ORIGINAL ARTICLE

Clinical Evaluation of Dibekacin in Urinary Tract Infection in Children

by

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Abstract

*Fifty selected cases of urinary tract infection (UTI) were treated with Dibe-
kacin with the dosage of 2 mg/kg. bw. IM. for seven days. Thirty five cases
classified as simple UTI and the rest fifteen cases as complicated urinary infec-
tion. Thirty one cases were injected once a day and the remaining nineteen pati
ents twice a day.*

*The clinical, laboratory and microbiological improvement was 84%, 86%
and 62% respectively. Complete improvement was and on 54% cases only. In
the group of simple UTI, no significant different result was found on different
interval time of drug injection. Similar result was also detected in the group of
complicated UTI. The only significant different result was obtained from the
comparison between simple and complicated urinary infection when the drug
was given twice a day, either it was separately assessed clinically, laboratory
and microbiologically or combined. Better result was more pronounced in the
group of simple UTI but we had to be cautious to interpret this finding. Single
daily injection could be recommended to reduce the dscomfort of parenteral
aaministration.*

Introduction

Urinary tract infection (UTI) is not an uncommon finding in children. It is potentially dangerous as a life threatening episodes and also could be the forerunners of severe renal disease in adulthood. The prevention of renal damage due to chronic pyelonephritis could be made by early diagnosis and eradication of UTI, early detection and correction of congenital anomaly and vesicoureteral reflux and also prevention and treatment of recurrent UTI.

Hitherto, many effective antimicrobial agents were available in the prevention of recurrent bacterial invasion on the urinary tract. One of them is Dibekacin (3.4-dideoxykanamycin-B), a semisynthetic drug derived from Kanamycin B by Umezewa et al, 1971.

This drug has a bactericidal action against gram positive and gram negative bacteria. Fujii in 1976 reported that in UTI, the efficacy rate was 88,8%. The study against this drug in Indonesia, especially in treating UTI has not been reported. Eventhough this drug is still considered as a second line drug for eradicating urinary infection, we still carried out this study to evaluate the effect of Dibekacin in the initial attack of UTI both in simple and complicated cases and to compare its effect on different interval of infection namely once and twice daily. The adverse effect of this drug was also noted with special references to ototoxicity and changes in renal function.

Material and Methods

All cases included into this study were selected from children (1-12 years) attending the outpatient department or hospitalized in the Department of child health, Dr. Cipto Mangunkusumo General Hospital, who showed symptomatic signs of urinary infection and proved with positive bacteriuria.

Systemic symptoms such as fever, poor weight gain, irritability, abdominal pain or vomitng without any obvious cause; and local symptoms such as dysuria, frequent micturation, loin pain, day or night wetting were considered as symptomatic signs of urinary infection. Positive bacteriuria was defined as the presence of 100.000 bacterial colonies or more in one ml cultured urine collected from midstream or catheter specimen, or the presence of any bacteria in urine collected from Supra pubic puncture.

Patients having symptoms of urinary infection with massive pyuria or severe local symptoms or fever will be immediately treated. Anyhow those patients without significant bacteriuria then will be excluded from this study.

On the others, treatment will be started after the result of urine culture have been received. Patients will be treated with Dibekacin in a dosage of 2 mg/kg b.w/day for seven days. If the symptoms still exist, the treatment will be prolonged for ten days. The selection of cases in this two types of drug injection (once or twice daily) were randomly assigned but in some cases treated ambulatory, injection was done once daily.

Patient regarded having UTI will be further investigated with intravenous pyelorgraphy and mictio-cysto-urethrography (MCU). All cases showing the signs of urinary obstruction, reflux or stasis of urine flow were classified as complicated UTI, while the remaining with normal radiographic findings were considered as non complicated or simple urinary infection.

Repeated urine culture will be done three days and two weeks after cessation of therapy. Biochemical blood examination (protein spectrum, cholesterol, urea, creatinine, TTT and bilirubin) will be done before treatment and one week after treatment to detect the possibility of side effects to the liver and renal tissue. The audiogram was not done but the possibility of hearing impairment was always kept in mind by asking directly to the patients or their parents for the presence of hearing impairment.

The efficacy of treatment should be judged from clinical, laboratory examination of urine and bacteriological point of view according to criterias specified as follows :

1. Clinical :
— improvement : clinical symptoms (fever, pain on urination etc) diminished or disappeared.
— no improvement : clinical symptoms persisted or became worse.

2. Urinalysis :
— improvement : pyuria subsided or absent.
— no improvement : pyuria persisted.

3. Microbiological :
— imprvovement : microorganism eradicated and remain so until two weeks post therapy.
— no improvement : colony persisted or superinfected with other microorganism.

Statistical analysis will be done by using Fisher exact test; p<0.05 was considered as statistically significant.

Results

Fifty selected cases fulfilled the cirteria for simptomatic UTI (34 males and 16 females) were available for evaluation. The age ranging from one to twelve years. Thirty five cases classified as simple UTI and the rest fifteen cases as complicated UTI. On thirty one cases injection were done once daily and the remaining twice a day. Forty two cases (84%) showed clinical improvement. On forty three cases (86%) pyuria subsided or absent. Bacteria was eradicated on 31 cases (62%) fifteen cases (30%) persisted. Superinfection with other microorganism was found on four cases (table 1).

Complete improvement (clinical, laboratory and bacterial eradication altogether) was found on 27 cases (54%) only. Four cases showing total failure or no response at all, either clinically, laboratory or microbiologically.

In simple urinary tract infection (UTI) no significant difference of improvement were noted, (p>0.05) neither with injection done once nor twice daily (table 2a). Thirty two cases (91,5%) showing clinical improvement.

TABLE 1 : *Result of treatment by causative organism*

Microorganism isolated from urine culture	Eradicated	Persisted	Superinfection	Total
E. coli	16	8	2	26
Proteus sp	7	3	—	10
Pseudomonas sp	1	3	—	4
Aerobacter aerogenes	3	—	1	4
Gram negative baccilli	2	—	—	2
Diphtheroid	1	—	1	2
Staphylococcus aureus	1	1	—	2
	31	15	4	50

I. Clinical judgement :

TABLE 2a : *Simple urinary infection : comparison of lag time of injection.*

Lag time	Improvement	No improvement	Total	
Once a day	19	1	20	
Twice a day	13	2	15	p > 0.05
T o t a l	32	3	35	

TABLE 2b : *Complicated UTI : Comparison of lag time of injection.*

Lag time	Improvement	No improvement	Total	
Once a day	8	3	11	
Twice a day	2	2	4	p > 0.05
T o t a l	10	5	15	

In complicated UTI, clinical improvement was noted on ten cases (66,6%). The different of improvement was also not significant (p > 0.05) in this group either it was injected once or twice a day (table 2b).

TABLE 2c : *A once a day administration of drug in simple and complicated UTI*

Classification	Improvement	No improvement	Total	
Simple UTI	19	1	20	
Complicated UTI	8	3	11	p > 0.05
	27	4	31	

Table 2c showed no different result between simple and complicated UTI on once a day administration of Dibekacin, but on twice a day injection, the difference of improvement become statistically significant (p < 0.05).

The improvement was more pronounced in simple UTI (table 2d).

TABLE 2d : *Twice a day administration of drug in simple and complicated UTI.*

Classification	Improvement	No improvement	Total	
Simple UTI	13	2	15	
Complicated UTI	2	2	4	p < 0.05
T o t a l	15	4	19	

II. Laboratory evaluation on urine examination.

TABLE 3a : *Simple UTI; comparison of lag time of injection.*

Lag time	Improvement	No improvement	Total	
Once a day	19	1	20	
Twice a day	14	1	15	p > 0.05
T o t a l	33	2	35	

TABLE 3b : *Complicated UTI; comparison of lag time of injection.*

Lag time	Improvement	No improvement	Total	
Once a day	9	2	11	
Twice a day	1	3	4	p > 0.05
T o t a l	10	5	15	

TABLE 3c : *The result of treatment on once a day administration of drug in simple and complicated UTI.*

Classification	Improvement	No improvement	Total	
Simple UTI	19	1	20	
Complicated UTI	9	2	11	p > 0.05
T o t a l		3	31	

TABLE 3d : *Twice a day administration of drug in simple and complicated UTI.*

Classification	Improvement	No improvement	Total	
Simple UTI	14	1	15	
Complicated UTI	1	3	4	p<0.05
T o t a l	15	4	19	

Table 3a and 3b showing that both in simple and complicated UTI, no significant difference of improvement were found on different lag time of drug injection.

On once a day drug injection there was no difference on laboratory improvement found neither in simple nor in complicated UTI (table 3c), but different result was obtained on twice a day injection (table 3d). Better result was found significantly in simple UTI compare to the group of complicated urinary infection (p<0.05).

III. Microbiological assessment.

TABLE 4a : *Simple urinary infection; comparison of lag time of injection.*

Lag time	Improvement	No improvement	Total	
Once a day	12	8	20	
Twice a day	12	3	15	p>0.05
T o t a l	24	11	35	

TABLE 4b : *Complicated urinary infection, comparison of lag time of injection.*

Lag time	Improvement	No improvement	Total	
Once a day	7	4	11	
Twice a day	0	4	4	p>0.05
T o t a l	7	8	15	

From table 4a and 4b, we concluded that both in simple and complicated urinary infection the result of treatment was not different (p>0.05) either the drug was given once or twice a day. Eradication rate was 68,6% in simple UTI and only 47% in complicated UTI group.

TABLE 4c : *The result of treatment on once a day injection in simple and complicated UTI.*

Classification	Improvement	No improvement	Total	
Simple UTI	12	8	20	
Complicated	7	4	11	p>0.05
T o t a l	19	12	31	

TABLE 4d : *The result of treatment on twice a day injection in simple and complicated UTI.*

Classification	Improvement	No improvement	Total	
Simple UTI	12	3	15	
Complicated UTI	0	4	4	p<0.05
T o t a i	12	7	19	

Microbiologically no different result was found on once a day of drug injection (table 4c), but on twice a day injection, the result was significantly better obtained in simple urinary infection compared with complicated UTI (p<0.05).

IV. Final assessment (Clinical, laboratory and microbiological evaluation together).

TABLE 5a : *The result of treatment in simple UTI.*

Lag time	Complete improvement	Failure	Total	
Once a day	12	8	20	
Twice a day	10	5	15	p>0.05
T o t a l	22	13	35	

TABLE 5b : *The result of treatment in complicated UTI.*

Lag time	Complete improvement	Failure	Total	
Once a day	5	6	11	p > 0.05
Twice a day	0	4	4	
T o t a l	5	10	15	

Complete improvement (Clinical, laboratory and microbiologically altogether) was found in 27 cases; 22 cases derived from simple UTI and five cases from complicated UTI group. The result was not significantly different for both in simple and complicated UTI whether the drug was given once or twice a day (table 5a and 5b).

TABLE 5c : *The result of treatment on once a day of injection*

	Complete improvement	Failure	Total	
Simple UTI	12	8	20	p > 0.05
Complicated UTI	5	6	11	
	17	14	31	

TABLE 5d : *The result of treatment on twice a day of injection.*

	Complete improvement	Failure	Total	
Simple UTI	10	5	15	p < 0.05
Complicated UTI	0	4	4	
	10	9	19	

On once a day injection group of patients, there were no different result of treatment neither in simple nor in complicated urinary infection but in the group of twice a day injection, better results were more pronounced in simple UTI, while in complicated urinary infection high serum urea and creatinine content observed none of them were treated successfully (table 5c and 5d).

Adverse reaction and side effect

There were two patients (no. 2 and 13) from complicated UTI group who had before treatment was started but on follow up none of them showed renal function deterioration.

On the others, not one case showed abnormal biochemical blood examination before and after treatment was done. Hearing impairment was not observed.

One patient suffered from severe pain and inflammation at the site of injection.

Discussion

The overall response rate to Dibekacin in this study showed us that clinical improvement was closely related to the improvement of laboratory findings (84% and 86% respectively).

Bacterial eradication rate was lower; 68,6% in simple UTI and only 47% on the group of complicated UTI.

Fujii in 1976 using the same dose with our study but with shorter period of treatment (5 consecutive days) reported a higher clinical efficacy rate (88,8%). Further analysis of table 1 revealed that the efficacy rate against Escherichia coli was 61,5% and proteus sp was 70%. These rates were lower compared to the report of Fujii (1976) who found the efficacy rate of 92.3% against Escherichia coli and 100% against Proteus.

Statistically speaking, the results separately analyzed from clinical, laboratory and microbiological point of view showed that no different results were observed either the drug was injected once or twice a day in cases of simple UTI. The same result was also noted in the group of complicated urinary infection. The only significant difference of the data obtained was from the comparison between simple and complicated UTI when the drug was given twice a day. It seemed that the improvement was more pronounced in the group of simple UTI but must be cautious to interpret this finding since we know that many factors could influence the outcome of the treatment in cases of complicated UTI. The type of urinary obstruction, the gradation of reflux and the degree of renal impairment for instance play an important role in the outcome of therapy. Statistical analysis of the group with simple UTI clearly showed us that no different result was obtained by either Dibekacin given once or twice a day. Based from this finding we could say that single daily injection of Dibekacin can be recommended in cases of urinary tract infection. The disadvantage and discomfort of parenteral administration thus could be diminished.

Final assessment revealed that only 27 cases (54%) showed excellent results or complete improvement. Further analysis against these data (table 5a — d) revealed the same result with previous findings in which each criteria was separately analyzed. We here are again faced with the fact that the only significant finding data was found in the intersubject of twice a day of drug injection. Here we saw that complete improvement was only noted from the group of simple UTI, while on the other group, none of them were treated successfully.

Once again we must be attentive to interpret this finding. Several factors other than the interval time of injection could influence this data. Besides that the

limited number of cases studied here should also be taken into consideration.

There was no adverse reaction or side effect of Dibikecin found on this study except in one patient who complained from severe pain and inflammation at the site of injection. Hearing impairment was not observed during the period of treatment.

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