Minocycline HCL in Urinary Tract Infection A Clinical Trial

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Abstract

Minocycline HCL was tried in 100 patients with urinary tract infections. It was highly effective in patients with E. coli and Strep faecalis infections. A convenient dose schedule, low recurrence and relatively low cost make it attractive in terms of patient compliance(JPMA 33 : 294, 1983).

The treatment of urinary tract infections is a difficult problem. One attack of UTI predisposes to a relapse or reinfection which then continues as a viscious circle. Apart from high urine output, change in the urinary pH, and removal of the precipitating cause, the main aim of the treatment is the administration of a suitable antimicrobial (Kitamoto et al., 1969). In this study efficacy of Minocydline a Semisynthetic derivative of Tetracycline in UTI was studied.

Material and Methods

The patients, included in this trial had established urinary tract infection. Sixty five were selected from North Surgical Unit, twenty from outpatient department and fifteen from the emergency room. They were divided into two groups (Table I).

Table I — Groups of Patients.

Group A				Group B	
Diagnosis	Operation		No. of Patients (50)	Diagnosis	No. of Patients (50)
Renal Calculus	a)	Pyelolithotomy	8	Pyelonephritis	14
	b)	Nephrolithotomy	2	Cystitis	15
Ureteric Calculus		Ureterolithotomy	4	Prostatitis and Posterior Urethritis	4
Vesical Calculus		Vesicolithotomy	12	Non-Gonococcal Urethritis	4
Benign Hyperplasia of Prostate		Prostatectomy	21	Gonococcal Urethritis	3
Ruptured Urethera		Retrograde Catheterization	3	Generalised UTI	10

Group ‘A’ consisted of 50 patients who underwent a surgical procedure. Remaining 50 patients (Group ‘B’) were treated conservatively. Of these 35 patients were treated as outpatients and 15 were hospitalised. Urinilysis, urine culture and sensitivity, complete blood count, blood urea and blood sugar

were done in all the cases. Radiological investigations were done only when indicated.
Children below 8 years, pregnant females and diabetics were excluded from the trial. Minocycline HCL was administrated orally or parenterally. Initial dose of 200 mg was followed by 100mg twice a day for 5-7 days in group 'A' and 10-15 days in Group 'B' depending upon the response in individual cases.

Results

The age and sex distribution of patients in two groups is shown in Table II.

Table II Age and Sex Distribution.

Age Group	A		B	
	Male	Female	Male	Female
10 years	2	–	–	–
10–20 years	4	2	6	2
21–30 years	5	2	8	2
31–40 years	6	3	6	3
41–50 years	7	2	4	3
51–60 years	8	–	6	2
61–68 years	9	–	6	2
	41	9	36	14

Diagnosis of urinary tract infection suspected clinically was established by urine culture studies.

Table III

Microorganisms in Urinary Tract infection.

Micro organisms	A	B	Total
E. coli	36	34	70
Pseudomonas	5	5	10
Strep faecalis	4	3	7
Proteus	3	3	6
Klebsiella	2	2	4
Gonococcus	–ve	3	3
	50	50	100

Table III shows the frequency of various organisms grown from urine specimen. Seventy percent of urinary tract infections were caused by E. coil and the remaining 30% by Pseudomonas, Strep faecalis, Proteus, kiebsiella and Gonococci.

Table IV Sensitivity Pattern in Urinary Tract Infections.

	E.coli 70%		Pseu-domonas 10%		Strep faecalis 7%		Proteus 6%		Klebsiella 4%		Gonococcus 3%	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1. Ampicillin	34	49	4	40	3	43	3	50	2	50	2	66
2. Cotrimoxazole	49	70	6	60	5	57	3	50	2	50	2	66
3. Nitro-furantoin	42	60	3	30	2	30	3	50	2	50	1	33
4. Tetracycline	30	43	1	10	2	30	2	33	0	Nil	1	33
5. Minocycline HCL	57	81	6	60	6	86	4	67	2	50	2	66

Table IV shows the sensitivity pattern of infecting organisms to Minocycline HCL and other commonly used antibiotics. Minocydline HCL was effective in 81% cases with E. coil and 86% with Strep faecalis infections. It showed a satisfactory response against pseudomonas, Proteus, Klebsiella and Gonococci. In mixed infections results were comparable to other antimicrobials and superior to tetracyclines.

Criteria for assessment of response to treatment in operated cases (group 'A') were:

a) Primary uneventful wound healing and apyrexial progress of the case.

b) Absence or improvements in the presence of pus cells and culture reports in the post operative period upto the time of removal of stitches.

c) Absence or improvement of urinary symptoms like frequency and dysuria. 72% of patients in group

'A' had a good response to Minocycline HCL (Table V).

Table V

Response to Treatment with Minocycline HCL in Group 'A'.

Diagnosis	Uneventful Recovery	Percentage
Pyelolithotomy	7/8	88
Nephrolithotomy	2/2	100
Ureterolithotomy	3/4	75
Vesicolithotomy	9/12	75
Prostatectomy	14/2!	67
Repair of ruptured Urethra	1/3	33
Total	36/50	72

Due to lack of a rigid follow-up in group 'B' the response was assessed clinically as "good" if symptoms disappeared within 48 hours, "satisfactory" when continued upto 96 hours and "poor" if persisted beyond 96 hours. Response was good in 27, satisfactory in 16 and poor in 7 cases (Table VI).

Table VI

Response to Treatment with Minocycline HCL in Group 'B'.

Diagnosis	Good	Satisfactory	Poor
Pyelonephritis	8	4	2
Cystitis	9	5	1
Prostatitis and posterior Urethritis	2	1	1
Non-Gonococcal urethritis	1	2	1
Gonococcal urethritis	2	1	–
Generalised UTI	5	3	2
Total	27	16	7

The results of cultures repeated 3 days after the cessation of therapy in group 'A' (Table VII)

Table VII

Results of Cultures 3 Days After Cessation of Minocycline HCL Therapy.

Microorganisms	Recurrence	Percentage
E.coli 4/36	11	
Pseudomonas	2/5	40
Strep faecalis	0/4	zero
Proteus	2/3	66
Klebsiella	1/2	50

showed persistence of microorganisms in only 11% of patients with E. coli infections. All patients with

Strep faecalis infection responded to treatment while results in other types of infections were not so promising. Pseudomonas, Kiebsiella and Proteus showed persistence in order of increasing frequency. The adverse reactions of Minocycline HCL are recorded in Table VIII.

Table VII

Results of Cultures 3 Days After Cessation of Minocycline HCL Therapy.

Microorganisms	Recurrence	Percentage
E.coli	4/36	11
Pseudomonas	2/5	40
Strep faecalis	0/4	zero
Proteus	2/3	66
Klebsiella	1/2	50

Drug was stopped in five patients due to these reactions.

Discussion

Minocycline was introduced as a semisynthetic derivative of Tetracycline in 1967 internationally and 1976 in Pakistan. Its chemical name is "7-dimethyl amino-6-deoxy-demethyl tetracycline". It belongs to the group known as "Polycyclic naphtahacane carboxamides" (Martell and Booth, 1967).
Minocycline HCL is rapidly absorbed after oral administration. Unlike most tetracyclines, its absorption is not significantly impaired by ingestion of food or milk (Haine, 1969). After single oral dose of 150mg minocycline HCL gives serum levels which are 2-4 times .higher than other tetracyclines. After 24hours serum level of Minocycline HCL (150mg) may be as high as 16 times than other tetracyclines (250mg) (Kanazawa and Kuamata, 1969). Its serum half life is 18 hours (Fedorko et al., 1968). Seventy percent of the drug is protein bound (Ory, 1970). Some drug is still detectable in the serum upto 96 hours after single oral dose. It is because the protein bound portion is gradually released and becomes active (MacDonald et al., 1973).
Minocycline HCL is widely distributed in body tissues (Colaizzi and Klink, 1969). Because of its high lipophffic properties it penetrates the epithelial membrane of the prostate in high concentrations (Brannan, 1975). Minocycline HCL is excreted partly through the kidney and partly through liver (Steigbigel et al., 1968). One third to half of the drug can be recovered from these cources, rest of the drug is metabolized in the liver (Bernard et al., 1971). A small percentage gets incorporated in the developing teeth and bone (Grossman et al., 1971).
Minocycline HCL like other tetracyclines acts by interfering with nucleic acid metabolism and protein synthesis of bacteria (Swenson and Sanford, 1970).
Minimum inhibitory concentration of Minocycline HCL in serum is 1-3 microgram/mI. With usual

dosage the level obtained is between 2-5 microgram/mI. It has wide margin of safety because the toxic effects appear at about 40-50 microgram/mi (Redin, 1967).

The value of Minocycline HCL in the treatment of urinary tract infections has been established in a number of trials (Steigbigel et al., 1968; Nakazawa et al., 1969; Frisk and Tunevall, 1969; Ronald et al., 1968). Of various antibiotics tested in the trial, Minocycline HCL was found to be most effective in E. coliC and Strep faecalis infections. Its efficacy against more resistant urinary pathogens like Pseudomonas, Kiebsiella, Proteus and Gonococci was comparable to other commonly used antibiotics. Infrequent adverse reactions, economy and convenience of dosage were responsible for higher patient compliance. In patients where oral therapy was not possible in early stages its availability in injectable form was found to be an added advantage.

Majority of our patients do not return for follow-up and repeated culture and sensitivity studies are not possible due to various economic and human factors. The use of an antimicrobial with low recurrence rate of infectiOn is therefore welcome to eradicate this potentially lethal disease (Carrol et al., 1970). Minocydline HCL with its effectiveness against E.coli infections, convenient dosage schedule and low recurrence rate of infection is likely to attain a certain place in the therapy of urinary tract infections.

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