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Amlodipine Besylate has no Adverse Effect on Male Hormonal Profile

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Abstract
Amlodipine besylate is a long-acting calcium channel blocker which has proved to be very potent in the curation of elevated blood pressure. It is a relatively new antihypertensive drug which is commonly prescribed as a single oral dose. Eleven (11) male wistar rats of 250g average body weight were used to determine the effect of Amlodipine besylate on the male reproductive hormones. Three dose levels (0.5, 1.0 and 10mg/kg) were used. The rats were all sacrificed on the eight day following treatment and the serum collected was sent for hormonal assay. The results obtained showed normal values of the reproductive hormones when compared with the control. This study strongly suggests that there was no significant reduction in the values of the reproductive hormones even at the highest dose administered. It could be said that Amlodipine besylate is good for the treatment of hypertension.

KEYWORDS: Hypertension, Serum, Amlodipine besylate, Reproductive hormones

INTRODUCTION

High blood pressure occurs when blood pressure is greater than lS0j90Hg. The types seen are primary or essential (no identifiable cause) and secondary (known cause) example endocrine such as cushing's disease, phaeochromocytoma: vascular as in renal artery stenosis. Atherosclerosis is a major predisposing factor to developing essential hypertension. Other factors that are implicated include stress, personality and dietary salt. Complications of hypertension include cardiac failure and stroke. (Hainsworth 1978, Espiner1989).

Amlodipine besylate is a dihydropyridine calcium antagonist that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. (Norvasc.com). The contractile processes of cardiac muscle and vascular smooth muscle are dependent upon the movement of extracellular calcium ions into the cells through specific ion channels. Amlodipine besylate inhibits calcium ion influx across cell membranes selectively, with a greater effect on vascular smooth muscle cells than on cardiac muscle cells. Serum calcium concentration is not affected by Amlodipine besylate. (Norvasc. com).

Within the physiology PH range, Amlodipine besylate is an ionized compound (PH=8.6) and its kinetic interaction with the calcium channel receptor is characterized by a gradual rate of association and dissociation with the receptor binding site, resulting in a gradual onset of effect. (Norvasc. com).

Amlodipine besylate is a peripheral arterial vasodilator that acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in blood pressure. After oral administration of theurapeutic dose of Amlodipine besylate, absorption produces peak plasma concerntration between 6 and 12 hours. It is extensively (about 90%) converted to inactive metabolites via hepatic metabolism with 10% of the parent compound and 60% of the metabolites excreted in the urine. (Norvasc. com).

Amlodipine besylate is used as first line treatment of hypertension in the majority of patients. The usual initial antihypertensive oral dose of Amlodipine besylate is 5mg once daily with a maximum dose of 10mg once daily. Small fragile or elderly individuals or patients with hepatic insufficiency may be started on 2.5mg once daily and this dose may be used when adding

Amlodipine besylate to other antihypertensive therapy. (Norvasc. com).

The most common side effects are headache and edema. But its effect on the reproductive hormones of male has not been documented; hence this research will go a long way to establish the effect of Amlodipine besylate on the hormonal profile of male wistar rats.

MATERIALS AND METHODS:

Eleven male wistar rats (Rattus norvegicus) were procured and bred in the experimental animal house of the College of Health Sciences, University of Port Harcourt Nigeria. The rats were fed with grower's mash (sanders feed, Port Harcourt) and tap water was provided ad libitum until they weighed 200g-300g.

The rats were divided into four groups, two in group A and three each in group B, C and D respectively. The first group (Group A) which was the control group was given distilled water. The second to fourth groups (i.e. Group B, C and D) were given 0.5, 1 and 10mg/kg orally by means of syringes respectively at twenty four hour intervals for seven days. The rats were then monitored and anesthetised on the eight day and blood was collected by cardiac puncture and centrifuged at about 3000 r.p.m. for 10 minutes. The supernatant serum was collected into sample bottles and stored at about -20°C until ready for hormonal assay. Assay was done using commercially available LH, FSH, testosterone and prolactin assay kits. The result was statistically analysised using SPSS a statistical computer software.

RESULTS:

Table 1 displayed the range, mean, standard deviation, standard error and percentage of reduction (%R) of serum LH assay of male wistar rats. The result shows that the reduction in the LH level across the group was not significant enough to cause an adverse effect on the fertility of the male wistar rats.

Table 1. Descriptive statistics of serum LH assay of male adult wistar rats.

Serum LH assay miu/ml	Min statistic	Max statistic	mean statistic	Std. error	STD. statistic	%R
GROUP A	2.80	3.00	29000	0.10000	0.14142	
GROUP B	2.40	2.60	2.4667	0.06667	0.11547	15.17
GROUP C	2.30	2.60	2.4667	0.08819	0.15275	15.17
GROUP	2.20	2.70	2.4500	0.25000	0.35355	15.51

Table 2 shows the range, mean, standard deviation, standard error and percentage of reduction (%R) of serum FSH assay of male wistar rats. The percentage of reduction 8.02, 15.05 & 24.73 for group B to D is not significant enough to cause an adverse effect on the fertility of the male wistar rats.

Table 2. Descriptive statistics of serum FSH assay of male adult wistar rats.

SERUM FSH ASSAY Mu/m	Min Statistic	Maximum Statistic	Mean Statistic	Std Error	Std Statistic	%R
GROUP A	413.70	14.20	13.950	00.25000	0.35355	
GROUP B	812.00	14.40	12,833	80.78387	1.35769	8.02
GROUP C	011.00	12.70	11.850	00.85000	1.20208	15.00
GROUP D	010.00	11.00	10.500	00.50000	0.70711	24.70

Table 3 presents the Range, mean, standard deviation, standard error and percentage of reduction of prolactin assay of male wistar rats.

Table 3. Descriptive statistics of serum prolactin assay of male adult wistar rats.

Serum Prolatin Mu/m	Fsh Mnm Statistic	Maximum Statistic	Mean Statistic	Std Error	Std Statistic	%r
GROUP A	3.00	3.10	3.0500	0.05000	0.07071	
GROUP B	3.40	3.70	3.5667	0.08819	0.15275	-16.72
GROUP C	3.20	3.80	3.4333	0.18559	0.32146	-12.45
GROUP D	2.80	3.80	3.3000	0.50000	0.70711	-8.19

Table 4 shows the range, mean, standard deviation, standard error and percentage of reduction (,X) R) of serum testosterone assay of male wistar rats. The result shows that the level of serum testosterone did not reduce significantly to cause an adverse effect on the fertility of the adult male wistar rats.

Table 4. Descriptive statistics of serum testosterone

assay of male adult wistar rats.

SERUM
testostarone

ASSAY	MN	MAXIMUM	MEAN	STD	%R
MU/M	MUM				
	Statistic	Statistic	Statistic	Std Error	Statistic
GROUP A	0.10	0.18	0.1400	0.04000	0.05657	
GROUP B	0.04	0.40	0.1667	0.11681	1.20232	-19.07
GROUP C	0.05	0.30	0.1567	0.07446	1.12897	-11.92
GROUP D	0.05	0.20	0.1033	0.04842	0.08386	26.21

DISCUSSION:

Amlodipine besylate is commonly prescribed as a single oral dose. It has proved to be a potent antihypertensive drug by acting as a calcium channel blocker. (Norvasc. com).

This study was to investigate the effect of Amlodipine besylate on the reproductive hormones when administered with doses normal and far above the normal dose.

The result from the determination of LDI00 and LD50 of the drug shows that they are greater than 200mg/kg, which confirms that Amlodipine besylate has a high therapeutic index.

From the result of our test, it shows that Amlodipine besylate did not have an adverse effect on the reproductive hormones of male wistar rats even at very high doses. This is because LH, FSH, prolactin and testosterone are all present in the serum at normal levels. It goes a long way to agree with the work done in which Amlodipine besylate was given at doses up to 10mg/kg/ day to male rats for 64 days with no effect on the fertility of the rats. (Norvasc. com).

In conclusion, patients been treated of elevated blood pressure with Amlodipine besylate should know that the drug is safe and highly recommended. However, further research should be carried out on the effect of long time use of Amlodipine besylate in the treatment of elevated blood pressure. Since high blood pressure patients are on long term therapy this will help them to take necessary precautions on the use of Amlodipine besylate

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