

Effect of fluoxetine and escitalopram on hypoglycemic response of repaglinide

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Abstract

The aim of the present study involves the effect of Fluoxetine and Escitalopram on hypoglycemic response of repaglinide. The whole data was obtained from the albino rats which are treated with Repaglinide along with antidepressant drugs like Fluoxetine &Escitalopram to observe their drug interactions in diabetic rats. The individual drugs were tested on healthy &diabetic induced albino rats to conform their effect on hypoglycemic activity. Fluoxetine, Escitalopram had shown no alterations in blood glucose levels when it is administered to healthy rat. Repaglinide had reduced blood glucose levels upto 6hours.Effect of treatment of Fluoxetine &Escitalopram on the hypoglycemic activity of Repaglinide in healthy albino rats had shown marked decrease in blood glucose levels. Fluoxetine and Escitalopram on blood glucose levels in diabetic albino rats did not show any alterations. Repaglinide had shown activity on decreasing the blood glucose levels in diabetic albino rats. Fluoxetine and Escitalopram had markedly reduced the hypoglycemic effect of Repaglinide in diabetic rats with out any change in duration of action. The present study indicates that Fluoxetine and Escitalopram have effect on hypoglycemic activity of Repaglinide.Both Fluoxetine &Escitalopram did not show any changes in glucose levels of normal albino rats. But they both increased the reduction of blood glucose levels of Repaglinide by 30 min in healthy rats& diabetic rats.

Key words: Fluoxetine, Escitalopram, Diabetes, Repaglinide, Depression.

Introduction

Diabetes mellitus is a chronic condition associated with abnormally high levels of sugar in the blood. People with diabetes either do not produce enough insulin or cannot use the blood stream.

Depression is a disorder that involves the body, mood and thoughts. It affects the way a person eats & sleeps, the way one feels about one self and the way one thinks about things[1].

The World Health Organization estimates that depression occurs at much higher rates (15-25%) in diabetic patients than in the general populations even though depression symptoms are frequently under diagnosed [2,3,4]. Some studies suggest that depression and/or anxiety may affect upto50% of young people with poorly controlled type1 diabetes. Depression may be a risk factor diabetes, (especially type2), due to its effects upon diet, exercise and smoking or drinking.

Repaglinide (PRASNDIN), a carbamoylmethyl benzoic acid derivative which was developed to specifically control meal-related glucose fluctuations in patients with type2 diabetes.

Escitalopram is an orally administered selective serotonin reuptake inhibitor used in depression[5]. Fluoxetine is a psychotropic drug for oral administration. It is also marketed for the treatment of premenstrual dysphoric disorder[6].

Treatment, with anti depressants for diabetic individuals must consider the variability in blood glucose level control at different times[7] and a comparison of the available antidepressant agents is always recommended.

Materials and Methods

Drugs and Chemicals

The experimental drugs Repaglinide, Fluoxetine & Escitalopram were collected from our Pharmacy. Tween 80%(Lobachemie), Alloxan monohydrate (Spectro chem. Ltd)and glucose estimation kit (Qualigens diagnostics) were obtained from the respective suppliers.

Grouping of animals

Albino rats (150-260 grams) of either sex were acclimatized under standard housing conditions of normal room temperature and relative humidity with light and dark cycles. The animals had free access to water and rat food. The animals used for study were approved by the Institutional Animal Ethical Committee (IAEC) of SRM college of Pharmacy, SRM UNIVERSITY, Kattankalathur, Kancheepuram (Dist) and the and the approval no. being IAEC/18/2007.The animals were grouped into 8. Among them healthy rats were grouped into 6 groups and diabetic rats were grouped into 2 groups.

The experiment was carried to find out normal blood glucose levels, effect of Fluoxetine(10mg/kg)and Escitalopram(5mg/kg)single dose treatment, effect of Repaglinide (0.2mg/kg)single dose treatment, effect of Fluoxetine(10mg/kg)and Escitalopram(5mg/kg) treatment for one week on the hypoglycemic activity of Repaglinide, on blood glucose levels of healthy albino rats before and after the treatment with above drugs by GOD/POD method[12]

In Alloxan induced diabetic rats the experiment was carried out to find out the effect of Repaglinide single dose treatment, effect of Fluoxetine &Escitalopram treatment on the hypoglycemic response of Repaglinide before and after the treatment with the drugs.

The results of all the groups were subjected to ANOVA one way test followed by Scheff's test using parametric statistics, IBM PC version1.01,LONDON SOFTWARE,INC.

Results

Table-1 Data showing the blood glucose levels after the administration of single dose of fluoxetine(10mg/kg)

	Blood	glucose	levels	in	% bg reduction after
Time in hrs	mg%				Fluoxetin treatment
0		99.29+2.	3		-
0.5		98.94+5.	1		0.3+0.12
1.0		99.38+4.	5		0.09 + 1.21
1.5		99.52+3.	6		0.23+0.23
2.0		98.14+2.	8		1.58 + 2.12
3.0		97.12+6.	1		2.81+0.32
4.0		96.14+4.	7		3.71+4.4
6.0		97.24+6.	2		2.06+0.12

Fluoxetine when administered as a single(10mg/kg p.o) did not exhibited any significant alteration in blood glucose levels in rats.

Table-2: Data showing	the blood	glucose	levels	after	the	administration	of s	ingle	dose	of
escitalopram (10mg/kg)										

Time in hrs	Blood glucose levels in mg%	%BG reduction after Escitalopram Treatment
0	94.99+4.5	_
0.5	99.09+7.3	0.3 + 2.02
1.0	99.59+5.1	0.24+0.23
1.5	100.21+4.1	-0.36+1.23
2.0	100.97+4.6	-0.09+1.09
3.0	100.35+12	-1.02+2.12
4.0	99.33+7.3	-0.51+0.28
6.0	99.02+6.2	2.06+0.12

Escitalopram when administered as a single (5mg/kg p.o) does not exhibited any significant alteration in blood glucose levels in healthy rats

Table-3: Data showing the blood glucose levels with repaglinide (0.2mg/kg) in healthy rat	S
before and after treatment of fluoxetine (10mg/kg)	

Time in hrs	BG in mg% befrore Fluoxetine treatment	BG in mg% after Fluoxetine treatment	% BG reduction before Fluoxetine treatment	% BG reduction after Fluoxetine treatment
0.0	96 88+5 5	89 12+2 3	-	_
0.5	81.12+3.6	63.99+4.9	16.21+1.4	28.23+1.25
1.0	70.26+3.1	38.69+4.7	27.06+4.1	56.61+4.2
1.0	50.07+3.8	38.69+2.5	48.83+1.4	45.53+1.9
2.0	59.58+2.6	48.58+1.2	38.42+3.8	39.42+3.0
3.0	75.79+1.4	53.98+10.1	21.72+6.1	19.56+3.9
4.0	80.76+4.9	71.66+1.7	16.61+2.8	14.60 + 1.2
6.0	85.03+6.1	80.07+4.7	12.1+0.9	10.14+3.4

Fluoxetine(10mg/kg,p.o) pretreated for 7 days followed by the single dose of Repaglinide has markedly reduced the hypoglycemic effect of Repaglinide.

Table-4: Data showing the blood glucose levels with repaglinide (0.2mg/kg) in healthy ra	ts
before and after treatment of escitalopram (10mg/kg)	

Time in hrs	BLG in mg% befrore Escitalopram treatment	BLG im mg% after Escitalopram treatment	% BG reduction before Escitalopram treatment	% BG reduction after Escitalopram treatment
0.0	99.88+2.3	99.17+6.1	-	-
0.5	84.11+3.8	80.23+9.7	15.8 + 3.8	19.08+6.2
1.0	71.38+1.6	44.77+1.2	28.40 + 4.1	54.85+1.6
1.0	50.08 + 5.8	53.72+8.2	49.83+3.8	45.78+3.8
2.0	68.17+3.2	69.01+6.1	31.78+3.3	30.39+3.54
3.0	73.03+3.9	77.94+4.8	26.79+6.2	21.38+1.4
4.0	82.52+2.9	84.82+4.3	17.29 + 2.2	14.43+3.4
6.0	88.23+2.9	89.90+1.8	11.71 + 1.7	9.27+2.1

Escitalopram(5mg/kg,p.o) pretreated for 7 days followed by the single dose of Repaglinide has markedly reduced the hypoglycemic effect of Repaglinide.

Table-5: Data showing the blood glucose levels with repaglinide (0.2mg/kg) in diabetic rats
before and after fluoxetine (10mg/kg) treatment

Time in hrs	BLG in mg% befrore	BLG im mg% after	% BG reduction	% BG reduction after
	Fluoxetine treatment	Fluoxetine treatment	before Fluoxetine treatment	Fluoxetine treatment
0.0	255.2+3.2	254.8+2.4	-	_
0.5	206.42+5.1	182.73+3.1	19.50+3.3	28.03+1.8
1.0	181.59+3.4	91.12+3.8	28.8+2.4	64.24+6.4
1.0	126.31+23.7	121.72+2.6	50.02+9.3	52.23+4.15
2.0	147.49+2.8	57.12+6.32	42.02+4.5	38.33+2.2
3.0	179.84+3.2	182.28+3.45	29.50+11.5	28.49+1.4
4.0	196.93+1.3	205.71+4.9	22.83+1.3	19.26+2.5
6.0	219.38+1.8	223.46+2.56	14.04+3.5	12.27+4.4

Fluoxetine(10mg/kg,p.o) pretreated for 7 days followed by single dose of Repaglinide(0.5mg/kg,p.o) has markly reduced the hypoglycemic effect of Repaglinide.

Table-6: Data showing the blood glucose levels with repaglinide (0.2mg/kg) in diabetic rats before and escitalopram (5mg/kg) treatment

Time in hrs	BLG in mg% befrore Escitalopram treatment	BLG im mg% after Escitalopram treatment	% BG reduction before Escitalopram treatment	% BG reduction after Escitalopram treatment
0.0	257.59+42	255.27+2.7	-	-
0.5	218+11.2	196.46+1.5	15.34 + 8.1	23.08+5.4
1.0	195.1+2.8	97.78+9.5	24.23+6.7	61.67+4.6
1.0	132.24+3.5	127.83+3.4	48.66 + 4.4	48.54+12.1
2.0	156.38+4.7	149.7+6.0	39.58+3.2	49.91+3.2
3.0	118.14 + 5.7	190.23+11.1	26.95+1.3	25.31+0.6
4.0	209.31+7.0	213.93+3.2	18.73+7.40	16.19+1.7
6.0	226.04+6.7	229.58+6.7	12.24 + 16.0	10.03 + 1.90

Escitalopram (5mg/kg, p.o) pretreated for 7 days followed by single dose of Repaglinide (0.5mg/kg, p.o) has markdly reduced the hypoglycemic effect of Repaglinide.

The experimental results in table-5&6 reveled that the Repaglinide (0.2mg/kg) exhibits the onset of action in 30mins and peak effect (49%) in 1.5hrs, the duration of action is about 6hrs.

The Fluoxetine (10mg/kg) and Escitalopram (5mg/kg) alone did not show any significant effect on blood glucose level in healthy albino rats.

The Fluoxetine and Escitalopram treatment for 7 days have shown significant changes in the hypoglycemic activity of Repaglinide in rats. These drugs have increased the blood glucose level reduction and also advanced the peak effect by 30 minutes. These drugs have failed to produce any changes in duration of action of Repaglinide. In healthy albino rats the Fluoxetine10mg/kg and Escitalopram 5mg/kg have established almost similar effect.

The Fluoxetine 10mg/kg and Escitalopram5mg/kg treated for 7 days in diabetic rats also increased the blood glucose reduction from 50.02%-64.24% (Fluoxetine), 48.66%-61.67% (Escitalopram) with advancement of peak effect. The percentage increase in blood glucose reduction was seen in diabetic rats are higher than the values observed in healthy albino rats. The duration of action of Repaglinide was not affected by Fluoxetine and Escitalopram treatment. The experimental results were summarized in the above tables.

Conclusion

From the experimental results observed during the study on effect of Fluoxetine and Escitalopram on hypoglycemic effect of Repaglinide was concluded that Fluoxetine(10mg/kg) and Escitalopram(5mg/kg) p.o did not show significant changes, Fluoxetine(10mg/kg p.o) treatment for 7days increased the reduction of blood glucose levels of Repaglinide in healthy albino rats. Escitalopram (5mg/kg po) treatment for 7days also increased the reduction of blood glucose levels of Repaglinide in healthy rats & diabetic rats. The Fluoxetine and Escitalopram at 10mg/kg po&5mg/kg po treatment for 7 days have advanced the peak effect of Repaglinide by 30minutes in healthy & diabetic albinorats.

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