Indian Journal of Drugs, 2014, 2(2), 36-38 ISSN: 2348-1684

Research Article

INVESTIGATION OF DIURETIC ACTIVITY OF OMEPRAZOLE IN ANIMAL MODELS

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Received: 29-03-2014
Accepted: 22-06-2014

Access this article online

Website:
www.drugresearch.in

Quick Response Code:

ABSTRACT

Diuretic agents are useful in reducing decrease plasma volume and venous return, this inturn reduce the cardiac overload, oxygen demand and plasma volume, thus decreasing blood pressure. Omeprazole is a proton pump inhibitor and mostly prescribed drug in the treatment of the peptic ulcer disease, GERD and zollinger-Elison syndrome. Some studies reveal that as omeprazole inhibits the carbonic anhydrase enzyme in gastric mucosa and erythrocytes. Present study is to determine the role of omeprazole in the diuretic action in healthy rats. All the values are shown as mean SEM and the results were statically analyzed using one way ANOVA followed by student t-test. The results of Omeprazole are compared with standard Furosemide and Acetazolamide drug. In the evaluation of diuretic activity, Urea treated rats showed a significant increase in volume of urine and urinary excretion of sodium, potassium, chloride ($P<0.01$) as compared with control. Omeprazole showed significant change urine excretion but effective in increasing the sodium ions and much less effect as diuresis. On the basis of the results, we conclude that omeprazole can be used as a diuretic agent at higher doses and the structural modification is recommended for the better activity.

KEY WORDS: Lipschitz method, Omeprazole, Furosemide, Acetazolamide, Carbonic Anhydrase

INTRODUCTION

Diuretics are the drugs that promote urine production, sodium excretion and adjust volume of body fluids in various clinical situations. They have been considered an effective treatment for diseases like hypertension, cardiac failure, nephritis syndrome and pulmonary edema. There are several classes of diuretics and they increase the excretion of water from the body by acting through different mechanisms[1,2]. Diuretics are capable of increasing the flow of urine and are useful in the treatment of disease related with the retention of fluids.Omeprazole is a proton pump inhibitor and mostly prescribed drug in the treatment of the peptic ulcer disease, GERD and zollinger-Elison syndrome. Some studies reveal that as omeprazole inhibits the carbonic anhydrase enzyme[3] in gastric mucosa and erythrocytes. Carbonic anhydrase enzyme inhibitors are the drug of choice in the treatment of oedema and omeprazole could inhibit the renal carbonic anhydrase enzyme as it is the mainstay of diuretic activity[4,5]. Hence the following study was undertaken for the investigating the diuretic activity in healthy rats. The method of lipschitz et al was employed for the assessment of diuretic activity.

Material and Methods

Experimental Animals:Male Wister albino rats were used for this study with the weight range of 180-200g. They were fed with standard diet and water *ad libitum*. The animals were housed in polypropylene cages maintained under standard environmental conditions (12h light/12h dark cycle: 25± 3°c 35-60% relative humidity).Drugs:Urea, Acetazolamide (Wyeth limited, Mumbai), Furosemide (Lupin Ltd, Aurangabad), Omeprazole (Dr. Ready's laboratories, Hyderabad) were procured from the pharmacy.Experimental:The method of lipschitz et al was employed for the assessment of diuretic activity[6], the urine output and sodium, potassium and chloride levels in the urine were measured. The animals were divided into five groups in each group containing six animals. The animals were deprived of food and water for 16hrs prior to the experiment. Group1 and 2 receive Saline and furosemide acts as control and standard groups. The other groups receive acetazolamide, omeprazole and

urea respectively. Before the oral administration of test drugs, the animals were dosed with 25ml/kg body weight of normal saline.Immediately after administration, the animals were placed in metabolic cages individually to allow separation of urine and faeces. The urine was collected for 5, 10, 15, 20, 24 hrs after administration of control, standard and test drugs. During this period no water and food was made available to animals. The urine volume was measured with graduated measuring cylinder.The parameters taken for each individual rat were total urine volume, urine concentration of sodium, potassium and chloride. Concentration of sodium and potassium was determined with flame photometer while chloride concentration was estimated by titrimetrically. The mean urine volumes were determined and diuretic potency was assessed by comparison of urine excretion due to test with respect to the standard drug frusemide[7,8].

STATISTICAL ANALYSIS

All the values are shown as mean SEM and the results were statically analyzed using one way ANOVA followed by student't' test.

RESULTS

The results of Omeprazole are compared with standard Frusemide and Acetazolamide drug. In the evaluation of diuretic activity, Urea treated rats showed a significant increase in volume of urine and urinary excretion of sodium, potassium, chloride ($P<0.01$) as compared with control. Omeprazole showed significant change urine excretion but effective in increasing the sodium ions and much less effect as diuresis [9,10] and Evaluated study is listed in table 1. All the tests showed significant Lipschitz values listed in table 2. Rats showed a significant increase in volume of urine and urinary excretion of Na^+, K^+ and Cl^- as compared to control[11] is listed in table 3.

Table 1: Diuretic activity of different drugs

Treatment	Dose(mg/kg)	Volume of urine (ml /100 gm)				
		After 5 hr	After 10 hr	After 15 hr	After 20 hr	After 24 hr
vehicle	-	2.0±0.1	2.7±0.2	3.5±0.3	3.9±0.1	4.4±0.1
Urea	1000	3.9±0.1	4.2±0.1	4.4±0.1	5.0±0.2	5.7±0.1
Furosemide	40	2.8±0.1	4.1±0.1	4.5±0.2	5.0±0.1	5.8±0.1
Acetazolamide	30	2.5±0.1	3.2±0.2	3.8±0.1	4.6±0.1	5.0±0.1
Omeprazole	20	2.3±0.1	2.9±0.1	3.5±0.1	3.9±0.1	4.5±0.1

All values are mean ±SEM (n=6); *p< 0.01 when compared to control.

Table 2: Lipschitz value of different drugs

Treatment	Dose(mg/kg)	Lipschitz value T/U value				
		After 5 hr	After 10 hr	After 15 hr	After 20 hr	After 24 hr
Furosemide	40	0.71	0.97	1.02	1.00	1.01
Acetazolamide	30	0.64	0.76	0.86	0.92	0.87
Omeprazole	20	0.58	0.69	0.79	0.78	0.78

All values are mean ±SEM (n=6); *p< 0.01 when compared to control.

Table 3: Parameters of diuretic activity of different drugs

Treatment	Dose(mg/kg)	Concentration of ions (meq./L) at 24 h			
		Na^+	K^+	Cl^-	Na^+/K^+
vehicle	-	62.67±0.04	54.65±0.02	53.64±0.02	1.15
Urea	1000	81.32±0.05	65.37±0.04	75.12±0.01	1.24
Frusemide	40	94.21±0.01	78.28±0.01	91.15±0.07	1.20
Acetazolamide	30	79.52±0.02	78.02±0.01	69.45±0.04	1.02
Omeprazole	20	84.25±0.01	74.23±0.04	81.91±0.06	1.13

All values are mean ±SEM (n=6); *p< 0.1 when compared to control.

DISCUSSION AND CONCLUSION

Diuretic agents are useful in reducing the syndrome of volume overload, pulmonary congestion including orthopnea and paroxysmal nocturnal dysponea. Theydecrease plasma volume and venous return, this inturn reduce the cardiac overload, oxygen demand and plasma volume, thus decreasing blood pressure. In present study, demonstrates the omeprazole diuretic activity by increasing the excretion of Na^+, K^+ and Cl^-. On the basis of the results, we conclude that omeprazole can be used as a diuretic agent at higher doses and the structural modification is recommended for the better activity.

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Cite this article as:
Abhinayani, G., Sravya, N., Somashankar, V. and Kishore, R.N. (2014).Investigation of diuretic activity of omeprazole in animal models. Indian J. Drugs, 2(2), 36-38.