ORIGINAL **PROF-679**

EFFECT OF ALPRAZOLAM THERAPY

DR. AHMAD DANYAL
Assistant Professor
Nishtar Medical College . Multan

DR. ABRA NAZIR
Assistant Professor
Nishtar Medical College, Multan

DR. KHALID MAHAMOOD QURESHI
Assistant Professor
Nishtar Medical College, Multan

Dr. Roohi Manzoor
Professor of Pharmacology
Nishtar Medical College, Multan

ABSTRACT
Alprazolam is a triazolabenzodiazepine which is metabolized by liver and excreted through kidneys. While passing through kidneys, it is expected that it may deteriorate the functions of kidneys especially if kidneys are malfunctioned due to some disease. To assess this hypothesis, tab alprazolam, 0.25 mg, P.O. was given to five control and fifteen renal insufficient persons for a< period of twenty one days. As creatinine clearance is a good indicator for renal functions, so it was used as a parameter to evaluate kidney functions. Ccr was assessed at day zero and day twenty one in both control and renal insufficient subjects during the course of alprazolam therapy. No remarkable difference in Ccr was found in between control group on day zero and twenty one. Also there was no difference in Ccr in renal insufficient patient on both days. But there was a sharp difference in mean values of Ccr on day zero and 21 when controls were compared with renal insufficient group on day zero and twenty one. So it was concluded that long term alprazolam therapy have no significant effect on Ccr in renal insufficient patients. Alprazolam is a benzodiazepine currently used as an anxiolytic drug. SETTING: In the department of Pharmacology and Therapeutics, BMSI Karachi,

KEYWORDS: Alprazolam , Creatinine clearance

INTRODUCTION

In addition, alprazolam may be useful in the treatment of reactive depression, which is commonly seen in medically ill patients with significant psycho social stressors e.g. patients with end stag renal disease[123]. In patients with impaired renal function, drug treatment is often complicated by altered kinetics, especially in the case of polar compounds eliminated predominantly by the kidneys. Many such substances have therefore been studied with renal failure and dosage recommendations have been made. On the other hand, it has assumed that elimination of lipid soluble drugs is not altered in uremia. As has been shown in the last few years, in chronic renal failure, metabolism of drugs may be enhanced, unaltered or slowed[4].

The level of creatinine is much less dependent on diet but is more related to age, sex and muscle mass. Once it is elevated, screen creatinine is a better guide to GFR than urea and so measurement of serum creatinine is a good way to monitor further deterioration in the GFR. Measurement of the GFR is necessary to define the exact level of renal function. It is essential when the blood urea or serum creatinine are within the normal range. Inulin clearance is not practical in

clinical practice. The most widely used measured is the Ccr[5]. In the light of above work, we decided to see the effect of alprazolam therapy is renal insufficient patients by evaluation of Ccr.

MATERIAL & METHODS

Fifteen male and female patients selected from Nephrology ward of JPMC, Karachi , who were suffering from different renal diseases (Mild to moderate). Age and weight range was 24-42 years and 45-60 Kg, respectively. Male to female ratio was 9:6. Patients with a history of liver diseases were excluded. Pregnant women or women taking oral contraceptives were also excluded. Normal subjects were normal by history, physical examination and laboratory screening. Male to female ratio was 2:3.AII gave written informed consent before the study.

Table-I. Ccr in control and renal groups on day zero and twenty

Dayo		Day 21
No.	Ccr (ml/min)	Ccr (ml/min)
1	70	71
2	79	79
3	73	71
4	76	80
5	80	79
Mean	75.60	76.00
S.D.	3.72	4.09
S.E.M	1.66	1.83
P>0.5		

STUDY PROTOCOL

Tablet alprazolam (by Upjohn), 0.25 mg, BD, P.O. was given to both groups for a period of twenty one days. Ccr, was measured two time during the course of alprazolam i.e. at day zero and twenty one. For this purpose, twenty four hours urine was collected and 3 ml of blood

drawn once in 24 hours. Serum and urinary creatinine was measured by an automatic analyzer using kits No. 303610030 and 303610550 by Eli Tech (diagnostics). Ccr was determined by following formula;

C = UV/P
where,
U = Concentration of creatinine in urine = mg/ml
V = ml of urine per minute = ml/minute
P = Concentration of creatinine in serum = mg/ml
C = Creatinine clearance = mg/ml
Normal range = 70 -130 ml/minute
Statistical analyses was done by applying student "t" test.

RESULTS

II. Renal patients		
1	58	60
2	41	40
3	52	56
4	42	41
5	38	40
6	39	39
7	41	42
8	52	39
9	37	39
10	40	43
11	38	35
12	39	40
13	41	39
14	38	38
15	28	32
Mean	41.80	41.53
S.D	7.38	6.98
S.E.M	1.90	1.80
P>0.5		

The mean values of Ccr (ml/minute) were 41.80 ± 1.90 on day zero and 41.53 ± 1.80 n day 21 in renal insufficient patients Ccr 75.60 ± 1.6 compared to those evaluated in control group which showed respectively. on day zero and 76.0 ± 1.83 on day 21.

Table-ll. Comparison of means of Ccr in control and renal groups on day 0 and 21

Parameter	Day 0			Day 21		
Cor (ml/min)	Control	Renal	PV value	Control	Renal	Pvalue
	75.60 - 1.60	41.80-1.90	<0.001	76.00 - 1.80	41.53 - 1.80	<0.001

DISCUSSION

As clear from our study on renal patients, there

was no significant 'effect on renal function (Ccr values), during long term therapy of alprazolam. Mean values of Ccr from day zero to day 21 shows no remarkable difference. Same was true in control group. Nevertheless, when control group was compared with renal group, there was a significant difference between these values.

Same work has been shown by Hermann et al in 1985, when he described the effect of alprazolam on digoxin kincties and creartinine clearance. Although, he have a single 1.5 mg dose of alprazolam to healthy persons, there was a tendency toward a reduction of creatinine clearance during alprazolam coadministration as compared with control, but the difference was not significant[6]. One research suggested dosage in renal insufficiency i.e. 0.125 mg to 0.25 mg, given two to three times daily. The dosage may be increased according to requirement[7].Our study was also in agreement with Hermann's evaluation.

CONCLUSION

From our study, it is suggested that no dosage modifications required in mild to moderate renal impairment, but adjust dosage in severe renal diseases due to possible decline in plasma protein, as obvious from other clinical studies.

REFERENCES

1. Dawson, GW, Jue SG and Brogden. RN Alprazolam A review of its pharmacodynamic properties and efficacy in the treatment of anxiety and depression. Drugs, 1984; 27: 132-147.

2. Imlah NW. An evaluation of alprazolam in the treatment of reactive or neurotic (secondary) depression. Br.J. Psychiatry, 1985; 146:515-519.

3. Rodin G and Voshart K. Depression in the medically ill. An overview Am.J. Psychiat, 1986;143:696-705.

4. Dieter K, Huempel M, Lerche V and Kessel M. Effects of uremia and hemodialysis on lormetazepam disposition, din. Pharmacol.Ther, 1981; 30(1): 77-85.

5. Baker, LRI. Renal disease. Clinical Medicine 3rd ed; 1994: P-436.

6. Hermann R, Greenblatt DJ and Birgitt Verburg. Effect of alprazolam on digoxin kinetics and creatinine clearance. Clin Pharmacol. Ther, 1985; 38:595-598. , ; ;

7. RxMed, Reviewed 1999.