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The Effects of Salicylates and Antihypertensive Drugs on Induced Hypoglycemia

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KEYWORDS

Salicylates, Antrihypertensives, Diabetes mellitus, Hypoglycemia

ABSTRACT:

Introduction:

Diabetes mellitus is a prevalent chronic disease globally, particularly in the elderly population Hypoglycemia, which is characterized by abnormally low blood glucose levels, is a common occurrence among people with diabetes. This study aimed to evaluate the effects of salicylates and antihypertensive drugs on induced hypoglycemia.

Methodology:

A prospective observational study was conducted for a duration of 6 months i.e., (September 2022-February 2023). Patient data (n=80) with salicylates and antihypertensive drugs collected from various departments like general medicine, gynaecology, endocrinology department were documented in documentation form and statistical analysis was done to acquire the results.

Results And Discussion:

Both in IP patients and OP patients there is a significant change in glucose levels when they are taken in combinations like hypoglycemic agents, anti-hypertensive, and aspirin. According to the inclusion criteria, a total of 80 diabetic and hypertension patients (n =80) were scrutinized. In the present study out of 80 subjects, 37 (46.25%) were females and 43(53.75%) were males. Among gender-wise distribution collected data males are more than females. In which the ratio is male: female. The greater number of cases were found in the age group 51-60(33.75%) in which male were 13 and female were 14.

Conclusion:

Blood glucose levels decreased in almost 59 out of 80 cases. The concomitant use of hypoglycemic agents and aspirin led to a moderate reduction in blood glucose levels.When compared to the other two combinations (hypoglycemics+aspirin) (hypoglycemics+antihypertensives), this drug combination (hypoglycemics+aspirin+anti-hypertensives) shows a significant decrease in glucose levels.

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Introduction DIABETES MELLITUS

Diabetes, marked by prolonged high blood sugar levels due to issues in insulin secretion, action, or both, has two main types. Type 1 results from an autoimmune response depleting insulin-secreting beta-cells, while Type 2 stems from an imbalance between blood sugar and insulin production. Gestational diabetes occurs during pregnancy. Insulin's role as an anabolic hormone leads to metabolic irregularities, primarily insulin resistance in tissues like muscles and adipose, impacting carbohydrates, lipids, and proteins. Symptoms vary with type and duration, with some experiencing polyuria, polydipsia, polyphagia, weight loss, and blurred vision. Type 2 diabetes may be asymptomatic initially. Untreated diabetes can lead to ketoacidosis or, rarely, nonketotic hyperosmolar syndrome, potentially causing coma or death if not addressed. [1].

CLASSIFICATION OF DIABETES MELLITUS:

Type 1 Diabetes Mellitus

Type 1 diabetes results from autoimmune destruction of pancreatic cells, driven by T cell-induced insulitis and B cell-initiated inflammatory reactions. Predominant in children and adolescents, this form is marked by a lack of insulin secretion. Symptoms include polydipsia, polyuria, enuresis, fatigue, polyphagia, weight loss, slow wound healing, infections, and blurred vision. In younger individuals, severe dehydration and diabetic ketoacidosis can also occur. [2] .

Type 2 Diabetes Mellitus

In type 2 diabetes, insulin resistance increases demand in target tissues, while pancreatic dysfunction hinders additional insulin supply. The gradual loss of beta cells leads to reduced insulin secretion over time, possibly shifting previously independent patients towards insulin dependence. [3].

One of the main distinctions from type 1 diabetes is the dependence on insulin. Other differences include the absence of ketoacidosis in the majority of type 2 diabetic patients and the absence of autoimmune cell destruction [4].

Along with diabetes, insulin resistance also manifests Obesity, Nephropathy, essential hypertension, dyslipidemia (hypertriglyceridemia, low HDL, decreased LDL particle diameter, increased postprandial lipemia, and remnant lipoprotein accumulation),ovarian hyperandrogenism and premature adrenarche, on-alcoholic fatty liver disease, systemic inflammation[5].

HYPOGLYCEMIA

Hypoglycemia is defined when plasma concentration decreases below 70mg/dL. Most people with type 1 diabetes and many people with type 2 diabetes experience recurrent morbidity from iatrogenic hypoglycemia, which can occasionally be fatal [6].

Symptoms Associated with Hypoglycemia

Whipple's triad: which includes symptoms that are consistent with hypoglycemia, a low plasma glucose concentration, and symptom alleviation when the plasma glucose concentration is restored, provides the strongest evidence for the clinical illness. Symptoms of neurogenic (autonomic) disorders include: palpitations, tremors, hunger, and sweating. Neuroglycopenic symptoms can include: seizure, coma, and even death. Neuroglycopenic symptoms frequently include: behavioural abnormalities, cognitive difficulties, and/or outright disorientation [7].

Causes Of Hypoglycemia

Hypoglycemia in diabetics is caused by a combination of relative or absolute insulin excess and weakened physiological protections against falling plasma glucose concentrations.

All insulin preparations and insulin secretagogues used to treat diabetes occasionally produce excessive amounts of insulin as a result of pharmacokinetic defects that are influenced by a variety of factors, including dietary intake, physical activity, drug interactions (including alcohol), altered sensitivity to insulin, and insulin clearance [8].

Diabetic hypoglycemia

Diabetes mellitus patients who have diabetic hypoglycemia have low blood sugar levels.

The danger of hypoglycemia exists in those who have type 1 diabetes who must take insulin to manage their

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blood glucose levels. Although it is typically less frequent, hypoglycemia can also occur in those who have type 2 diabetes who use insulin and/or specific additional drugs (such as sulfonylureas, meglitinides) [9].

Causes

Being insulin-dependent too much, cutting out a meal, mistimed insulin delivery, youthful individuals and the elderly, Individuals with reduced liver or kidney function, Individuals who have been living with diabetes for an extended period [10].

SALICYLATES:

Aspirin

Acetylsalicylic acid, commonly known as aspirin, is a medication that is used to relieve pain, reduce fever and inflammation. Aspirin has antithrombotic properties, making it useful in preventing blood clots. Aspirin is used to treat certain inflammatory conditions such as Kawasaki disease, pericarditis, and rheumatic fever [11].

Mechanism of action:

Aspirin is a type of NSAID and part of the salicylate group, which all have salicylic acid as the active ingredient.

Aspirin has similar pharmacological effects as salicylates and is also influenced by the actions associated with salicylic acid itself, as well as having additional, independent effects due to its reactive acetate group. Aspirin is thought to provide pain relief through both peripheral and central mechanisms. On a peripheral level, it stops the production and release of prostaglandins. In terms of its central effect, it reduces pain at a specific area in the hypothalamus, although the exact way it works is unknown [12].

ANTI HYPERTENSIVES:

Medications called anti-hypertensives are used to reduce high blood pressure, which is a condition characterized by excessively high force of blood against blood vessel walls. This can increase the likelihood of heart disease, stroke, and kidney disease.

BETA BLOCKERS:

Betablockers reduce the workload of the heart and slow down the heart rate; these drugs inhibit glycogenolysis. However, it is believed that taking Beta blockers may raise the chances of severe or prolonged low blood sugar levels by suppressing the early warning signals of hypoglycemia. Non selective beta blockers block 2-adrenoreceptors and decreases the flow of glucose from the liver into the bloodstream which is due to prevention of gluconeogenesis and glycogenolysis stimulation in the liver. Since beta blockers can prevent pancreatic islets from secreting insulin in response to glucose, glucagon, or arginine, they have a detrimental effect on glucose homeostasis. By preventing the sympathetic response to hypoglycemia, beta antagonists can also lead to hypoglycemic unawareness [13].

ANGIOTENSIN CONVERTING ENZYME INHIBITORS:

Angiotensin converting enzyme inhibitors inhibits the angiotensin II hormone formation which can constrict blood vessels and increases blood pressure. Studies have suggested a possible association between the use of ACE inhibitors and hypoglycemia in diabetic patients. In diabetic patients, especially those using other hypoglycemic medications, particularly sulfonylureas, ACE inhibitors might enhance insulin sensitivity, which can result in an approximately three- to four-fold increased risk of hypoglycemia. The ACE inhibitors also modify the hormone bradykinin's expression, which has been demonstrated to have a tussive impact via the kininogen-kinin pathway, causing cough as a side effect and having hypoglycemia as its aetiology. Intensive insulin therapy that improves metabolic control dramatically raises the risk of hypoglycemia. In diabetic individuals with microalbuminuria, intensive insulin therapy is frequently tried, and many of these patients may also be taking ACE inhibitors. Some individuals, especially those with type 2 diabetes, experience hypoglycemia after taking ACE inhibitors. This is hypothesised to happen as a result of the angiotensin converting enzyme being inhibited, which results in less insulin being secreted and more insulin receptors being degraded [14].

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ANGIOTENSIN II RECEPTOR BLOCKERS:

ARBs can rarely cause hypoglycemia this occurs because ARBs can impair glucose-stimulated insulin secretion and reduce insulin sensitivity, leading to decreased glucose utilization and increased insulin resistance. Various studies have found varying incidences of hypoglycemia linked to ARBs, with reported rates ranging from 0.1% to 2.7% [15].

CALCIUM CHANNEL BLOCKERS:

1. Rarely CCBs can also cause hypoglycemia (low blood sugar). This happens as a result of CCBs ability to prevent calcium from entering the pancreatic cells that secrete insulin, which reduces insulin production and causes hypoglycemia as a result. CCBs with longer half-lives, such as verapamil and diltiazem, are more likely to have this impact than those with shorter half-lives, like nifedipine. Additionally, taking insulin or other glucose-lowering drugs increases the risk of hypoglycemia among diabetics [16].

2. Objectives

AIM & OBJECTIVES:

AIM:

The study aims to evaluate the hypoglycemic effect of Aspirin and anti-hypertensive drugs in a tertiary care hospital.

OBJECTIVES:

- To study the decreased levels of glucose in patients with diabetes mellitus who receive aspirin to prevent cardiovascular events in combination with hypoglycemic agents.
- To identify the effect of anti-hypertensives on glucose levels.
- To monitor the glucose levels in patients taking salicylates and anti-hypertensives along with oral hypoglycemics
-

3. Results

A total of 80 cases were collected according to inclusion criteria (n=80) in which 63 cases (78.7%) are collected from general medicine, 13 cases (16.2%) are collected from endocrinology, 4 cases (5%) are collected from gynaecology in that total of 43 male patients and 37 female patients were identified.

TABLE 1: Categorizing cases based on age

S. No.	AGE	GENDER		NO. OF CASES	PERCENTAGE
		MALE	FEMALE		
1	0-10	1	0	1	1.25%
2	Nov-20	1	2	3	3.75%
3	21-30	1	1	2	2.50%
4	31-40	5	6	11	13.75%
5	41-50	10	4	14	17.50%
6	51-60	13	14	27	33.75%
7	61-70	12	10	22	27.50%
TOTAL		**43**	**37**	**80**	**100%**

- A higher number of cases were gathered among the age group 51-60, with 27 cases in total - 13 of which were male and 14 were female.
- A lower number of cases were gathered among the age group 0-10, with only 1 case observed, which was male and no female cases were reported

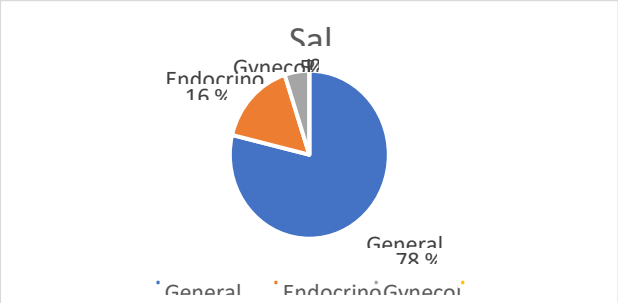

FIGURE 1: Classification of cases based on department

➢ The greater number of cases are collected from general medicines that are 63 cases (78.7%)

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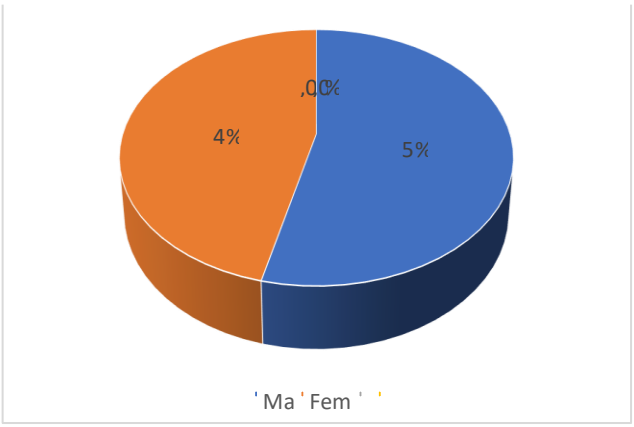

FIGURE 2: Graphical representation of gender wise distribution of cases

The total number of cases collected were 80 in which 43(54%) were male and 37 (46%) were female.

➢ Among the total collected cases we observed that male cases were more.

TABLE 2: Organisation of age wise distribution of drugs

S.NO	age group	hypoglycemic+ antihypertensives	hypoglycemic+ antihypertensives + aspirin	hypoglycemics + aspirin
1	0-10	1	0	0
2	11-20	2	0	1
3	21-30	1	0	0
4	31-40	8	3	0
5	41-50	5	6	4
6	51-60	8	14	6
7	61-70	6	13	2

The patients are categorized into 3 categories. They are:

- Patients taking hypoglycemic agents along with anti-hypertensives.
- Patients who are taking hypoglycemic agents, anti-hypertensives along with aspirin.
- Patients who are taking oral hypoglycemics along with aspirin.
- The above table is about age wise distribution of cases according to drugs.

TABLE 3: Arrangement of drug wise decrease of glucose levels

Category	No. of cases with Decreased blood glucose levels	No. of cases with no Change in blood glucose levels
HYPOGLYCEMIC DRUGS + ANTI HYPERTENSIVES DRUGS	21	11
HYPOGLYCEMIC+ANTI HYPERTENSIVES+ASPIRIN	26	9
HYPOGLYCEMIC+ASPIRIN	11	2

- The number of cases with decreased blood glucose levels were more in patients who used combination of oral hypoglycemics + antihypertensives+aspirin i.e., 26 cases.

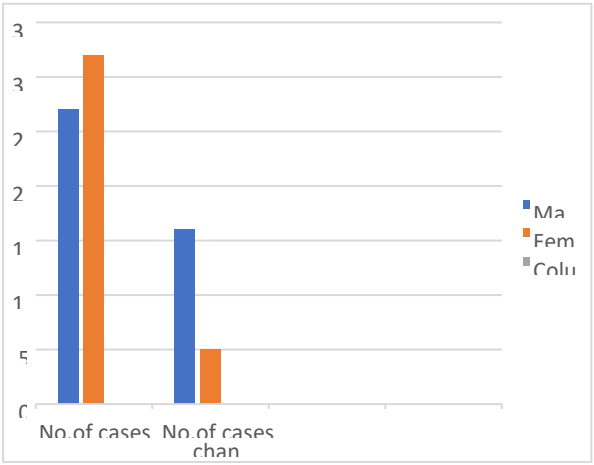

FIGURE 3: Change in Glucose Levels According to Gender

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The number of cases with decreased blood glucose levels were more in female.

TABLE 4: Drugs given in combination

Drugs	**No of patients**	**No of patients with decreased glucose levels**
Beta Blockers		
Atenolol + OH	6	4
Propronolol+OH	5	4
Carvedilol+OH	2	2
ACE		
Enalpril +OH		6
ARB		
Telmisartan +OH	9	4
CCB		
Amlodipine +OH	3	1
COMBINATION WITH ASPIRIN		
Aspirin + OH	13	11
Aspirin +OH +ANTIHTN	35	26

The majority of patients with decreased glucose levels are present in aspirin and hypoglycemics and anti-hypertensives that is 26 patients.

4. Discussion

The present study aimed to evaluate the efficacy of various medication combinations in managing blood glucose levels among patients with comorbid diabetes and hypertension. Our findings suggest that certain medication combinations, including hypoglycemic agents, anti-hypertensives, and aspirin, may have a significant impact on lowering blood glucose levels in this patient population.

Firstly, our study observed a predominance of male cases among the evaluated subjects, consistent with previous literature indicating a higher prevalence of diabetes and hypertension in men.

Regarding age distribution, our study primarily included patients aged 51-70, reflecting the higher incidence of diabetes and hypertension in older age groups.

Our findings regarding specific medication combinations are noteworthy. Carvedilol, a non-selective beta blocker, demonstrated a consistent decrease in blood glucose levels when administered alongside oral hypoglycemics. Similarly, amlodipine, a calcium channel blocker, exhibited promising results in lowering blood glucose levels in one patient.

Furthermore, our study observed favorable outcomes with the use of ACE inhibitors and angiotensin receptor blockers (ARBs) in combination with oral hypoglycemics. Enalapril, an ACE inhibitor, was associated with decreased blood glucose levels in the majority of patients, highlighting its potential as an adjunct therapy for glycemic control in individuals with concurrent hypertension. Similarly, ARBs such as valsartan demonstrated a beneficial effect on fasting blood glucose levels when combined with oral hypoglycemics, indicating a potential mechanism of action beyond blood pressure regulation.

The combination of aspirin, hypoglycemic agents, and anti-hypertensives emerged as particularly effective in our study, with a significant proportion of patients experiencing reductions in blood glucose levels.

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