



A Narrative Review of the Effects of Polypharmacy on Compliance in Type 2 Diabetes Mellitus

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Abstract

This article provides a comprehensive summary of recent work done on the effect of polypharmacy on compliance in Type 2 Diabetes Mellitus (T2DM). It is intended to see how polypharmacy effect compliance in T2DM as the potential for polypharmacy will continue to rise with time because of the complications and comorbidities associated with T2DM.

Background:

The term Polypharmacy is used for patients who take several medications at a time. The most common form of diabetes, that accounts for over 90% of diabetes cases, is T2DM. The use of Polypharmacy is appropriate in treating complex conditions like diabetes along with their comorbidities like cardiovascular diseases or other chronic illnesses. A cluster of comorbidities is associated with T2DM patients, including various complications; this has been said to cause a considerable increase in Polypharmacy in T2DM patients, but How Polypharmacy affects the compliance of these patients is still under research.

Methods:

Electronic database search is performed by using PubMed and Google Scholar to identify the relevant research. While searching the data key words Type 2 DM, Polypharmacy, compliance, and adherence to treatment were used. Only the articles meeting the following criteria were included:

- 1) Analyzing the compliance or adherence to treatment in patients on polypharmacy.*
- 2) Which describes polypharmacy as use of 5 or more medicines to analyze the effect on compliance.*

The articles which were duplicated, incomplete or in language other than English were excluded. The articles on the effect of polypharmacy in Type 2 DM published before January 2015 were also excluded.

Results

A total of 160 articles appeared as a result of our search strategy. 93 articles were retrieved on PubMed and 5 on google scholar using Polypharmacy and compliance, and 62 using Polypharmacy and T2DM.

Conclusion:

The rising age, multiple comorbidities, neuropathies and microvascular impediments of diabetes complicate the Management of a disease this leads to practicing polypharmacy for betterment of the patients. The lack of knowledge, mental state, and cost-effective drugs all factors can affect a patient's compliance towards treatment. Taking various medications for disease and visiting different specialists for the comorbidities makes them non-adherent towards the treatment process. The care of diabetic patients shall focus on all the patients and caregiver aspects and a comprehensive attitude shall opt with the primary goal focused on improving patient health. There is a need for additional research to evaluate the risk benefits of various medications and interventions in regard to polypharmacy and the effects on real life applications.

Keywords

Type 2 DM, Polypharmacy, compliance, adherence.

Introduction**Polypharmacy**

The term Polypharmacy is used for patients who take several medications at a time [1]. Many researchers state that the simultaneous intake of more than five drugs refers to polypharmacy [1]. Polypharmacy is a concerning issue in clinical practice, the practice of prescribing a variety of drugs is on the rise, and this practice is most commonly seen in patients over 65 years of age [2]. The complications caused by Polypharmacy are very alarming; this is why most healthcare givers have advised the prescription of fewer drugs at a time for a single patient.

However, in treating complex conditions like cardiovascular diseases or other chronic illnesses, using Polypharmacy is appropriate [3]. Polypharmacy is beneficial in treating chronic conditions where evidence-based prescriptions are made. It can become challenging with the use of inappropriate medications or drug interactions [3]. Therefore it is associated with surplus challenges concerning the patient's safety with a high prevalence of contrary results, which includes a high risk of mortality, adverse drug-to-drug interactions, and prolonged hospital stays [4].

According to a review on Polypharmacy, the elderly population has reported an escalation of drug interaction, prolonged hospitalization and a high mortality rate. Polypharmacy was the main reason behind 90% of hospitalizations in older people [5]. There was a decline in physical activity (PA), thinking ability and reduced compliance towards medications because of polypharmacy [3].

Type 2 diabetes mellitus (T2DM)

The most common form of diabetes, accounting for over 90% of diabetes cases, is T2DM [6]. Diabetes plays a huge role in the economic burdon of communities [6]. In the past few decades, there has been a fourfold increase in the incidence of T2DM worldwide; the estimated increase since 1980 was 108 million, which rose to 463 million in a survey done in 2019 [7]. According to the 'International diabetes federation diabetes atlas', around 463 million individuals in 2019 were living with T2DM, which makes it 9.3% (20–79 years) of the world's population. The numbers are anticipated to rise to around 578 million (10.2%) by 2030 and to around 700 million, making it 10.9% of the world's population by 2045 [8].

T2DM is usually treated with different medications depending upon the complexity and severity of the disease. Usually, the prescription includes drugs for glycemic control, cardiovascular problems, and other comorbidities, if there are any [9]. As a consequence, individuals with T2DM are more likely exposed to the practice of Polypharmacy [10]. The prevalence of Polypharmacy is increasing in T2DM patients day by day; there is an estimated prevalence of 57% -99% in these patients [10, 11]. A cluster of comorbidities is associated with T2DM patients, including various complications; this has been said to cause a considerable increase in Polypharmacy in T2DM patients.

Compliance

For two decades, the term compliance has been the center of major clinical studies [12]. Fundamentally when a particular treatment regimen is followed, it refers to the patient's compliance. It is an important term in clinical research and primary healthcare. The outcome of any treatment highly depends on compliance in health care. It is significant in all the phases of health care.

The World Health Organization (WHO) has reported that 50% of people adhere to long-term therapies [13]. In the developing countries the rates are even lower. Noncompliance towards medications causes around 125000 annual deaths, demanding 25% of nursing facilities and leading to around 10% of hospital admittance [13]. 33–69% of hospital entries are due to noncompliance in the United States (US). Noncompliance leads to more hospital entries causing almost \$100 billion annual cost burden in the US. At the same time, compliance towards treatment regimens has been reported to have good health outcomes with a reduced economic burden on the economy of a country [13, 14].

Review

Polypharmacy is a significant area in medical practice; from the past few years, research regarding Polypharmacy has gained interest, but the data available in terms of effects of polypharmacy on compliance, and the use of opposing medications is very diverse and still not clear. Furthermore, let us take the example of T2DM patients. There is limited reliable data on to what extent polypharmacy is effective in these patients and how it can affect the compliance of these patients towards treatment which can influence glycemic control and the outcome results.

Methods

Objective

The main objective of the current review is to find out how practicing Polypharmacy affects the compliance of T2DM patients.

Design

To identify the relevant studies, we searched different electronic databases, including MEDLINE (accessed by PubMed), and Google Scholar, from 2015 to 2023.

The search was filtered to the English language only and included search/MESH terms polypharmacy, T2DM, and compliance. Additionally, the references of published studies were manually searched. Only the full-text articles available in English were considered eligible for review.

The search terms used for Medline included (Polypharmacy [MeSH Terms]) AND (type 2 diabetes mellitus [MeSH Terms]). The term compliance and adherence is interchanging, so both were considered in the search.

Inclusion criteria

Articles analyzing the compliance or adherence to treatment in patients on polypharmacy were included in the study. The articles describing polypharmacy as use of 5 or more medicines to analyze the effect on compliance were considered. The articles, reviews and trials on the effect of Polypharmacy in T2DM published after January 2015, till May 2023, which were freely available and written in English, were considered for the review.

Exclusion criteria

The articles which were duplicated, incomplete or in a language other than English were excluded in this review. Articles published after January 2015 were excluded from the review.

Results

Using the above-explained search method, a total of 160 articles appeared. Ninety-three articles were retrieved on PubMed, five on google scholar using Polypharmacy and compliance, and 62 using Polypharmacy and T2DM.

Expert opinion

Low compliance with treatment regimens is a multifocal problem, especially in individuals with chronic illnesses. It is considerably destabilizing the welfare of health care. Chronic conditions like T2DM are very complex in terms of treatment; they require compliant behavior from the patient's end to control the disease. It will include timely intake of medications with regular blood sugar, exercise and dietary control checkups for good glycemic control.

Noncompliance with diabetes can result in many complications ranging from various infections, micro and macro vascular diseases, neuropathies and nephropathies. A respectful attitude of a patient towards diabetes care is of utmost importance. This helps halt the disease and prevents some of these complications from happening. Studies suggest that Polypharmacy is a more dominant condition in the elderly diabetic population. Unfortunately, many people are unaware of the importance and role of a positive attitude and compliance towards a disease leading to an estimated rate of 50%-80% of noncompliance [12].

According to literature Polypharmacy is said to play a significant role in noncompliant attitude of a patient towards a treatment regimen. Along with a noncompliant attitude there is increased number of medications leading to inappropriate intake of drugs, drug side effects with increased hospitalization and more mortality [15, 16]. Reasonable glycemic control is essential for T2DM patients, unfortunately according to M Badedi et al.; Polypharmacy is said to be associated with poor glycemic control, which can lead to complications in these patients [17]

According to our literature search, there are mixed reviews related to Polypharmacy. Some studies state that it can result in hypoglycemia, reduced quality of life, long hospital stays due to drug interaction and mortality [18, 19]. While some studies have stated that educated patients with polypharmacy shows good compliance. It is recommended that caregivers shall be able to differentiate between the terms 'appropriate' and 'inappropriate' drug prescription. The difference between these two is based on what is the risk and benefit quotient and how important it is to go more than one drug at a time for a patient [20].

Discussion

How Polypharmacy Effects Treatment Compliance in T2DM Patients

Patients with T2DM encompass multiple comorbidities [21]. These existing comorbidities exposes the patient to polypharmacy. The reason behind the physician opting polypharmacy is for the betterment of their patients to achieve optimal glucose readings. According to a study reported by Joseph et al., 60% of the diabetic patients have at least a single co-morbidity and around 40% of them are suffering from three [21]. Due to this reason majority of the patients require complex treatment options to management the disease. As T2DM is a chronic condition, multiple drugs have to be taken by the patient as a standard care, which makes polypharmacy completely unavoidable. Around 81% of the patients who are on antidiabetic drugs involving insulin are practicing polypharmacy [21].

A study by Joseph et al., reported that in a population of 92 T2DM patients the most commonly found comorbidities high blood pressure, lipid dysregulation, and Gastric disorder, depression and altered wound healing [21]. Each condition required different drugs for proper control [21]. Making patients prone to polypharmacy despite the complex nature of medication their study reported a high compliance level as a result of polypharmacy [21].

As some studies have reported positive adherence to drugs as a result of polypharmacy on the other hand some studies have reported a negative effect of polypharmacy on compliance in T2DM patients with comorbidities. Araya et al., reported that patients undergoing polypharmacy for T2DM were 7.19 times more non-compliant than the patients receiving a single dose of medication [22]. At the same time they also reported that patients showing better adherence towards polypharmacy was attributed to their good monthly income, accessibility towards health care facilities and right counseling regarding the importance of polypharmacy in T2DM [22]. A study Ayele et al. reported that patients showed improved compliance towards treatment with polypharmacy [23]. A study by Kirkman et al.; reported noncompliance towards polypharmacy in T2DM patients [24]. Complex treatment regimens of polypharmacy require better cognitive skills of a patient to realize and recall timely intake of medications [22].

The Characteristics of the Patient

Numerous research studies have worked on how a patient's demographics plays a role in polypharmacy and it affect a patient's compliance towards a treatment. There are many mixed reviews regarding the topic.

Polypharmacy is more commonly found in patients with older age this can be due to that fact that 90% of the older patients have one or more existing comorbidities [25]. It is reported that with advancing age, the patient becomes more compliant towards a treatment regimen, while some studies report no effects or relationship between age and compliance [26, 27]. Badr et al.; have reported that compliance for treatment in the elderly is very much related to the knowledge and educational level of the patient [28]. They reported an excellent adherence towards drugs with more exposure to knowledge [28].

Some studies have identified that the gender of a patient does not play any role in patients' compliance towards any drug therapy [29]. At the same time, some studies have identified females as more noncompliant than their male counterparts [29]. The negative and optimistic effect of Polypharmacy with antidiabetic drugs was said to be related to adherence. A period greater than 10 years was associated with more adherence towards medication [29].

Another contributing factor to the adherence of the patients was found to be depression. Patients with comorbidities were likely to be depressed because of their health situation. These patients were more likely to be noncompliant than non-depressed diabetic patients [29].

Smoking can also play a role in noncompliance towards a treatment. Non-compliers towards a medication are more likely to be smokers than nonsmokers [29, 30].

Ahmed et al., in 2017, reported that one of the significant reasons behind patients' noncompliance towards treatment was non-adherence to regular clinical checkups [30]. Polypharmacy comes with complex Management of the disease with multiple drugs, which can be cost-effective for the patient and can cause drug interaction or side effects [30]. These can be attributed to the effects of Polypharmacy leading to noncompliant patients.

Priyanka et al., in a study conducted in 125 T2DM patients reported a high adherence rate in polypharmacy patients [31]. They reported that the weight of the patients undergoing polypharmacy can also play a role in compliance with normal weight patients showing more compliance than obese. Their results also reported that patients with existing co morbidities shows more compliance towards polypharmacy than the one without co morbidities. This because the people who had positive beliefs regarding polypharmacy and who were aware of the importance showed a positive compliance. Patients showing concerns with the long-term effects of drug side effects showed fewer compliance [31]. Their results encouraged care givers towards practicing polypharmacy prescribing for the betterment of patients [31]. The beliefs of a patient towards a

medication also plays a role in compliance and it can affect future health which can result in good overall compliance [31].

Sinha et al., reported that T2DM patients have chronic conditions along with other comorbidities. This leads to use of polypharmacy for treatment of these conditions and makes the compliance of the patient challenging. They reported a low compliance rate of 47% towards polypharmacy in their study population. The reasons how polypharmacy was affecting the patient compliance were misinterpretations of doctors instructions, this were due to low literacy rates, language barriers, busy schedules of the doctors and fewer doctor to patient communication [32]. These were consisted with the findings of Ayele et al. [23].

Improving treatment compliance

As diabetes is a complex phenomenon, there should be an exchange of opinions with the physician, and they should involve the patient in the treatment process. The caregivers shall opt for patient-centered care to treat various long-lasting diseases with proper medications regularly. The patient-centered approach can be defined as 'providing care that is respectful of and responsive to individual preferences, needs, and values and ensuring the patient values guide all clinical decisions' [33]. The general practitioners shall involve patients in decision-making by explaining the various treatment choices so they can benefit from them in terms of the patient's general health. Eventually, the patient's choice to implement or decline the specific therapy is based on what they need. This will result in good compliance towards polytherapy.

Future directions

In order to ensure that polypharmacy is practiced properly its very essential that the medications which are prescribed to the patients are reviewed properly, it should be ensured that all the necessary laboratory tests done timely, all the drug interactions and side effects shall be monitored and brought into notice, patients shall be provided with the necessary information and they shall be engaged regarding the decisions about their medications, and those therapies shall be optimized. It is very important to review the prescriptions of the patients undergoing polypharmacy carefully and the consultation shall be given proper time so that patients comes to know the importance of polypharmacy. The patient shall me made aware of the fact that the repeated visits of the patients with chronic disease are to ensure proper review of the medication from time to time.

There is a need for additional research to evaluate the risk benefits of various medications and interventions in regard to polypharmacy and the effects on real life applications.

Conclusion

Chronic disease like diabetes comes along with the gift of comorbidities and complications related to diabetes are unavoidable. Therefore, the treatment of this chronic state needs treatment with different medication for those complication. Polypharmacy, makes in use multiple drugs at a time in treating T2DM patients. Our study concludes that the rising age, multiple comorbidities, neuropathies and microvascular impediments of diabetes complicate the Management of the disease. These aspects also affect the compliance of a patient towards treatment. Taking various medications for disease and visiting different specialists for the comorbidities makes them non-adherent towards the treatment process. The care of diabetic patients shall focus on all the patients and caregiver aspects and a comprehensive approach shall be opted, where the primary goal shall be to focus on improving patient health.

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