

PHARMACOKINETIC PARAMETERS OF CIPROFLOXACIN IN BANGLADESHI VOLUNTEERS: A PRELIMINARY EVALUATION

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ABSTRACT

The present study has attempted to establish a High-performance liquid chromatography (HPLC) method to determine ciprofloxacin in plasma, in order to evaluate the bioavailability of ciprofloxacin. In this study, initially 8 (eight) Bangladeshi Bangalee healthy male volunteers and 7 (seven) Bangladeshi Tribal healthy male volunteers received 500 mg tablet of pioneer brand of ciprofloxacin in oral route. Blood samples were collected at 0, 30, 60, 120, 180, 360, 540 and 720 minutes after drug administration. After 1 week of washout period, same volunteers of two groups received 200 mg injection of pioneer brand of ciprofloxacin in intravenous route. HPLC with ultraviolet detection was used to quantify plasma ciprofloxacin concentrations. In case of oral route, AUC_{0-12hr} , C_{max} , T_{max} and $T_{1/2}$ values for Bangladeshi Bangalee and Tribal healthy volunteers were 545.53 ± 32.35 & 655.74 ± 16.57 $\mu\text{g min/mL}$, 2.19 ± 0.16 & 2.49 ± 0.20 $\mu\text{g/mL}$, 75.00 ± 27.77 & 94.29 ± 32.07 min and 241.96 ± 13.53 & 242.02 ± 19.88 min respectively. In case of intravenous route, the AUC_{0-12hr} , C_{max} , T_{max} and $T_{1/2}$ values for Bangladeshi Bangalee and Tribal healthy volunteers were 344.07 ± 29.31 & 343.31 ± 25.34 $\mu\text{g min/mL}$, 2.47 ± 0.17 & 2.46 ± 0.18 $\mu\text{g/mL}$, 30.00 ± 0.00 & 30.0 ± 0.0 min and 278.16 ± 1.74 & 272.74 ± 4.42 min respectively and the difference between these two groups of volunteers was not significant. The difference in AUC_{0-12hr} , C_{max} , T_{max} and $T_{1/2}$ values between these two groups of volunteers was significant. The mean percent absolute bioavailability in Bangladeshi Bangalee and Tribal healthy volunteers was 64.04 ± 3.21 and 76.81 ± 6.71 respectively. In conclusion, pharmacokinetic parameters of ciprofloxacin significantly varied among Bangladeshi Bangalee and Bangladeshi Tribal healthy volunteers indicating necessity of further study on population pharmacokinetic in these groups of people.

Keywords: Ciprofloxacin; Bangladeshi Bangalee; Bangladeshi Tribal; healthy volunteers; Pharmacokinetic parameters; Bioavailability

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INTRODUCTION

Bangladesh features different disease pattern than that of the developed countries because of its' socioeconomic and geographical difference. Infections are the main reason of morbidity and mortality, though recently burden of non-communicable diseases are increasing. Consequently, antimicrobials constitute a significant proportion of drug budget of Bangladesh.¹⁻⁵ In addition, emergence of resistance has worsened the situation. These issues jointly led to a position, where antimicrobials warrant immediate attention as the most important drug to watch in Bangladesh.^{2,6-7} Detail understanding about local, regional, and national antimicrobial susceptibility surveillance data is required in order to assist choice of appropriate agents.⁸ Though there are few studies on susceptibility pattern, however, very little is known about pharmacokinetic status of the Bangladeshi population regarding the antimicrobials.

Fluoroquinolones are extensively prescribed to treat different bacterial infections.⁹ Among the fluoroquinolones used in different level of health facilities of Bangladesh, ciprofloxacin is the most commonly consumed one.¹⁰ The commonly recommended oral dosage for adult patients is 250–500 mg twice a day. Whenever taken orally, the drug usually recommended to be taken after 2 hours of meal.¹¹ In order to explain the success and failure of antimicrobial therapy, there was effort to establish relationship between the in-vivo pharmacokinetic variability of ciprofloxacin at target site with the pharmacodynamics.¹² Though, the pharmacokinetic parameters of ciprofloxacin in Bangladeshi population are not yet known. Therefore, the variability of response with ciprofloxacin is now only partially explained by the available sensitivity data, nevertheless detail understanding about its' pharmacokinetic parameters is required to explain that further. Inadequate information about the pharmacokinetic status of Bangladeshi people led to necessity of research to enable scientists to understand these issues.

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This is generally perceived that our knowledge of the pharmacokinetics and pharmacodynamics of antimicrobials has achieved a significant advance. Though there are different fluoroquinolones, they have their common pharmacokinetic and pharmacodynamic properties. Contrasting to the β -lactams and aminoglycosides, fluoroquinolones are not remaining limited to the blood. Fluoroquinolones penetrate mucosal tissues effectively to reach concentrations several times greater than serum, which has particular clinical relevance. Polymorphonuclear leucocytes and macrophages concentrate the fluoroquinolones to varying degrees, usually in excess of four times than that of the serum. The pharmacokinetic study shows that ciprofloxacin is bioequivalent when given in different formulations.¹³ Solubility improvement converts the medicines as potential candidate for bio-waiver of in vivo bioequivalence (BE) testing for oral dosage forms of ciprofloxacin.¹⁴

There are different methods to estimate ciprofloxacin in plasma, especially by HPLC^{9, 15-16}, however, the initial challenge was to establish a suitable method to estimate plasma ciprofloxacin in laboratories of Bangladesh. Therefore, the aim of this study was to establish a method of estimation of ciprofloxacin in plasma as well as to get preliminary idea about the pharmacokinetic behaviour of Bangladeshi healthy volunteers of two different ethnic groups.

MATERIALS AND METHODS

Subject population

The present study was conducted in two ethnic groups of Bangladeshi healthy volunteers e.g., Bangalee and Tribal. The family and anthropometric history was considered for confirmation of categorization. This study included 8 (eight) Bangladeshi Bangalee male healthy volunteers, aged 23–25 years (23.88 ± 0.83 years), weighing between 50–60 kg (55.88 ± 3.44 kg) & within 15% of the ideal bodyweight and 7 (seven) Bangladeshi Tribal male healthy volunteers, aged 23–25 years (24.14 ± 0.69 years), weighing between 50–60 kg (54.14 ± 3.72 kg) & within 15% of the ideal bodyweight. Volunteers were screened to ensure that they have no cardiac, renal, hepatic, hematological, neurological, gastrointestinal and pulmonary disorders and allergy to ciprofloxacin. The volunteers were requested to stay away from any medication for two weeks prior to the study and up to its completion. Moreover, they were requested not to take any beverages like alcohol, coffee and tea in 48 h prior to first dose and until the collection of last blood sample.¹⁷

Medicines

Commercially available pioneer brand of ciprofloxacin 500 mg tablets and 200 mg injections were used.

Medicine administration schedule

This study was conducted in an open label design with one-week washout period between oral and intravenous doses. At the time of study, the volunteers were exclusively hospitalized at Z H Sikder Women's Medical College & Hospital, Dhaka, Bangladesh. Initially, all volunteers received oral dose of 500 mg ciprofloxacin tablet. After one-week wash period, the same volunteers received intravenous dose of 200 mg ciprofloxacin. The volunteers were monitored by principal researcher (an experienced physician) to detect adverse effects (if any) during the study.

Blood sample collection

For collection of blood samples, a catheter *in situ* was placed in one arm by the researcher with all aseptic precaution. The catheter was removed immediately if phlebitis develops, otherwise normally after the study period. Seven blood samples (3 ml at each occasion) were obtained at 0, 30, 60, 120, 180, 360, 540 and 720 minutes after drug administration and placed in sterile tubes with 100 μ L of 10% EDTA solution. Immediately after each blood collection, the samples were centrifuged at $3000 \times g$ for 15 min and plasma was then separated and stored at -70°C . The stored samples were then studied by HPLC in appropriate method.¹⁴⁻¹⁶

Sample analysis

Ciprofloxacin plasma concentrations were measured by HPLC. Specificity, linearity, lower limit of quantification (LLOQ), inter-day and intra-day precision and accuracy as well as absolute recovery and stability of ciprofloxacin was evaluated.

Chromatographic analysis

Ciprofloxacin analysis was performed using previously adapted and validated methods.¹⁸⁻²⁰

Chromatographic Condition

HPLC: Alliance HPLC, Origin: Waters USA (Separation Module, Model: Waters 2695; Detector, Model: Waters 2487 and Empower software)

Column: Symmetry C18 (2.5 cm x 4.6 mm), Waters-USA

Flow rate: 1.30 mL/min

Run Time: 10 min

Column Temperature: Ambient

Detector: UV detector

Test wave length: 278 nm

Cell temperature: 40°C

Injection Volume: 50 μ L

Reagents

Sodium Dihydrogen Phosphate Dihydrate (MW=156.01) – Analytical Reagent Grade
Acetonitrile – HPLC Grade.

Preparation of 0.025 M phosphoric acid buffer, pH=4.0

1.5 ml of conc. H₃PO₄ was taken in 1.0 L volumetric flask and then diluted with H₂O pH was adjusted at 4.0 with 5 M NaOH solution

Preparation of Mobile Phase

0.025 M phosphoric acid buffer: Acetonitrile = 80:20

Preparation of Diluent for Stock solution and Working Standard

Water: Acetonitrile = 95: 5

Preparation of stock solution

110.90 mg of Ciprofloxacin HCl (100 mg of Ciprofloxacin) was taken in 100ml volumetric flask. Then that was dissolved and diluted with H₂O

Preparation of Working Standard from Stock Solution (Concentration: 1000µg/mL)

Working Standard 1µg/mL: 0.1 mL of stock solution was taken in 100 mL of volumetric flask, diluted and then volume increased up to mark with diluent.

Working Standard 10µg/mL: 1.0 mL of stock solution was taken in 100 mL of volumetric flask, diluted and then volume increased up to mark with diluent.

Working Standard 100µg/mL: 10.0 mL of stock solution was taken in 100 mL of volumetric flask, diluted and then volume was increased up to mark with diluent.

Preparation of Lomefloxacin Solution

107 mg of Lomefloxacin (equivalent to 100 mg of Lomefloxacin) was dissolved in 100 mL volumetric flask, diluted and later volume increased up to the mark with Methanol (1000 µg/mL). 10 mL of this solution was taken in 100 mL volumetric flask and volume increased up to mark with methanol (100µg/mL). Then 0.15 mL of this solution was taken and 0.85 ml of methanol was added to make 1 mL of Final solution (15µg/mL).

Preparation of sample Solution:

0.1 mL of plasma was mixed with 0.90 ml of MeOH to make 1.0 mL of sample solution.

Injection Step

Step 1: 1 mL of drug free plasma + 9 mL MeOH = 10 mL solution as a blank

Step 2: 1 mL of drug free plasma + 1 mL Lomefloxacin (15µg/mL) + 8 ml MeOH = 10 mL solution

Step 3: 1 mL of drug free plasma + 1 mL of Ciprofloxacin (20µg/mL) + 1 ml Lomefloxacin (15µg/mL) + 7 mL MeOH = 10 mL solution

Step 4: Working Standard

Step 5: Samples

Specificity

The specificity of the method was determined by comparing the chromatograms obtained from the samples containing ciprofloxacin and internal standard with those obtained from blank samples.

Calibration and validation

Standard Ciprofloxacin samples were prepared in control plasma using standard stock solutions of Ciprofloxacin (1.00, 10.00 and 100.00 µg/mL). The overall coefficient of correlation between fluorescence and standard drug concentrations was 0.99+0.009 and the standard curve obtained was linear and followed Beer's law from 0.07 to 1.15 µg/mL. The overall recovery of Ciprofloxacin from plasma standard solutions was 98.85±1.86 per cent with a range of 98.85 to 100.41 per cent. The interday coefficient of variation of the recovery from standards in the above mentioned range was 2.21±1.83 per cent.

Pharmacokinetic and data analysis

Maximum observed plasma concentration (C_{max}) and time taken to reach it (T_{max}) were obtained from drug concentration vs. time curves. The areas under the ciprofloxacin concentrations vs. time curves from 0-12 hours (AUC_{0-12h}) were calculated using the trapezoidal method. $T_{1/2}$ was calculated through determining k_{el} by utilizing the intravenous data. C_{max} and AUC_{0-12h} data were analyzed statistically using parametric test, i.e., one-way ANOVA. A customized non-compartmental pharmacokinetics data analysis Excel template was developed to calculate and analyze the parameters.

Ethical clearance

The protocol of this study was approved by the National Research Ethics Committee of Bangladesh Medical Research Council. Informed written consent was obtained from all participants after explaining the nature, risk and benefits of the study to them.

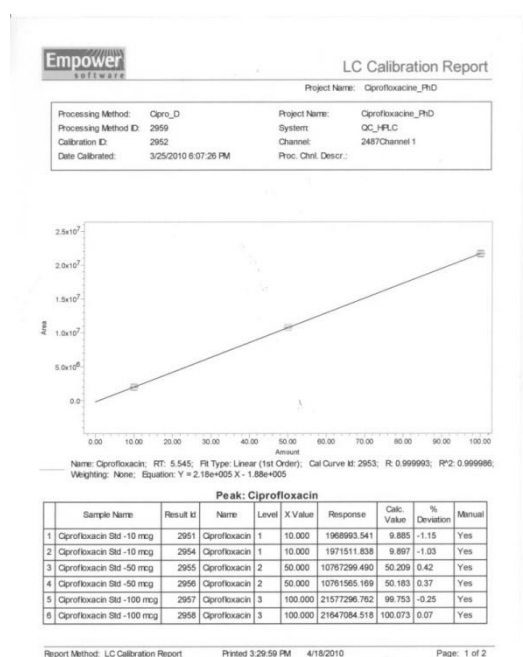
STATISTICAL ANALYSIS:

Data were analyzed by using SPSS soft-ware version 18. The values for quantitative data were expressed as mean, mean ± SD, while that of qualitative data were presented as percent.

RESULTS

All volunteers completed the study without any event, which was ascertained by thorough medical examination after study completion.

HPLC was sensitive in quantifying ciprofloxacin in plasma (limit of quantification = 0.1 µg/mL; $R^2 = 0.9996$). Fig 1 shows the calibration curve for the HPLC method.


Figure 1

Presentation of result with adjustment: In order to minimize the effect of variation in weight of the volunteers, the obtained actual plasma concentration was adjusted as per mg of ciprofloxacin per kg bodyweight and then used for calculation of different pharmacokinetic parameters. Therefore, the AUC_{0-8h} and C_{max} were calculated with two

values, one with the original plasma concentration of amoxicillin detected in HPLC and the other was with value obtained after adjustment. The Mean Percent Absolute Bioavailability was calculated by using the adjusted values.

Table I shows that there was no significant ($p>0.05$) difference between the subjects of two study groups in respect of different parameters.

Table II shows that in case of oral route, the AUC_{0-12h} for Bangladeshi Bangalee and Tribal healthy volunteers were 545.53 ± 32.35 & 655.74 ± 16.57 $\mu\text{g min/mL}$ respectively and the difference was statistically significant ($p<0.05$). The C_{max} values for Bangladeshi Bangalee and Tribal healthy volunteers were 2.19 ± 0.16 & 2.49 ± 0.20 $\mu\text{g/mL}$ respectively and the difference was statistically significant ($p<0.05$). The T_{max} for Bangladeshi Bangalee and Tribal healthy volunteers were 75.00 ± 27.77 & 94.29 ± 32.07 min and the difference was not statistically significant ($p>0.05$). The $T_{1/2}$ for Bangladeshi Bangalee and Tribal healthy volunteers were 241.96 ± 13.53 & 242.02 ± 19.88 min respectively and the difference was not statistically significant ($p>0.05$). The C_{trough} values for Bangladeshi Bangalee and Tribal healthy volunteers were 0.11 ± 0.01 & 0.12 ± 0.01 min respectively and the difference was not statistically significant ($p>0.05$).

Table III shows that in case of intravenous route, the AUC_{0-12h} for Bangladeshi Bangalee and Tribal healthy volunteers were 344.07 ± 29.31 & 343.31 ± 25.34 $\mu\text{g min/mL}$ respectively and the difference was not statistically significant. The C_{max} values for Bangladeshi Bangalee

Table I

Age, weight, height, Body Mass Index (BMI), serum creatinine, serum ALT and Prothrombin time of the Bangladeshi Bangalee and Tribal healthy volunteers

	Bangalee (n=8) Mean \pm SD	Tribal (n=7) Mean \pm SD	t	P value
Age (years)	23.88 \pm 0.83 (23.00 - 25.00)	24.14 \pm 0.69 (23.00 - 25.00)	0.68	>0.05
Weight (kg)	55.88 \pm 3.44 (51.00 - 60.00)	54.14 \pm 3.72 (51.00 - 60.00)	0.93	>0.05
Height (cm)	165.00 \pm 4.00 (160.00 - 172.00)	164.00 \pm 3.00 (160.00 - 170.00)	0.69	>0.05
Body Mass Index (BMI)	20.50 \pm 1.22 (18.87 - 22.58)	20.15 \pm 1.70 (18.59 - 23.15)	0.45	>0.05
Serum Creatinine (mg/dL)	0.76 \pm 0.09 (0.60 - 0.80)	0.74 \pm 0.08 (0.60 - 0.80)	0.45	>0.05
Serum ALT (U/L)	35.88 \pm 3.94 (30.00 - 45.00)	35.29 \pm 3.86 (30.00 - 40.00)	0.29	>0.05
Prothrombin Time (seconds)	9.88 \pm 0.83 (9.00 - 12.00)	10.29 \pm 0.49 (10.00 - 12.00)	1.18	>0.05

and Tribal healthy volunteers were 2.47 ± 0.17 & 2.46 ± 0.18 $\mu\text{g/mL}$ respectively and the difference was not statistically significant. The T_{max} for Bangladeshi Bangalee and Tribal healthy volunteers were 30.00 ± 0.00 & 30.0 ± 0.0 min and the difference was not statistically significant. The $T_{1/2}$ for Bangladeshi Bangalee and Tribal

healthy volunteers were 278.16 ± 1.74 & 272.74 ± 4.42 min respectively and the difference was statistically significant ($p < 0.05$). The C_{trough} values for Bangladeshi Bangalee and Tribal healthy volunteers were 0.07 ± 0.03 & 0.02 ± 0.01 min respectively and the difference was statistically significant ($p < 0.05$).

Table II

Pharmacokinetic parameters following oral administration of 500 mg ciprofloxacin tablet in Bangladeshi Bangalee and Tribal healthy volunteers

Pharmacokinetic parameters	Bangalee (n=8) Mean \pm SD	Tribal (n=7) Mean \pm SD	ANOVA	t	P value
AUC_{0-12h} ($\mu\text{g min/mL}$)	545.53 ± 32.35 (498.09 - 586.91)	655.74 ± 16.57 (637.71 - 683.09)	65.71	2.34	<0.05
C_{max} ($\mu\text{g/mL}$)	2.19 ± 0.16 (2.00 - 2.41)	2.49 ± 0.20 (2.27 - 2.77)	10.89	3.25	<0.05
T_{max} (min)	75.00 ± 27.77 (60.00 - 120.00)	94.29 ± 32.07 (60.00 - 120.00)	0.00	1.24	>0.05
$T_{1/2}$ (min)	241.96 ± 13.53 (222.88 - 258.29)	242.02 ± 19.88 (209.53 - 262.83)	0.00	0.01	>0.05
C_{trough} ($\mu\text{g/mL}$)	0.11 ± 0.01 (0.10 - 0.12)	0.12 ± 0.01 (0.10 - 0.13)	0.75	0.83	>0.05
AUC_{0-12h} ($\mu\text{g min/mL per mg/kg}$)	61.54 ± 3.66 (57.37 - 66.91)	71.04 ± 5.83 (65.38 - 81.97)	14.67	3.72	<0.05
C_{max} ($\mu\text{g/mL per mg/kg}$)	0.25 ± 0.02 (0.22 - 0.27)	0.27 ± 0.03 (0.23 - 0.32)	2.93	1.64	>0.05

With adjusted value means the original values obtained was later adjusted for per mg of ciprofloxacin/kg bodyweight

Table III

Pharmacokinetic parameters following intravenous administration of 200 mg ciprofloxacin in Bangladeshi Bangalee and Tribal healthy volunteers

Pharmacokinetic parameters	Unit	Bangalee (n=8) Mean \pm SD	Tribal (n=7) Mean \pm SD	ANOVA	t	P value
AUC_{0-12h}	($\mu\text{g min/mL}$)	344.07 ± 29.31 (299.31 - 373.79)	343.31 ± 25.34 (312.08 - 382.43)	12.28	0.02	>0.05
C_{max}	($\mu\text{g/mL}$)	2.47 ± 0.17 (2.22 - 2.68)	2.46 ± 0.18 (2.21 - 2.74)	4.08	0.17	>0.05
T_{max}	(min)	30.00 ± 0.00	30.00 ± 0.00	0.00	0.00	NA
$T_{1/2}$	(min)	278.16 ± 1.74 (275.63 - 280.68)	272.74 ± 4.42 (267.02 - 277.97)	12.83	3.05	<0.05
C_{trough}	($\mu\text{g/mL}$)	0.07 ± 0.03 (0.03 - 0.10)	0.02 ± 0.01 (0.01 - 0.03)	15.92	4.23	<0.05
AUC_{0-12h}	($\mu\text{g min/mL per mg/kg}$)	96.16 ± 4.80 (89.79 - 103.90)	92.57 ± 2.47 (87.98 - 95.61)	3.16	1.85	>0.05
C_{max}	($\mu\text{g/mL per mg/kg}$)	0.69 ± 0.03 (0.67 - 0.74)	0.66 ± 0.01 (0.64 - 0.69)	6.47	2.66	<0.05

With adjusted value means the original values obtained was later adjusted for per mg of ciprofloxacin/kg bodyweight

Table IV

Mean Percent Absolute Bioavailability (MPAB) of ciprofloxacin in Bangladeshi Banglaee and Tribal healthy volunteers

	Banglaee n = 8			Tribal n = 7			ANOVA	t value	p value
	Oral	IV	MPAB	Oral	IV	MPAB			
Subject 1	60.47	89.79	67.35	65.53	95.61	68.54	6.65	4.59	<0.01
Subject 2	60.96	89.79	67.89	65.38	93.81	69.70			
Subject 3	62.35	97.91	63.69	81.97	93.62	87.55			
Subject 4	57.37	95.08	60.34	71.67	91.34	78.47			
Subject 5	57.68	97.18	59.35	73.97	93.80	78.86			
Subject 6	66.91	100.03	66.89	71.31	87.98	81.05			
Subject 7	66.76	103.90	64.26	67.47	91.82	73.48			
Subject 8	59.77	95.58	62.54						
Mean	61.54	96.16	64.04	71.04	92.57	76.81			
SD	3.66	4.80	3.21	5.83	2.47	6.71			

Calculated on the basis of adjusted AUC from plasma concentrations obtained after oral (500mg) and intravenous (200mg) administration of ciprofloxacin and expressed as per mg ciprofloxacin/kg bodyweight

Table IV shows that the Mean Percent Absolute Bioavailability in case of Bangladeshi Banglaee and Bangladeshi Tribal healthy volunteers was 64.04 ± 3.21 and 76.81 ± 6.71 respectively. The difference between these two values were highly significant ($p < 0.01$).

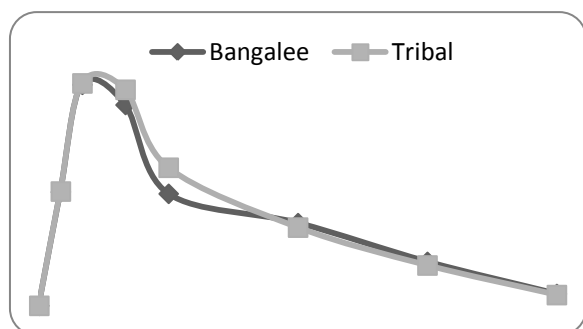


Figure 2: Time concentration curve obtained by plotting the mean plasma concentrations of ciprofloxacin estimated at different point of time (in oral route)

Figure 2 showing the time concentration curves obtained in the oral route. There are difference in the shape, slope and peak between the curves of Bangladeshi Banglaee and Tribal healthy volunteers. Difference is particularly observed in the mean concentrations obtained at 120, 180 and 230 minutes.

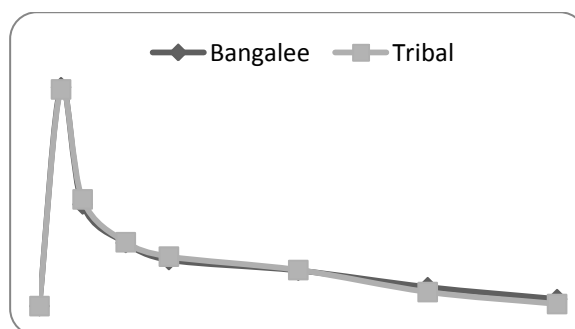


Figure 3: Time concentration curve obtained by plotting the mean plasma concentrations of ciprofloxacin estimated at different point of time (in intravenous route)

Figure 3 showing the time concentration curves obtained in the intravenous route. The curves reflect no difference in the shape and slope between the curves of Bangladeshi Banglaee and Tribal healthy volunteers. The C_{max} is calculated by backward extrapolation of data up to 0 minute. The C_{max} in case of Banglaee and Tribal derived through extrapolation is 2.46 and 2.47 $\mu\text{g/mL}$ respectively.

DISCUSSION

Pharmacokinetic parameters of ciprofloxacin have been investigated at different doses of 250, 500, 750 and 1000 mg.¹⁹⁻²² Previous studies using chromatography have reported C_{max} values of 2.18 µg/mL after oral administration of 500 mg ciprofloxacin,¹³ and 1.5 µg/mL after 250 mg ciprofloxacin.²³ The C_{max} observed in the present study after oral administration was modestly higher in case of Tribal and lower in case of Bangalee Bangladeshi in relation to the findings of the previous studies probably due to the dissimilarity in the population studied. Regarding intravenous route, one study¹⁶ has provided idea about the AUC_{0-12h} and C_{max} , which are in cystic fibrosis patients and were 48.3 µg h/mL and 2.9 µg/mL respectively.

The AUC_{0-12h} obtained in the present study for intravenous route both in case of Tribal and Banglaee was very low in comparison to the result observed by Montgomery et al 2001.¹⁶ The AUC_{0-12h} obtained in the present study for oral route in case of Tribal was comparable to the findings of previous study,¹³ although the values for Bangalee were low.

Nevertheless, the T_{max} observed in the present study was parallel to the values revealed by previous researcher¹³ using same dose but that is different with findings with another study.²³ However, the similarity in these findings reiterating the fact that different doses of the same drug have no influence on T_{max} values.

For $T_{1/2}$ values, different studies revealed a range of 2.9 hours to 5.37 hours with a mean of 100 minutes²¹⁻²⁴ and the present study finding is similar to those observations.

The Mean Percent Absolute Bioavailability obtained in both Bangalee and Tribal volunteers in the present study appears to be lower than the previous report.²⁵

In order to explain the significant difference observed in the present study, different meta-analysis and reviews were considered. Meta-analysis and reviews revealed that metabolism of different drugs has little association with CYP2C19 genotype.²⁶ Study also suggests that the dose can be increased in populations with high frequencies of HomEMs or HetEMs.²⁷

The pharmacokinetic parameters of amoxicillin in ethnically different Bangladeshi populations were revealed in a previous study, which was similar to the findings of the present study reiterating the necessity of further study with this focus.²⁸ The pharmacokinetic parameters of orally administered ciprofloxacin tablet are well understood as a result of series of studies.²⁹⁻³³ In general, ciprofloxacin tablets dissolve rapidly in the gastrointestinal tract and are absorbed in the duodenum and jejunum. Following oral dosing, the bioavailability of ciprofloxacin is between 70% and 80%.³⁴

The revealed significant difference between two groups of Bangladeshi healthy volunteers is really an interesting finding, which require further exploration with especial emphasis into genetic correlation. Further exploration might help to develop a population pharmacokinetic model,³⁵ which will enable the researcher to suggest prescriber regarding optimum dosage calculation at an individual level applicable for Bangladeshi population. This type of difference in pharmacokinetic properties of Bangladeshi healthy volunteers needs to be correlated with therapeutic outcome as well.

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