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Research Article

URINARY EXCRETION OF THIAMPHENICOL FOLLOWING PARENTERAL ADMINISTRATION IN GOATS

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ABSTRACT

Present study was conducted in goats to determine the urinary excretion of thiamphenicol following extravascular and intravascular administration at the dose rate of 30 mg/kg. Renal excretion was the major route of elimination of thiamphenicol as more than 50% of the drug administered was excreted through urine. Excretion after i.v. administration was very fast. Almost one-third of the total administered dose was excreted within first three hours. Almost comparable amount of the drug was excreted in six h following i/m route and 12 h following s/c route. About 50% of the total administered dose was excreted in 6 h, 12 h and 30 h following i/v, i/m and s/c route of administration, respectively. The cumulative per cent excretion of the total dose of thiamphenicol, within detectable limit of 6 µg/ml by microbiological assay, was 60.27±1.67%, 55.21±1.40% and 51.11±1.32% following i/v, i/m and s/c route of administration, respectively during 24, 36 and 42 h, respectively. However, thereafter, the drug could not be detected in urine.

Key words: Thiamphenicol, urinary excretion, intravascular, extravascular

Thiamphenicol (TAP) is a broad spectrum antibiotic and closely related to chloramphenicol (CAP). It is active against both Gram-negative and Gram-positive bacteria and is especially effective on anaerobes. Thiamphenicol is intended for treatment and control of respiratory and intestinal infections of animals usually cattle and poultry (European Agency for the Evaluation of Medicinal Products, 1997) and is also intended for intramammary administration in both lactating and dry cows. Its pharmacokinetics has been studied in many species of animals including goats (Kumar *et al.*, 2003 a and Kumar *et al.*, 2003 b) following various routes of administration. Urinary excretion data of TAP in animals including goats is scarce, therefore, the present study was undertaken to determine the urinary excretion of TAP in goats following intravascular and extravascular routes of administration.

MATERIALS AND METHODS

Present study was undertaken on five male beetal goats of 1 to 1½ year age weighing 15 to 22 kg. Thiamphenicol (Technical grade, Sigma, USA) was dissolved in N, N-dimethylacetamide to prepare 30 % solution (w/v) for parenteral administration. Thiamphenicol was administered to goats through intravenous, intramuscular or subcutaneous routes at the dose level of 30 mg/kg body weight. All the animals had free access to feed and water through out the study. Urine of goats was collected with the help of specially designed urine collecting bags. The total volume of urine voided by animals during different time intervals was collected and measured. An aliquot of each urine sample was then filtered through filter paper (Whatman No. 1) and centrifuged at 4500 rpm for 30 min and stored in freezer of refigerator (-7°C) until analysed for the level of thiamphenicol within a weak of collection. The concentration of thiamphenicol in urine was determined by agar well diffusion assay according to the method of Arret *et al.* (1972). The *Micrococcus luteus* (MTCC 1541) was used as the test organism. The minimum detection limit of the assay was 6 µg/ml of thiamphenicol. The data was presented as mean±S.E. (Snedecor and Cochran, 1967).

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RESULTS AND DISCUSSION

The urinary excretion data of thiamphenicol are summarized as drug excreted, cumulative drug excreted, percent drug excreted and cumulative percent drug excreted following different routes of administration (Table 1).

Thiamphenicol could be detected in urine up to 24 h post-administration following single i/v dose. The total drug excreted in urine in 24 h was 319.08±26.97 mg which is 60.27±1.67% of the administered dose. More than 50 per cent of total drug administrated was excreted within first 6 h. From 6 h onwards, the excretion was very low as almost eight per cent of the drug was excreted between 6 and 24 h post-administration.

Thiamphenicol is concentrated in urine possibly in unchanged state and could be detected in urine for up to 24 h. Such a high excretion of TAP in urine of goats suggests a strong ability of kidneys of goats to concentrate TAP in urine. Kumar *et al.* (2003b) reported short elimination half-life (1.56±0.09 h) of TAP following intravenous administration which indicated rapid clearance of drug from the central compartment. Distribution was rapid while transfer of drug from peripheral to central compartment was slow (k_{21}=1.62±0.10 < k_{12}=3.86±0.19 h^{-1}). Therefore based on the pharmacokinetic determinants (Kumar *et al.*, 2003b), it may be suggested that TAP probably readily concentrate in kidney and excreted in urine. Urinary excretion of florfenicol, a congener of thiamphenicol, following i/v administration in veal calves was slightly more than 50% of the administered dose during 30 h (Varma *et al.*, 1986)

Urinary excretion data of thiamphenicol following i/m administration (30 mg/kg) in goats is shown in the table. During first three hours post-drug administration the total excreted drug was 120.31±6.40 mg but during the next three hours, it was lesser than the first spell of three hours and the total amount of drug excreted was 92.99±5.91 mg. Nearly 50 per cent of the total administered drug was excreted up to 12 h; however, TAP could be detected in urine for upto

Table 1

Mean excretion of thiamphenicol in urine following single parenteral administration in goats (n=5)

Duration (h)	Drug excreted (mg)			Cummulative drug excreted (mg)			Per cent drug excreted			Cummulative per cent drug excreted		
	i/v	i/m	s/c	i/v	i/m	s/c	i/v	i/m	s/c	i/v	i/m	s/c
0 – 3	183.03 ±15.29	120.31 ±6.40	78.53 ±4.70	183.03 ±15.29	120.31 ±6.40	78.53 ±4.70	34.62 ±1.33	20.53 ±0.84	11.70 ±1.05	34.62 ±1.33	20.53 ±0.84	11.70 ±1.05
3 – 6	93.16 ±9.33	92.99 ±5.91	80.81 ±2.09	276.19 ±24.21	213.30 ±11.08	159.34 ±5.67	17.54 ±0.80	15.81 ±0.54	11.99 ±0.60	52.16 ±1.91	36.34 ±0.98	23.69 ±1.56
6 – 9	28.07 ±2.24	48.85 ±6.21	50.64 ±6.19	304.26 ±25.43	262.15 ±11.63	209.98 ±10.09	5.32 ±0.30	8.35 ±0.97	7.61 ±1.17	57.49 ±1.65	44.69 ±0.76	31.30 ±2.59
9 – 12	6.94 ±0.94	28.84 ±5.89	33.93 ±4.66	311.27 ±26.32	290.99 ±16.53	243.91 ±9.81	1.31 ±0.12	4.82 ±0.81	4.96 ±0.53	58.79 ±1.76	49.52 ±1.12	36.25 ±2.43
12 – 18	6.03 ±1.24	16.78 ±1.11	59.05 ±6.24	317.23 ±26.76	307.78 ±16.49	302.95 ±7.70	1.13 ±0.20	2.91 ±0.31	8.64 ±0.72	59.92 ±1.66	52.42 ±1.32	44.90 ±1.92
18 – 24	1.85 ±0.21	6.89 ±0.66	27.28 ±6.37	319.08 ±26.97	314.66 ±16.93	330.23 ±7.32	0.35 ±0.02	1.16 ±0.08	3.98 ±0.90	60.27 ±1.67	53.59 ±1.27	48.88 ±1.48
24 – 30	-	4.21 ±0.67	8.71 ±2.49	-	318.87 ±17.30	338.94 ±9.53	-	0.72 ±0.10	1.25 ±0.34	-	54.30 ±1.32	50.12 ±1.40
30 – 33	-	2.93 ±0.45	3.02 ±0.75	-	321.80 ±17.46	341.96 ±9.86	-	0.50 ±0.08	0.44 ±0.10	-	54.81 ±1.37	50.56 ±1.35
33 – 36	-	2.36 ±0.57	1.82 ±0.56	-	324.16 ±17.70	343.78 ±10.14	-	0.40 ±0.10	0.26 ±0.08	-	55.21 ±1.40	50.82 ±1.34
36 – 42	-	-	1.98 ±0.49	-	-	345.77 ±10.32	-	-	0.29 ±0.07	-	-	51.11 ±1.32

36 h. The total amount of drug excreted in urine was 324.16±17.70 mg. In terms of percent values it is equal to 55.21±1.40 per cent of the total drug administered. Total urinary recovery of TAP in calves has been reported to range between 22 and 59 % (EAEMP, 1997) following a single i/m injection at the rate of 25 mg/kg.

Following s/c administration the excretion of TAP was almost equal during first two intervals of 3 hours each, i.e. 78.53±4.70 mg and 80.81±2.09 mg in first and second interval of three hours, respectively and constituted about 12 per cent of the total drug administered per three hours. Therefore, nearly 24 per cent of the drug administered was excreted within 6 h. There after urinary excretion of thiamphenicol was very slow and the drug could be detected in urine up to 42 hours. The total thiamphenicol excreted during 42 h was 51.11±1.32 per cent of the administered dose.

Following all the parenteral routes, more than 50 % of the drug administered dose or TAP was excreted through urine. Excretion was fastest following i/v route and slowest following s/c route of administration. About 50 per cent of the total dose administered was excreted in 6 hours following i/v route, 12 hours following i/m route and 30 hours following s/c route. The cumulative per cent excretion of the total dose of thiamphenicol was 60.27±1.67% following i/v route in 24 h, 55.21±1.40% following i/m route in 36 h and 51.11±1.32% following s/c route in 42 h. Thus suggesting that urinary excretion of TAP is influenced by its absorption from the site of drug administration, and also possibly due to slow distribution.

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