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INTERVENTIONS TO IMPROVE MEDICATION ADHERENCE IN ORAL HYPOGLYCEMIC AGENTS: AN INSIGHT ON BARRIERS AND FACILITATORS

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ABSTRACT

Over 347 million people worldwide have diabetes, which is on the rise. To treat hyperglycemia, oral antidiabetic drugs are being used more and more often. The rising use of oral antidiabetic drugs brings up questions of adherence in the management of diabetes, particularly recognizing the difficulties associated with taking oral antidiabetic drugs. Non-compliance with anti-diabetic medication might result in inadequate glycemic control and increase patient problems. This review focuses on research on patient adherence to targeted oral anti-diabetic medication for glycemic control. Following that, we go over adherence challenges and a diabetic adherence improvement strategy. Lastly, we go through further research directions that will be necessary to define and enhance oral antidiabetic drug adherence.

KEYWORDS: Hyperglycemia, Oral Antidiabetic Drugs, Adherence, Improvement, & Glycemic Control.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic condition that affects a broad population and is becoming more and more common worldwide. It is defined by high blood sugar and a deficiency in insulin production, action, or resistance.

An increasing number of people throughout the world—347 million—are affected with DM. The World Health Organization (WHO) predicts that DM will rank as the seventh greatest

cause of mortality in 2030, with 75% of cases coming from low-income nations where Type 2 diabetes would affect the majority of the population. The different anti-diabetic drugs have been shown to control hyperglycemia. Together with medicines, lifestyle changes (such as diet and exercise) can considerably aid with DM control. The management of DM is crucial for improving the patient's quality of life by reducing the symptoms and avoiding illness complications. There are six kinds of oral antidiabetic drugs that can be used for therapy. Based on the illness severity, mono, dual, or triple oral medication combination treatment is advised.

The management of diabetes is crucial for preventing future complications; patients must take their medications as prescribed for the rest of their lives and concentrate on lifestyle management, which includes weight loss through a decrease in caloric intake and an increase in physical activity. This is because the associated complications and clinical manifestation, in addition to the chronic nature of the disease, make managing DM very challenging. Notwithstanding all the challenges involved in maintaining treatment adherence, including dietary changes, regular exercise, foot care, and home glucose monitoring, medication delivery is crucial for disease management. It has been discovered that the key to managing Type 2 DM is medication compliance. This review summarizes research on diabetic patients' adherence to oral anti-diabetic drugs, obstacles to specific oral anti-diabetic medications, and interventions to increase adherence.

TAKING ANTIDIABETIC MEDICATIONS ORALLY

Compliance: - The WHO defines it as the degree to which a person's conduct complies with the accepted advice from a healthcare professional. It is an ongoing process that evolves over time. Patients and medical professionals believe that the advice below is a good way to take your medicine. To guarantee positive health outcomes, oral antidiabetic medication compliance is essential. Diabetes can affect regular social contacts in any way, such as being overly busy, travelling, under stress, or in other ways.

Adherence is often measured in patients who adhere to correct instructions. The choice of whether or not to take medication is based on empirical reasoning.

Insulin resistance and a relative lack of insulin production, with progressively less secretion over time, describe type 2 diabetes mellitus, a chronic condition. Family history of diabetes, obesity (BMI > 25 kg/m2), habitual inactivity, hypertension, high cholesterol, and PCOS are

some of the risk factors that might lead to type 2 DM. The majority of people with type 2 diabetes have abdominal obesity, which in turn leads to insulin resistance. The majority of people can attain normal glycemia with oral antidiabetic drugs, however some people need insulin as a stand-alone treatment or in conjunction with oral antidiabetic medications to regulate their long-term glycemic levels. For the treatment of type 2 DM, oral anti-diabetic medications are widely accessible nowadays. There are several medication classes available, each with a unique mechanism of action, safety profile, and side effects. Biguanides, sulphonylureas, rapid-acting secretagogues, thiazolidinediones, alpha-glucosidase inhibitors, suppressors of glucagon release (GLP-1 Analogues), stimulators of insulin secretion (Biguanides), enhancers of insulin action (thiazolidinediones), delaying the absorption and digestion of intestinal carbohydrate (alpha-glucosidase (DPP-IV Inhibitors). The medicine metformin is most frequently used to treat type 2 diabetes. The primary adverse effects include skin rashes, weight loss, anorexia, and Vitamin B12 malabsorption. It should not be used if you have kidney failure, liver illness, a heart issue, or pregnancy. Sulphonylurea, which lowers HbA1c by 1-1.5 percent, is the best medication option for slim people. Weight gain, hypoglycemia, and Gl fluctuations are some of its negative side effects, although research found that it lowers the incidence of micro and macrovascular problems in high-risk individuals. The oral anti-diabetic medications are gradually increased in dose based on the glycemic response, which is assessed by the measurement of glycosylated haemoglobin (HBA1c) concentration. The majority of prescription combinations for the treatment of the condition include a secretagogue and either a biguanide or a thiazolidinedione.

Adherence to the recommended prescriptions is ultimately what ensures the quality of healthcare. In the event of a chronic illness like diabetes, noncompliance with the prescribed medicine causes the therapy to fail, ultimately increasing mortality and morbidity. Adherence to oral antidiabetic treatment is shown to range from 36 to 93% in type 2 diabetes. Nonadherence to therapy is one of the main causes for diabetes to be poorly managed.

OBSTACLES TO ADHERENCE

Previous assessments have found a number of obstacles to OHM adherence. Several factors, including timing with eating, side effects, cost, patients' poor educational levels, nutrition, physical inactivity, the complexity of the dosage regimen, and polytherapy are currently being researched as hurdles to adherence for OHMs. But many factors, including age, gender, stress, self-esteem, the quality of the relationship between the patient and the healthcare

provider, social support, and the patient's ability to maintain adherence to the changing circumstances in their life, have been identified as having an impact on adherence to the treatment for diabetes.

DIET AND EXERCISE

Diabetes patients must also take medicine to maintain a normal glycosylate level due to their excessive glucose levels. Diet is the most crucial element. When you have type 2 diabetes, it's crucial to follow a low-carbohydrate diet to preserve your quality of life. Yet, if you don't, your condition will worsen, increasing your risk of morbidity and death. Research was done in Kuwait with 334 adult men to examine the obstacles to diet adherence. From the study samples, it was shown that 63.5% of patients were not following any diets and 90.4% were overweight or obese. The greatest obstacles to diet adherence were reluctance (48.6%), social gatherings (13.7%), and difficulties getting the rest of the family to follow the diet (30.2%).

According to the same survey, comorbid ailments (35.6%), unfavourable weather (278. %), and a lack of time (390. %) were the greatest obstacles to exercising.

Food, which is very high in fat and calories (79.9%), frequent social gatherings (59.6%), stress (&)>&%), an abundance of maids (54.1%), and excessive car use (83.8%) were the main obstacles to people in Kuwait adhering to lifestyle measures. This illustrates how the sedentary lifestyle of the population ultimately increases morbidity and mortality of the patient.

COMPLEXITY OF DOSING REGIMENS

Because the condition is chronic and progressive, patients must take many drugs and must continue to take them for the rest of their lives, which adds to the regimen's complexity. According to a US survey, between 1991 and 2001, the percentage of patients who were taking at least five medicines rose from 18.2% to 29.9%. Individuals with type 2 diabetes may take 10 pills per day because they may also have additional complicated issues. The likelihood of non-adherence rises as dosage complexity rises. Typically, patients start their treatment with metformin and subsequently add more medications to keep their blood sugar levels stable. Although type 2 diabetes is chronic and progressive, oral medications are often used by patients who are having trouble keeping their HbA1c levels under control.

TOLERABILITY AND SAFETY

A treatment's unfavourable side effects might potentially be the cause of nonadherence. The primary negative effects of OHMs include headaches, hypoglycemia, Gl side effects, and weight gain. In cross-sectional research including 285 patients, non-obese patients were shown to be 10.87% more likely than obese patients to be compliant with their medication ($p = 0.0024$). Oral antidiabetic treatment is connected with medications that raise CVS risk and promote weight gain, which is the reason for nonadherence.

Gastrointestinal abnormalities and other adverse effects are also thought to be causes of nonadherence. In a review carried out in the US between 2006 and 2008, 2074 patients with type 2 diabetes who were using more than one OHA were included. Of these, 71.7% reported at least one adverse event, with Gastrointestinal side effects being the most common. 49.7% of people had more than 2 occurrences. A negative incident and adherence had a statistically significant relationship.

Economic consideration: Poor adherence to treatment regimens may result from prescription costs. Cross-sectional research in Ethiopia comprising 285 managed diabetic intervention trials revealed that 54.6% of patients cited the cost of medicine as a factor in their failure to adhere to treatment regimens. A patient-reported questionnaire was used in French research to assess a number of adherence-related parameters. Low family income, a lack of family and social support, and medication adherence were all substantially correlated.

ACTIONS TO IMPROVE MEDICATION ADHERENCE IN DIABETIC PATIENTS

Several research have looked at treatments to increase adherence to OHMs, and many more are in progress. Many types 2 DM control treatments have been found; however, they have not been successful in improving medication adherence. To encourage patient adherence to OHMs, however, a variety of strategies have been established. Medication adherence was evaluated using a variety of techniques, including electronic measurements, patient self-report, and pharmacy refills.

The effectiveness of interventions to increase drug adherence has been mixed. Many studies have been done, but none of them have been successful in increasing adherence. Nevertheless, some of them have shown improvement in HbA1c alone, while others have shown improvement in both HbA1c and adherence.

Self-reported tools were the most prevalent tool (described in 50 papers), followed by electronic measurements[33], data on pharmaceutical refills and claims[26], and pill counts.[25] The three types of adherence measurements that were most often employed in studies were electronic measures, patient self-reports, and claims data. Some individuals evaluated adherence using the medication subscale items in the summary of diabetes self-care activities (SDSCA) questionnaire. The Morisky-green test, the short medication questionnaire, the Medication Adherence Report Scale, and the Hill Bone Compliance Questionnaire were the additional self-reported instruments. The most popular self-reported tool was SDSCA. The intervention was effective because it used several different tactics.

Inpatient adherence has improved as a result of elements including education, behaviour techniques, emotional components, interactive technology, human behaviour, greater patient education, and financial or economic reasons.

According to several studies, individuals who comprehend the value of the medications they are taking to enhance their health are more likely to stick to prescribed regimens. The first step in raising awareness and assisting patients in sticking to the prescription is educating patients about their disease and the significance of taking their medication. The easiest and most effective ways to assist patients comprehend their illness state and, as a result, motivate them to take medicine and improve their health outcomes, include booklets, electronic media, and verbal communication.

A substantial improvement in medication adherence was seen in patients getting OHMs in a randomized experiment where the patient got 10 phone calls from their health educator over the course of a year at 4–6-week intervals. To enhance adherence, innovative techniques must be used to see if the patient's behaviour has changed, or the patient and provider's communication must be increased.

The majority of diabetes medications, including sulfonylurea and thiazolidinediones, have several side effects, including weight gain and hypoglycemia. Patients who have a normal glucose level with fewer side effects are more likely to stick with their treatment regimen than those who use medications that cause more side effects. Nevertheless, certain more recent drugs, such as DPP-4 inhibitors and glucagon (GLP-1) receptor agonist, have fewer of these adverse effects, which lowers cardiovascular problems and improves adherence.

Financial concerns are a significant issue for someone who has a chronic illness like diabetes. Several studies carried out in the US have demonstrated that low-income patients are less likely than high-income patients to stick to their treatment regimens. Nevertheless, there haven't been as many studies on economic issues, so more research is required to understand how these affect adherences. In Australia, a study was carried out in 2005 to determine whether or not raising co-payments under the pharmaceutical benefits scheme by 24% would have an impact on adherence, but it was discovered that there had been a decrease in the dispensing of various medications, including those for diabetes. It demonstrates that it promotes adherence if the reimbursements and expenditures are restricted to the medications that the patient is taking.

The ideas that are included in the majority of adherence interventions are known as affective components. It uses a variety of tactics, such as peer supporters acting as interventionists, addressing lifestyle factors like nutrition and exercise, and integrating cutting-edge methods like integrated health coaching to the emotional component. In order to make novel therapies more self-centered, patient counselling or other awareness programs can also be used. Many psychological factors, including mood, disorders associated with diabetes, quality of life, attitudes towards the disease, and cognitive capacities, have been identified as crucial factors in the management of diabetes.

A patient must take a lot of pills each day after they begin using anti-diabetic medicine. However, the adjustments can mean taking fewer medications each day. The patient must take a lot of medications each day for the management of diabetes and another cardiovascular risk connected with treating the disease's complication. Many studies have demonstrated that polypharmacy and various dose regimens contribute to non-adherence to the prescribed medicine. The research of 76 patients revealed that an increase in daily other medications considerably decreased the mean dosage taking compliance.

Now that a variety of fixed-dose combinations of diabetic treatment drugs have been identified, the administration process is made simpler and patient adherence is increased. A fixed-dose combination was shown to result in a lower HbA1c than monotherapy or dual therapy in a meta-analysis study of treatments for type 2 diabetes, and an increase in adherence was therefore seen. Moreover, adherence has been demonstrated to be worse with a daily program requiring more doses than a once-day plan.

PREDISPOSING FACTORS	TREATMENT FACTORS	POSSIBLE INTERVENTIONS
Patient characteristics **-Psychological state** **-Social state** **-Quality of life** **-Health beliefs** **-Understanding of disease/ therapy** **-Disease characteristics**	**Complexity of regimens** **-Food interaction** **-Side effect of regimens** **-Cost of drug** **-Cost of follow up care**	Reduced treatment complexity Reduced treatment cost Education and increased knowledge Use assessment of tools Refer to support group Encourage tools to help with adherence -Pill boxes, alarms, calendars Consider initiate nurse led phone calls to home to address adherence, side effects or aby barriers Provide literature on side effects Improved continuity of care

Table 1: Cost effectiveness analyses and % price variation among sulfonylurea group.

Drug	Formulation	Dose(mg)	Min Price (Rs)	Max Price (Rs)	% price variation
Glibenclamide	3	1.25	2.23	6.05	171.30
		2.5	2.75	6.00	118.18
		5	3.73	19.50	422.78
Gliclazide	4	30	23.55	31.25	32.69
		40	15	50	233.33
		60	36	52	44.44
		80	19	76	300
Glimepiride	4	1	11.90	79	563.86
		2	18.54	117.4	533.22
		3	35	129	268.57
		4	22.93	110.50	381.90
Glipizide	3	2.5	3.10	5.35	72.58
		5	4.83	13	169.15
		10	19	22.76	19.78

Table 2: Cost Effectiveness and % price variation Biguanides and Thiazolidinediones group.

Drug	Formulation	Dose(mg)	Min Price (Rs)	Max. Price (Rs)	% price variation
Metformin	4	250	4.34	7.90	690
		500	6	39	550
		850	10.32	36	248.84
		1000	19	39	105.26
Pioglitazone	2	15	12.50	80	540
		30	23	84	265.21

Table 3: Cost Effectiveness and % Price Variation among Alpha- glucosidase inhibitor group.

Drug	Formulation	Dose (mg)	Min. Price (Rs)	Max. Price (Rs)	% price variation
Acarbose	2	25	36	68	88.88
		50	38	117	207.89
Miglitol	2	25	50	65.70	31.4
		50	60	123	105
Voglibose	2	0.2	37	102	175.67
		0.3	52	100	92.30

Table 4: Cost Effectiveness and % Price Variation between Meglitinides group.

Drug	Formulation	Dose	Min. Price (Rs)	Max. Price (Rs)	% price variation
Nateglinide	2	60	30	45	50
		120	50	80	60
Repaglinide	3	0.5	29	90	210.34
		1	48	148	167.94
		2	78	209	208.33

Table 5: Cost Effectiveness and % Price Variation among combination.

Drug	Formulation	Dose(mg)	Min. Price (Rs)	Max. Price (Rs)	% Price variation
Glibenclamide + Metformin	2	2.5 + 400	8.15	23	182.20
		5 + 500	12	29	141.66
Glicazide + Metformin	5	30 + 500	35	80	128.57
		40 + 500	20	28.34	41.7
		60 + 500	50	129	158
		80 + 500	21	66	214.28
Glimepiride + Metformin	4	1 + 500	10	70	600
		2 + 500	15.50	126.50	716.12
		1 + 1000	33.08	48	45.10
		2 + 100	45	68	51.11
Glipizide + Metformin	2	2 + 400	4.09	8.90	117.60
		5 + 500	7.45	14.50	94.63
Pioglitazone + Metformin	2	15 + 500	26.75	65	142.99
		30 + 500	34.90	70	100.57
Pioglitazone + Metformin + Glimepiride	2	15 + 500 + 1	39.50	80	102.53
		15 + 500 +2	45	90	100

Table 6: FDA approved drug.

Drug Class	Drug Name	Brand Name	Year Approved	Mechanism of Action
Sulfonylureas	Glimepiride Glipizide Glyburide	Amaryl Glucotrol, Diabeta, Glynase presTab,	1984	Increase insulin secretion by pancreatic beta cells
Biguanides	Metformin	Glucophage	1959	Inhibit glucose production by the liver
Meglitinides	Repaglinide Nateglinide	Prandin Starlix	1997 2000	Increase insulin secretion by pancreatic beta cells
Thiazolidinediones	Pioglitazone Rosiglitazone	Actos Avandia		Increase glucose uptake by skeletal muscle
Alpha-glucosidase inhibitor	Acrabose Miglitol	Precose Glyset	1995 1996	Inhibit carbohydrate absorption in the small intestine

CONCLUSION

According to several research, Type 2 diabetes is a chronic, progressive condition with a wide range of consequences. Treatment management requires both pharmaceutical and nonpharmacological interventions. In order to control the condition and lower complications so as to maintain quality of life, adherence to pharmacologic therapy is therefore crucial, but it is very poor. The intricacy of dosage regimens, side effects, the patient's lack of knowledge, age, the expense of pharmaceuticals, social and psychological variables, and other considerations are only a few of the many causes of nonadherence to therapy. Adherence is also impacted by a number of adverse effects, including weight gain, hypoglycemia, poor patient-doctor communication, and physicians' inability to control the condition. For individuals who don't comply with the treatment, a variety of different techniques must be developed to promote adherence. To boost adherence to the OHMs, many strategies have been implemented, including lower prices, reminder systems, greater doctor-patient contact, educational campaigns, simpler regimens, fixed-dose combinations, and inexpensive medication.

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