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Study of effect of Amlodipine on Blood Sugar level

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Abstract

Objective: To study the effect of AMLODIPINE on blood sugar levels in hypertensive patients.

Method: It is a prospective study in which patients were selected from Princess Esra hospital, Hyderabad.

Results: This study was done on 20 mild to moderate newly detected hypertensive patients. Statistical analysis shows a highly significant rise in blood sugar level with 'P' value < 0.001 after 2 and 4 weeks of using 2.5 to 5 mgm (once daily) amlodipine.

Conclusion: As calcium channels are involved in the release of insulin from the β cells of pancreas, calcium channel blockers like amlodipine may cause hyperglycemia when used in hypertensive patients. Further studies are required in this field on a larger number of patients.

Keywords: Amlodipine; Calcium channel blockers; Diabetes Mellitus; Hypertension

1. Introduction

A changing lifestyle in developing countries like India, has enormously increased the statistical figures of chronic diseases like diabetes mellitus. A survey depicts that 4% of the adults in India suffered from diabetes in the year 2000 and it is expected to increase to 6% by the year 2025.[1] Most of the patients have coexisting hypertension. Calcium channel blockers are a class of drugs and natural substances that disrupt the calcium (Ca2+) conduction of calcium channels. The main clinical usage of calcium channel blockers is to decrease blood pressure by blocking calcium channels. It is for this action that they are used in individuals with hypertension. Calcium channels are also involved physiologically in the release of insulin from the ß cells of the pancreas. It is therefore important to look for any relation between calcium channel blockers and the occurrence of hyperglycaemia. As amlodipine is the most commonly prescribed calcium channel blocker this study was planned to monitor the effect of amlodipine on blood sugar level of hypertensive patients.

Voltage-dependent calcium channels (VDCC) are a group of voltage-gated ion channels found in excitable cells (e.g., muscle, glial cells, neurons, etc.) with a permeability to the ion Ca2+.[2-3] At physiologic or resting membrane potential, VDCCs are normally closed. They are activated (i.e., opened) at depolarized membrane potentials and this is the source of the "voltage-dependent" epithet. Activation of particular VDCCs allows Ca2+ entry into the cell, which, depending on the cell type, results in muscular contraction, excitation of neurons, up-regulation of gene expression, or release of hormones or neurotransmitters.[4]

Table 1: Sensitivity of dihydropyridines to different types of calcium channels

Current Type	1,4-dihydropyridine sensitivity (DHP)	ω-conotoxin sensitivity (ω-CTX)	ω-agatoxin sensitivity (ω-AGA)
L-type	blocks	resistant	resistant
N-type	resistant	blocks	resistant
P/Q-type	resistant	resistant	blocks
R-type	resistant	resistant	resistant

Structure: Voltage-dependent calcium channels are formed as a complex of several different subunits: α1, α2δ, β1-4, and γ. The α1 subunit forms the ion conducting pore while the associated subunits have several functions including modulation of gating.[2]

Channel subunits: There are several different kinds of high-voltage-gated calcium channels (HVGCCs). They are structurally homologous among varying types; they are all similar, but not structurally identical. In the laboratory, it is possible to tell them apart by studying their physiological roles and/or inhibition by specific toxins. High-voltage-gated calcium channels include the neural N-type channel blocked by ω-conotoxin GVIA, the R-type channel (R stands for resistant to the other blockers and toxins) involved in poorly defined processes in the brain, the closely-related P/Q-type channel blocked by ω-agatoxins, and the dihydropyridine-sensitive L-type channels responsible for excitation-contraction coupling of skeletal, smooth, and cardiac muscle and for hormone secretion in endocrine cells (table-1 & 2).

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α1 Subunit: The α1 subunit is the primary subunit necessary for channel functioning in the HVGCC, and consists of the characteristic four homologous I-IV domains containing six transmembrane α-helices each. The α1 subunit forms the Ca2+ selective pore, which contains voltage-sensing machinery and the drug/toxin binding sites. Total ten α1 subunits have been identified in humans.[2]

Table 2: Different types of calcium channels

Type	Associated subunits	Most often found in
L-type calcium channel ("Long-Lasting" AKA "DHP Receptor")	$\alpha_2\delta$, β, γ	Skeletal muscle, smooth muscle, bone (osteoblasts), ventricular myocytes (responsible for prolonged action potential in cardiac cell; also termed DHP receptors), dendrites and dendritic spines of cortical neurones
P-type calcium channel ("Purkinje") /Q-type calcium channel	$\alpha_2\delta$, β, possibly γ	Purkinje neurons in the cerebellum / Cerebellar granule cells
N-type calcium channel ("Neural"/"Non-L")	$\alpha_2\delta/\beta_1$, β_3, β_4, possibly γ	Throughout the brain and peripheral nervous system.
R-type calcium channel ("Residual")	$\alpha_2\delta$, β, possibly γ	Cerebellar granule cells, other neurons
T-type calcium channel ("Transient")		neurons, cells that have pacemaker activity, bone (osteocytes)

2. Materials and Methods

Patients & Methods: This was a prospective study in the outpatient department of Internal Medicine at Princess Esra hospital, a tertiary care hospital attached to Deccan College of Medical Sciences, Hyderabad, India.

Newly detected hypertensive patients who were prescribed amlodipine were enrolled in this study.

Inclusive criteria:

Age: 30-70 years

Sex: Both men & women

Exclusive criteria:

Age: Below 35 and above 70 years

Associated diseases: Any associated disease (ischemic heart disease), chronic or complicated cases.

Patients satisfying the inclusion and exclusion criteria were selected. The baseline fasting blood sugars only were done on account of non-cooperation of the patients. The fasting blood sugars were repeated after an interval of two and four weeks. Statistical analysis was done after four weeks. Total twenty cases were studied.

3. Results

Fasting blood sugar levels at 0, 2 weeks, 4 weeks of newly detected hypertensives treated with amlodipine were noted.

The mean blood sugar levels at - 0 weeks was 85 mg %.

2 weeks was 92 mg %

4 weeks was 97 mg %

Statistical analysis shows that there is a highly significant rise in blood sugar level with 'P' value < 0.001 after 2 and 4 weeks of observation (table 3; fig-1).

Table-3: Fasting blood sugar levels in mg% at 0, 2, 4 weeks in non-diabetic hypertensive patients

Case No.	Blood Sugar Levels in mg %			Change in Blood Sugar levels	
	0 weeks	2 weeks	4 weeks	After 2 weeks	After 4 weeks
1	120	126	132	6	6
2	74	78	69	4	9
3	68	74	84	6	10
4	99	100	100	1	0
5	78	76	80	2	4
6	68	75	108	7	30
7	80	82	78	2	4
8	96	105	110	9	5
9	64	70	75	6	5
10	79	79	80	0	1
11	64	74	78	10	4
12	100	131	139	31	8
13	104	111	115	7	4
14	70	72	72	0	0
15	100	121	126	21	5
16	70	74	84	0	10
17	104	112	120	8	6
18	100	112	120	12	8
19	98	98	100	0	2
20	69	76	77	7	1
Total	**1705**	**1846**	**1947**	**139**	**122**
Mean	**85**	**92**	**97**	**--**	**--**
% increase	**--**	**8.2%**	**14%**	**--**	**--**

Values of	0-2 weeks	2-4 weeks
Standard deviation	7.4039	6.42
T-value	4.199	4.864
P-value	<0.001	<0.001

P<0.001 when compared to values at 0 week

4. Discussion

The calcium channel blockers (CCBs) are subdivided into 3 groups:

1. Dihydropyridines : Nifedipine, amlodipine, nimodipine.

2. Phenylalkylamines: Verapamil

3. Benzothiazepines: Diltiazem

Mechanism of action

Calcium channel blockers act by blocking voltage-gated calcium channels (VGCCs) in cardiac muscle and blood vessels. This decreases intracellular calcium leading to a reduction in muscle contraction. In the heart, a decrease in calcium available for each beat results in a decrease in cardiac contractility. In blood vessels, a decrease in calcium results in less contraction of the vascular smooth muscle and therefore an increase in arterial diameter. Vasodilation decreases total peripheral resistance, while a decrease in cardiac contractility decreases cardiac output. Since blood pressure is determined by cardiac output and peripheral resistance, blood pressure drops. Calcium channel blockers block only voltage sensitive L-type channels. The dihydropyridines are the most potent Ca^{2+} channel blockers.

AMLODIPINE: It belongs to the class of dihydropyridines of calcium channel blockers. The other members belonging to this class are nifedipine, nicardipine, felodipine, nimodipine etc. Amlodipine (as besylate, mesylate or maleate) is a long-acting calcium channel blocker used as an anti-hypertensiveand an antianginal drug . Like other calcium channel blockers, amlodipine acts by relaxing the smooth muscle in the arterial wall, decreasing total peripheral resistance and hence reducing blood pressure; in angina it increases blood flow to the heart muscle. In hypertension it is given in a dose of 2.5-10 mgm once daily.

Different types of calcium channels play an important role in the various cellular activities including the release of insulin from β cells of pancreatic islets of Langerhans. This adds to the pharmacodynamics of insulin, that the same calcium channels which are responsible for the release of insulin may also be affected or blocked by using calcium channel blockers in addition to L-type of channels.

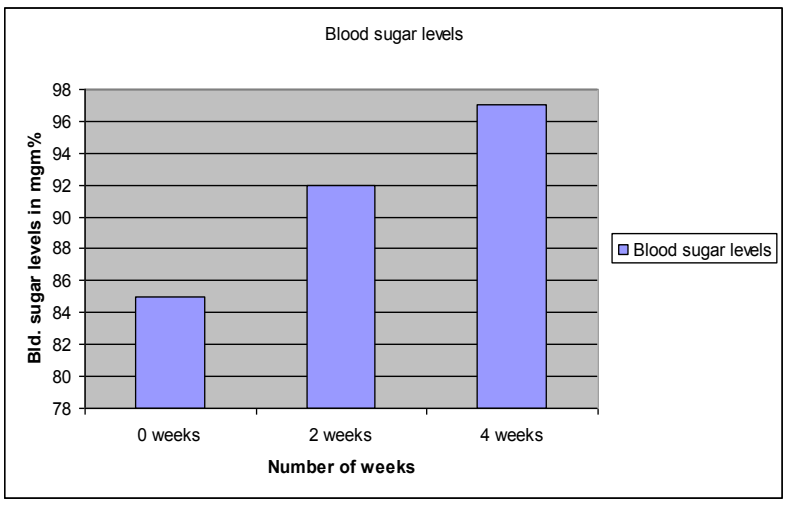

Fig 1: Blood sugar level

The present study done only on twenty patients reveals that there is statistically highly significant (P value < 0.001) rise in blood sugar levels after using amlodipine in a dose of 2.5 – 10 mg once daily This has to be confirmed on post lunch blood sugars and on a larger number of patients in further studies.

5. Conclusion

As calcium channels are involved in the release of insulin from the β cells of pancreas, calcium channel blockers like amlodipine may cause hyperglycaemia when used in hypertensive patients. Calcium channel blockers have shown a statistically significant rise in fasting blood sugar levels in a small group of patients over a short period of time (2-4 weeks). Further studies are required to confirm this as calcium channel blockers form a very commonly prescribed group of antihypertensive drugs today.

6. References

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