growth (sterile).

Results

ment with pipemidic acid. These patients consisted of 16 boys and 15 girls, their age

There were all thirty one patients treat- ranged from 2 to 14 years. The body weight ranged from 11 to 40 kg with an average of 25.5 kg.

Table 1: Age and sex distribution

Age (Years)	S e x		
	Boys	Girls	
2 - 4	3	4	
5 - 9	6	9	
10 - 14	7	5	
Total	.16	15	

Table 2: Body weight and sex distribution

Body Weight (kilogram)	S e x		
	Boys	Girls	
10 - 19	7	5	
20 - 29	6	9	
30 - 40	3	1 %	
Total	16	15	

Table 3: Etiology of the urinary tract infection

Microorganisms	Total	percentage (%)	
E. Coli	14	45,20	
Alkaligenes	5	16,20	
Enterobacter	3	9,60 9,60 9,60 6,50 3,30	
Staphylococcus	3		
Pseudomonas	3		
Paracolon	2		
Proteus	1		
Total	31		

The results revealed that on the 6th day of treatment in 27 patients (87,09%) were no bacteriuria, while on the 11th the urine

of 29 patients (93,54%) was sterile. In this study no drug side effect was observed.

Table 4: Result of the pipemidic acit treatment

Duration of treatment	Significant bacteriuria		
Darwing of treatment	absent	present	
5th day	27 (87,09%)	4 (12,91%)	
10th day	29 (93,54%)	2 (6,46%)	

Discussion

Pipemidic acid belonging to the quinolone group which includes some other chemotherapeutic agents such as nalidixic acid, oxolinic acid and piromidic acid, represents a new compound as there is a piperazine nucleus present in it. This chemical change gives pipemidic acid a broader antibacterial spectrum in comparison with the other components of the group, covering not only the gram negative germs, but also the gram positive ones, which were more frequently found in urinary tract infections. It has also a very low toxicity (Hori et al., 1975; Senda et al., 1975. Pipemidic acid is rapidly and completely absorbed after oral administration, reaches high concentrations in the kidney and in the excretory tract, where it also exerts a powerful bactericidal action on Pseudomonas aeruginosa, against which most of chemoantibiotics proved ineffective

(Shimizu et al., 1975; Ueda et al., 1978).

According Senda et al. (1975), there were only few side effects of pipemidic acid. One hundred and eleven (5,57%) among 1992 patients treated with pipemidic acid, showed side effects of nausea (1,96%), epigastric pain (1,15%), anorexia (0,95%) and skin rash (1,05%). As far as toxicity is concerned dogs and monkeys given pipemidic acid during 30 consecutive days, showed no loss of appetite or body weight and in autopsy there were no pathological changes of the organs. Administration of pipemidic acid to dogs with a doses of 100, 200, 400 mg/kg and to rats of $50 - 3.200 \, mg/kg/day$ for 6 months gave the same results. There was no fatal case in that study.

In our present study, the effectiveness of pipemidic acid treatment for 5 days was no statistically significant difference between these two regimens.

Table 5: Effectiveness of pipemidic acid treatment in different studies

Authors	Year	Dose	Cases	Duration of treatment	effectiveness
Hori	1975	50 mg/kg/day	17	10	82,35
Ueda	1975	l g/day	30	3 - 10	80,00 %
Lydia	1987	15 - 20 mg/kg/day	31	5 days	87,09 %
			10 days	93,54 %	

Conclusion

The causative agents of 31 cases of urinary tract infection were E. Coli (45,20%), Alkaligenes (16,20%), Enterobacter (9,60%), Staphylococcus (9,60%), Pseudomonas (9,60%), Paracolon (6,50%) and Proteus (3,30%).

The effectiveness of a 5 days treatment of pipemidic acid was 87,09% and in 10 days it was 93,54%. It was proved that a 5 days pipemidic acid treatment is effective for urinary tract infection in children.

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REFERENCES

- ALATAS, H.: Masalah infeksi saluran kemih pada anak. Majalah Dokter Keluarga. 3: 17-122 (1984).
- CHANTLER, C.: Urinary tract infection in children. Hongk. J. Pediat. 2: 235 – 244 (1985).
- CICMANEC, J.F; EVANS, A.T.: Classification of urinary tract infections by biotype identification of the pathogens. J. Urology, 124: 68 - 69 (1980).
- FAIELEY, K.F.; WHIWORT, A.Y.: Problems in treatment of urinary tract infection. Med. Prog. 7: 39 (1980).
- GAN, S.; SUHARTO, B.; SYAMSUDIN, U.; SETIABUDY, R.; SETIAWATI, A.; GAN, V.H.: Farmakologi dan Terapi ed. 2 hal. 469-473. (Bagian Farmakologi FK UI, Jakarta, 1980).
- GAUTHIER, B.; EDELMAN, C.M.; BAR-NETT, H.L.: Nephrology and Urology for the Pediatrician 1st ed. pp. 73 - 85. (Little Brown, Boston, 1982).
- HORI, M.; KOHNO, S.; JOH, K.; OKAMO-TO, K.; TOTANI, M.: Clinical experience with pipemidic acid in bacterial infections of children. Chemother. 23: 2880 - 2888 (1975).
- KEMPE, C.H.; SILVER, H.K.; O'BRIEN, D.: Current Pediatric Diagnosis & Treatment 7th ed. pp. 497 - 526 (Lange Med. Publ. Los Altos, 1982).
- MOFFET, H.L.: Pediatrc Infectious Diseases 2nd ed. pp. 347 - 354 (William Morrow, New York, 1981).

- ONGKIE, A.S.: Penatalaksanaan infeksi saluran kencing pada anak. Simposium Nasional Nefrologi Anak II. Kumpulan Naskah hal. 111-124 (Ikatan Dokter Anak Indonesia Jawa Timur, Surabaya, 1983).
- PETER, G.; GIEBINK, G.S.; HALL, C.B.; PLOTKIN, S.A.: Report of the committee on infectious diseases 20th ed. pp. 485. (American Academy of Pediatrics, Illionois, 1986).
- SENDA, H.; FUJIMOTO, G.S.; HALL, C.B.; TATSUMI, H.: Toxicological studies of pipedimic acid. Chemother 23: 2739 - 2764 (1975).
- SHIMIZU, M.; NAKAMURA, S.; TAKASE, Y.; KUROBE, N.: Pipemidic acid; absorption, distribution and excretion. Antimicrob. Agents Chemother. 7: 441 - 446 (1975).
- SIDOR, T.A.; RESNICK, M.I.: Urinary tract infection in children. Pediat. Clins N. Am. 30: 323 - 332 (1983).
- TUNE, B.M.; MENDOZA; BRENNER, B.M.; STEINB, J.H.: Pediatric Nephrology 1st ed. pp. 155-181 (Churchill Livingstone New York, 1984).
- UEDA, Y.; MATSUMOTO, F.; SAITO, A.; OHKOSHI, M.; KAWAMURA, N.; NISHIU-RA, T.; KAWADA, Y.; BAN, Y.: Clinical studies on pipemidic acid. Jap. J. Antibiot. 31: 528 - 535 (1978).
- CLINICAL, V.C.; MACKAY, R.J.; BEHR-MAN, R.E.: Textbook of Pediatrics 11th ed. pp. 1543 1548. (Saunders, New York, 1981).