Pak. j. life soc. sci. (2003), 1(1): 57-58

Pakistan Journal of
Life and Social Sciences

Urinary Excretion of Trimethoprim in Female Volunteers

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Abstract

The urinary excretion of free trimethoprim (TMP) was studied in eight healthy adult female volunteers. Urine samples were collected at predetermined time intervals after giving a single therapeutic dose (160 mg trimethoprim + 800 mg sulfamethoxazole) orally. The concentration of trimethoprim in urine was determined by spectrophotometery. The total urinary excretion of free trimethoprim is 6.26 percent during 12 hours. It was concluded that urinary excretion of TMP was high in foreign subjects due to difference in environmental conditions. The study was conducted in month of July so the rate of urine flow was less.

Key words: Excretion, Trimethoprim, human volunteers

Introduction

Trimethoprim is a broad spectrum antibacterial agent. It is used to treat infections of upper and lower respiratory tract, urinary tract and middle ear.

Trimethoprim is most often combined with sulfa drugs, like sulfamethoxazole. It was demonstrated that trimethoprim and sulfamethoxazole potentiated each other, with the result that together their antibacterial effects were greatly enhanced. The action of combination proved to be bactericidal, whereas, components separately were bacteriostatic. (Mandell and Petri, 1996).

The urinary excretion of trimethoprim has been described in human beings (Black, Israel and Farid, 1977, Nielson and Rasmussen, 1977; Jarl and Erik, 1982; Babar, 2002). The optimal therapeutic regimen of a drug is best determined in human beings under environment in which the drug is to be applied. In view of this, the urinary excretion of trimethoprim has been investigated in female human volunteers in the present study.

Materials and Methods

The project was designed to study the urinary excretion of free trimethoprim in female human beings after the oral administration of therapeutic dose. The study was conducted on eight clinically healthy female volunteers aging between 21 to 23 years.

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The average weight of the volunteers was 57 kg (range 49 to 65 kg), average height 5′-3″ inches (range 5′-2″ to 5′-6″ inch), average blood pressure 109/71 mmHg (range 100/60 to 120/80 mmHg) and average body temperature 96.8°F (range 94 to 98°F). the experiments were conducted in the month of July.

Drug administration

Septran DS ("Galaxo-Welcome Pakistan Limited") was administered as a single dose (160 mg trimethoprim + 800 mg sulfamethoxaozle) orally to each volunteer.

Collection of urine samples

A blank urine sample was collected from each volunteer before administration of drug. Urine samples were collected at 60, 120, 180, 240, 360, 480 and 720 minutes after oral administration of trimethoprim. The pH and total volume of urine voided during this time period were recorded. Urine samples were stored at –20°C for further analysis.

Analysis of drug in urine

Sample of urine with standard concentrations of (2, 4, 6, 8, 10, 12, 14 and 16µg/mL) trimethoprim were prepared in drug free/control urine. TMP was extracted from urine samples by chloroform and then back extraction was done in aqueous media using 0.1 N H_2SO_4. The aqueous extract was analyzed by spectrophotometer at 271 nm (Clarke, 1974). Absorbance versus concentrations of standards were plotted and linear curve was obtained.

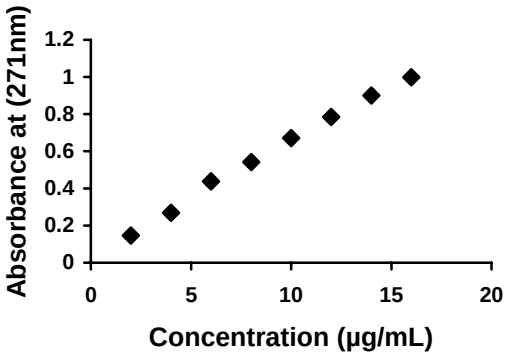

Fig. 1. Standard curve of trimethoprim in urine of female volunteers

The percent cumulative dose excreted during 720 min was determined and average ±SE value was calculated (Steel and Torrie, 1992).

Results and Discussion

The urinary excretion of free TMP was studied in eight female volunteers. The average percent cumulative dose excreted in urine during 12 hours is 6.26% (Table 1).

In other studies the total urinary excretion were less than 15% (Nielsen and Rassmussen, 1975), 9.24% in 12 hours (Babar, 2002), 35% in 24 hours (Black *et al.*, 1977) and 66 to 95% in 120 hours (Jarl and Erik, 1982). Here the difference in values is due to the difference in season with the fact that evaporatory loss of the body water reduces urine flow during summer while lower environmental temperature increases rate of urine flow (Nawaz and Shah, 1984). The difference is also due to gender variability, fluctuation in urine pH, environmental conditions and nutritional ingredients (Nawaz, 1994).

Glomerular filteration rate, passive tubular reabsorption, tubular molar clearance, plasma osmotic pressure, antidiuretic harmone (Guyton, 1996) and blood pressure also affect the rate of urine flow (Frandson, 1974).

Table 1: Percent cummulative dose of Trimethoprim excreted in urine of female volunteers after oral administration (160 mg).

Time (min)	Volunteers									
	A	B	C	D	E	F	G	H	Average	±SE
60	0.856	0.505	0.221	0.650	0.337	0.681	0.462	0.457	0.521	0.067
120	1.73	1.03	0.477	1.31	0.734	1.37	1.19	1.30	1.14	0.129
180	2.61	1.59	0.884	2.26	1.14	2.35	2.19	2.33	1.92	0.211
240	3.50	2.29	1.30	3.31	1.59	3.34	3.58	3.52	2.80	0.310
360	4.42	3.12	1.80	4.37	2.15	4.35	5.04	4.80	3.76	0.409
480	5.41	3.98	2.30	5.43	2.86	5.41	7.42	6.13	4.87	0.565
720	6.55	5.31	2.86	6.61	4.05	6.73	10.41	7.57	6.26	0.757

Table 2: cummulative amount (mg) to Trimethoprim excreted in female volunteers after oral administration (160 gm).

Time (min)	Volunteers									
	A	B	C	D	E	F	G	H	Average	±SE
60	1.37	0.808	0.353	1.04	0.539	1.09	0.739	0.731	0.834	0.107
120	2.77	1.65	0.763	2.10	1.17	2.19	1.91	2.07	1.83	0.207
180	4.18	2.55	1.41	3.62	1.83	3.76	3.51	3.72	3.07	0.335
240	5.61	3.67	2.07	5.30	2.55	5.35	5.73	5.63	4.49	0.497
360	7.08	5.00	2.87	7.00	3.44	6.97	8.06	7.67	6.01	0.655
480	8.67	6.37	3.68	8.70	4.58	8.66	11.87	9.79	7.79	0.903
720	10.49	8.49	4.57	10.59	6.48	10.77	16.66	12.10	10.02	1.21

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