Effect of "Polypharmacy" and "Frequency of Drug Dosing" on Rate of Compliance among Diabetic and Hypertensive Patients:

A Survey Study in Palestine

تأثير تعدد الأدوية و الجرعات الدوائية على الأنضباط الدوائي بين مرضى الضغط والسكري:

دراسة مسحية في فلسطين

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Abstract

The objective of this study was to investigate the influence of polypharmacy and frequency of drug dosing on the rate of compliance among hypertensive and diabetic patients in the Palestinian community. The rate of compliance of 321 hypertensive and diabetic patients was assessed using graded questionnaire. The overall rate of compliance for the tested sample was 42.1%. Both, diabetic and hypertensive patients tend to have better compliance and less noncompliance when the number of medications is decreased. The best rate of compliance in both cases was obtained when patients have simple one drug regimen. Both, diabetic and hypertensive patients tend to have better compliance on once daily dosing (ODD) versus multiple daily dosing (MDD). However, diabetic but not hypertensive patients tend to have better compliance on once daily dosing versus twice daily dosing. These results indicate that although once daily dosing is associated with higher compliance but it is not always the best especially in treatment of hypertension as the treatment of some type of hypertension requirs more than one drug more daily doses, depends on the type of hypertension, as well as dirbetic melitiies. These results should encourage physicians in the hypertension and diabetes mellitus clinics of the Palestinian Ministry of Health (MOH) to minimize the number of prescribed medications to improve compliance, therapeutic outcome and to minimize cost.

ملخص

هدف هذه الدراسة هو بحث تأثير تعدد الأدوية والجرعات الدوائية على الأنضباط الدوائي بين مرضى الضغط والسكري في المجتمع الفلسطيني. تمت معاينة الأنضباط الدوائي على ٣٢١ مريضا" حيث كان معدل الأنضباط الدوائي الجيد يساوي ٤٢,١%. عند مرضى الضغط والسكري كان الأنضباط الدوائي أفضل حيثما قل

عدد الأدوية المستعملة. الأنضباط الدوائي كان أفضل ما يمكن عندما كان عدد الأدوية المستعملة هو واحد. عند
مرضى الضغط والسكري كان الأنضباط الدوائي أفضل عندما كانت عدد الجرعات الدوائية هي واحدة يوميــا"
مقارنة" بعدة جرعات يوميا". ولكن, عند مرضى السكري وليس الضغط كان معدل الانضــباط الـدوائي مــع
الجرعة الوحدة يوميا" أفضل من جرعتين يوميا". هذه النتائج تشير الى أنة مع الرغم أن الجرعة الواحدة يوميا"
مصحوبة بمعدل انضباط دوائي مرتفع الا أنة ليس دائما" الأفضل وبالذات عند مرضى الضغط. حيث أن العلاج
وخاصة لمرضى ضغط الدم يتطلب في كثير من الاحيان استعمال أكثر من دواء واحد، وذلك حسب نوع ضغط
الدم الذي يعاني منه. كما أن داء السكري قد يتطلب في بعض الأحيان أكثر من نوع من الأدوية أو أكثر مــن
جرعة واحدة يومياً. هذه النتائج يجب أن تشجع الأطباء العاملين في عيادات الســكري والضــغط فــي وزارة
الصحة الفلسطينية أن يقللوا من عدد الأدوية الموصوفة لتحسين الأنضباط الدوائي والعلاجي ولتخفيف التكاليف.

Introduction

Polypharmacy is defined as too many or multiple medications prescribed for the patient[1]. Polypharmacy patients are usually elderly people with multiple chronic diseases and tend to be at high risk of adverse drug reactions [2-3]. The similarity in appearance (e.g. size, color, or shape) of certain drugs creat confusion among patients using multiple drugs. This confusion would ultimately lead to noncompliance[4]. Compliance or adherence is defined as the extent to which a person's behavior coincides with health-related advice[5]. Many studies have indicated that noncompliance is a major cause of poor blood pressure and blood glucose control among patients with hypertension and diabetes mellitus respectively[6-7]. There are many other reasons why patients fail to follow medical advice[8]. Poor patient – doctor communication increases the risk of noncompliance[9]. Patients with chronic disorders, particularly asymptomatic conditions, such as hypertension and hyper-cholesterolemia are more likely to be non-compliers[10-11]. The consequences of medication noncompliance may not only be dangerous for patient's health, but also dramatically increase the financial costs of public health services[14].

Among other factors that also negatively affect patient compliance (adherence) are multiple drug regimen, multiple drug dosing (MDD), chronic duration of therapy, and symptoms of the disease [15 -17]. While the symptomatic nature and the chronicity of diseases may not be changed, the number pf prescribed drugs and daily dose frequency may be altered. For many types of medications, switching from multiple daily dosing to once or twice daily dosing will decease cost and risk of adverse reactions[18]. Single daily dosing of glibenclamide was found to be safer and more effective than multiple daily

dosing in treatment of type 2 diabetes mellitus[19]. Physicians often change multiple dose regimens to once daily in the belief that this improves compliance. Previous reviews of the literature on medication compliance have confirmed the inverse relationship between number of daily doses and rate of compliance[20]. However studies comparing once daily dosing with twice daily dosing in hypertensive and diabetes mellitus patients are few and inconclusive. Studies in Canada have shown that once-daily dosing of glipizide oral hypoglycemic is associated with better compliance than twice-daily dosing[21]. Other studies demonstrate that with antihypertensive medications, once daily dosing regimens are associated with higher rates of adherence than either twice or multiple daily dosing[22]. A third study showed that once a day is not always the best, particularly when compared with twice daily regimens[23].

Few studies about patient compliance in Arab countries have been published. Two studies were conducted in Saudi Arabia. The first study is about compliance and knowledge of hypertensive patients in Al-Khobar city[24]. The second study was carried out at Al-Manhal Primary Health Care Center, and aimed to identify determinants of compliance among diabetic patients attending that clinic[25]. A third study was conducted in Sudan on hypertensive patients[26]. Of the various methods available for assessing compliance, none is without disadvantages, however self reports and interviews with patients are the simplest and most common method for measuring compliance[27-28].

The objective of this study is to investigate the effect of multiple drug therapy (polypharmacy) on diabetic and hypertensive patient's rate of compliance.

Method and Design of the Study

The population of this study consisted of patients with chronic diseases in the clinics of Ministry of Health (MOH) in Northern Palestine. The sample consisted of 321 male and female patients. The medical record of those patients revealed that they had hypertension or diabetes mellitus for at least five years. The medical records also showed that the patients were undergoing fixed drug therapy for at least the past six months. The patients who were enrolled in the present study were registered in the MOH as chronic patients and they get their medication for free from the MOH pharmacy units.

The compliance was studied using a 3-domain questionnaire. The first and second domains contain questions related to patients' demographic characteristics and factors affecting compliance. The third domain contained ten

graded questions to assess compliance. Each item of the third graded domain has four possible answers. Each answer has 1 to 4 points. Patients collecting more than 75% of the points were considered in the good compliance group. Patients collecting less than 50% of the points were considered in the noncompliance group and finally patients collecting between 50 and 75% of the points were considered in the poor/partial compliance group.

Statistical Packages for Social Science (SPSS) was used to analyze the data obtained from the questionnaire. Chi-square test and contingency coefficient test were used to analyze the significant correlations between compliance and the tested factors. For certain two variables, when p value is less than 0.05, there is a statistically significant relationship between the two variables.

Results

1. Rate of Compliance

Compliance is defined as patient's adherence with the general medical instructions given to him regarding his medications and disease. The sample tested contained 46.4% males and 53.6% females. The educational level of the patients in the sample was classified as high, middle or illiterate. The majority of the pateints in the sample belong to the illiterate class (62.3%), while those that belong to the middle level education were (24.3%) and finally those that belong to the high level of education were the minority and count for 13.4%. The patients in the sample were also classifeid based on age group as those who are above 60 (46.5%), those who are between 40 and 60 (36.2%) and finally those who are less than 40 years of age (17.3%). Among the hypertensive patients, beta blockers (atenolol) and angiotensin ezyme blocking agents (enalapril) were the most commonly used ones. Among the diabetic patients, the sufonylureas (Glibenclamide) and the Biguanides (metfromin) were the most commonly used drugs. Results of patient's rate of compliance are shown in the Table (1). Almost more than half of the patients were in the poor or noncompliance category while less than half of the patients were in the good compliance category.

Table (1): Results of the rate of compliance among the patients in the tested sample.

Category	Number of patients in the category	Percentage

Good compliance	135	42.1%
Poor compliance	165	51.4%
Noncompliance	21	6.5%

2. Rate of compliance among hypertensive and diabetic patients

Table 2 shows the degree of general compliance with respect to the type of the disease. The results show that there is a significant difference in the degree of general compliance with respect to the type of the disease based on the contingency test.

Table (2): Rate of compliance with respect to the type of disease. The contingency coefficient is 0.241, and the approximate significance is 0.003.

Category of Compliance	Diabetes Mellitus	Hypertension
Good	41.7%	36.6%
Poor / Partial	55.9%	49.1%
noncompliance	2.4%	14.3%

3. Effect of polypharmacy on the rate of compliance among diabetic patients:

Table 3 shows the degree of general compliance with respect to the <u>number of drugs</u> taken by diabetic patients. The results show that there is a significant difference in the degree of compliance with respect to the number of medications taken by diabetic patients based on the contingency test. Good compliance decreases and the total of poor plus the noncompliance increases with increasing the number of medications.

Table (3): Rate of compliance in diabetic patients with respect to the number of drugs taken daily. Contingency coefficient is found to be 0.271, and approximate significance is 0.039.

Number of drugs taken by the patient daily	Noncompliance	Poor/Partial	Good
One	2.9%	34.4%	63%
Three or more	2.6%	69%	28%

4. Effect of polypharmacy on the rate of compliance among hypertensive patients:

(Table 4) shows the degree of general compliance with respect to the <u>number of drugs</u> taken by hypertensive patients. The results show that there is a

significant difference in the rate of compliance with respect to the number of medications taken by hypertensive patients based on the contingency test. Again, the rate of good compliance decrease and the poor and noncompliance increases with increasing number of medications.

Table (4): Rate of compliance in hypertensive patients with respect to the number of drugs taken daily. Contingency coefficient is found to be 0.194, and approximate significance is 0.355

Number of drugs taken	Noncompliance.	Poor/partial	Good
One	0.0%	33.3%	66.7%
Three and more	15.4%	51.3%	33.3%

5.   Effect of frequency of dosing on rate of compliance among diabetic patients

The table below (table 5) shows the degree of general compliance with respect to the frequency of drug dosing taken daily by diabetic patient. The results show that there is a significant difference in the degree of general compliance with respect to the frequency of drug dosing in diabetic patients as tested by the contingency test.

Table (5): Rate of compliance with respect to the frequency of drug dosing taken daily by diabetic patients. Contingency coefficient is 0.322, and approximate significance is 0.003.

Frequency of daily drug dosing	Poor + Non Compliance	Good Compliance
Once	33.3%	66.7%
Twice daily	62%	38%
Three or more	60.9%	39.1%

6.   Effect of frequency of drug dosing on rate of compliance among Hypertensive patients:

The table below (table 6) shows the degree of general compliance with respect to the frequency of drug dosing in hypertensive patient. The results show that there is a significant difference in the degree of compliance with respect to the frequency of drug dosing in hypertensive patients as tested by the contingency test.

Table (6): Rate of compliance among hypertensive patients with respect to the frequency of drug dosing. Contingency coefficient is found to be 0.311 and approximate significance is 0.018.

Frequency of drug Dosing	Poor and Non - Compliance	Good Compliance
Once	66.7%	33.3%
Twice	46.7%	53.3%
Three or more	75.9%	24.1%

Discussion

The results showed that 6.5% of the hypertension and diabetes mellitus patients who attend the clinics of the Palestinian MOH belong to the noncompliance group, 51.4% belong to the poor/partial compliance group and 42.1% belong to the good compliance group. A French study that used similar assessment method found similar rates of noncompliance suggesting that compliance behavior is independent of culture or health education [29].

Our study also shows that the rate of compliance among diabetic patients is higher than that for hypertensive patients (41.7% versus 36.6%). The lower rate of compliance among hypertensive patients may be attributed to the asymptomatic nature of hypertension. On the other hand, the high compliance rate among diabetic patients may be attributed to the profound symptomatic nature of diabetes mellitus that signals the patient to comply with drug instructions. Furthermore, in the tested sample, hypertensive patients have higher age average than diabetic patients (83% of diabetic patients in the tested sample were above 40 years old, while 99% of hypertensive patients were above 40 years old). With increasing age, there is an increase risk of polypharmacy, adverse reactions and noncompliance [30].

The results clearly show there is an inverse relation between rate of compliance and multiple drug therapy in both hypertensive and diabetic patients. The good compliance clearly improves in diabetic and hypertensive patients when the number of prescription medications are reduced from, for example, three drugs to one drug regimen.

The noncompliance in hypertensive patients dramatically jumps from zero percentage to approximately 15% when the number of medications is increased. Actually, combinational therapy is very common in treatment of elderly hypertensive patients and that might explain the low compliance rate of hypertensive compared to diabetic patients (36.6% versus 41.7%). The degree of non-compliance among diabetic patients tends to insignificantly change upon changing the number of medications. So, although the number of medications

affects both good compliance and noncompliance among hypertensive patients, only the good compliance is affected by the number of medications among diabetic patients. Again, this might be due to the nature of diabetes mellitus. Diabetic patients might be more willing to use multiple drug therapy to reduce the profound symptoms of hyperglycemia, although one drug regimen would be better for them than many drugs. Finally, it should not be understood that multiple drug therapy means noncompliance, actually, the results show that in multiple drug therapy, most compliant patients become poor/partial compliers rather than non-compliers.

Results also show that when diabetic patients are switched from multiple daily dosing (MDD) to once daily dosing (ODD) the rate of compliance improved from 39.0% to 66% and the rate of poor/noncompliance has been decreased from 60% to 33%. Thus, for diabetic patients, rate of compliance is inversely related to dosing frequency. It is noticeable that in diabetic patients, compliance rate is statistically the same in twice or multiple daily dosing indicating that in diabetic patients, once daily dosing is the best.

Results of rate of compliance in hypertensive patients are more complicated and it is not easy to draw straightforward conclusions regarding the association between the rate of compliance and frequency of daily dosing. The results here shows that once daily dosing is better than multiple daily dosing but it is not the best. Actually for hypertension, twice daily dosing is the best regimen that can give the best compliance rate. This might be surprising for some physicians who always try to reduce the frequency to get the best rate of compliance. It might be understandable why once daily dosing is the best for diabetic patients. Most diabetic patients like to be injected once daily and do their best to control blood glucose with diet restriction. It is important to note that although once daily dosing in diabetic patients would achieve the best compliance rate, but it does not necessarily mean that it would achieve the best therapeutic outcome. For hypertensive patients, it might be the nature of the disease and the pharmacokinetic properties of the anti-hypertensive medications available at the clinics that make the twice daily dosing to be the best. For most classes of antihypertensive drugs available at the clinics so far, twice daily dosing achieve better control of blood pressure than once daily dosing. Finally, although further studies are necessary to compare the effect of twice and once daily dosing frequency on rate of compliance, probably the single most important action that health care providers can take to improve compliance is to select medications that avoid multiple daily dosing.

This study should encourage the health policy makers in Palestine to implement strategies to reduce non-compliance and thus to reduce national health costs. One strategy is to minimize the number of drugs prescribed for the patients. The MOH should also develop better follow up for the patients medications. Finally, although this study is the first of its type in Palestine, it has few limitations and further studies are needed.

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