Original article
Adherence and Nonadherence to Inhaled Corticosteroids in Asthma Patients; Factors and Consequences.

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Abstract
Objectives: Asthma is one of the commonest chronic illnesses worldwide. Inhaled corticosteroids (ICS) are critical components in this disease therapy. Incompliance to prescribed treatment is a major factor leading to poor asthma control and many factors could be responsible for this issue.Our aim is to clarify the relation between adherence to treatment and level of asthma control and to evaluate the role of some factors affecting the compliance of asthmatic patients to prescribed inhaled corticosteroids (ICS).
Subjects and methods;A prospective descriptive study was held at internal medicine, thoracic medicine, and pediatric clinics located at Prince Rashed Hospital (PRH), North of Jordan, on asthmatic patients over a period of six months starting from 15 July 2014. Factors that may affect adherence to therapy were studied. These factors included age, sex, residence; level of education, asthma education, Type of inhalation device, and combinations with long acting β2 agonist (LABA).A structured questionnaire to collect the data was used. Adherence to ICS was determined according toModified Morisky Scale (MMS).Global Initiative for Asthma (GINA) 2011 guidelines were used to assess the level of asthma control. For statistical analysis SPSS window software was used. P- Value below 0.05 was considered as significant.
Results: Total of 110 asthmatic patients, of them 50 (45%) males, were included in the study.53 patients (48%) were adherent and only 10patients (9%) have a fully controlled asthma. Adherent patients are more likely to have controlled asthma. Adherence was significantly promoted by increased level of education, being older, having asthma education, using dry powder inhaler (DPI), and using ICS and LABA by the same device. On other hand, sex and residence have no significant effect on adherence.
Conclusion: Nonadherence to ICS is prevalent and it is significantly worsening the clinical outcome in asthmatic patients. National efforts are mandatory to improve the knowledge of general population about such chronic and correctable illnesses as bronchial asthma in order to increase the adherence to treatment and improve the outcome of these diseases.

Keywords: Bronchial asthma, Inhaled Corticosteroids, Compliance, Prince Rashed Hospital, North of Jordan.

Introduction

Asthma is the major chronic illness among children and adults and it is a major cause of avoidable visits to emergency room and hospitalizations (1). The available data indicates that bronchial asthma is increasingly prevalent in the countries of Middle East with hospital admission rates of 150- 200 per 100,000 per year in some countries especially among children. In the recent years many efforts have been conducted in order to achieve appropriate self-management behaviors aiming to improve asthma control .Inhaled corticosteroid currently are considered as a first- line therapy in the treatment of bronchial asthma and are approved for chronic use in adults and children(2). Data extracted from the biopsies and bronchoalveolar lavage showed that correct use of inhaled steroids can reduce cellular infiltrates and inflammatory proteins and the appropriate adherence to ICS leads to better quality of life making the exacerbations and hospitalizations significantly fewer(3,4). In the last decade many ICS delivery systems have been developed with the pressurized metered dose inhalers (MDI) and dry powder inhaler(DPI) being the two most commonly used devices(5). Two factors, proper inhalation technique and adherence to ICS, are a major detriments In order to achieve good asthma control (6). On other hand, bad technique and poor compliance, which are very common, can lead to recurrent exacerbations and hospitalizations (7). Noncompliance is multifactorial and can be divided into two main categories –nonintentional and intentional-.Non intentional nonadhernce is the inability of patient to take ICS as a result of practical barriers-e.g.forgeting, misunderstanding the medication instruction, poor inhaler technique, financial and supply difficulties, etc. Intentional nonadherence is due to perceptual barriers when the patient decides not to take ICS. Both of these barriers require different approaches in order to be solved (8).Although the cost of efforts to improve adherence are high in the short run, it still persistently needed as the long-term cost savings gained by improved adherence can significantly exceed it.This makes adherence promotion a worthy "investment" in managing asthma outcomes(9). In this contextasthma education has essential part of the treatment of this disease. Healthcaresystem must establish a partnership with the patient and his family in order to establish a management plan which the patient will voluntarily follow (10).

The objective of our study is to evaluate how our asthma patients are compliant to ICS therapy and to assess factors that may promote the compliance.

Subjects and methods

A prospective descriptive study was held from July 2014 to January 2015 on internal medicine, thoracic medicine, and pediatric clinics at PRH-North of Jordan-on asthmatic patients using face to face interviews based on a structured questionnaire. All our patients are supposed to be under regular ICS treatment either alone or combined with LABA. Complete medical history was taken every visit in order to assess the compliance of patients to their asthma medication and the level of asthma control. A total of 110 patients who were seen at internal medicine, thoracic medicine, and pediatric clinics and agreed to participate in the study during the study period were included and interviewed. These patientswere studied for Factors possibly affecting adherence to therapy. Includedfactors were age, gender, residence, education level, asthma education, ICS device and whether ICS was used alone, with LABA in separate devices or with LABA bythe same device. Anasthma education program for six weeks was organized by investigators before the study period. The basic components of this program were definition of asthma, how to diagnose asthma, asthma treatment, advantages of ICS therapy, relievers, and 'preventers, consequences of incompliance to treatment, and removing myths (table1).All the points included in this program in addition to proper inhalation technique were discussed and explained repeatedly. To determine the adherence of asthmatic patients to their therapy we used the Modified Morisky Scale (MMS) (Table2).Global Initiative for Asthma 2011 (GINA) (1) was used to evaluate the level of asthma control. Accordingly to these guidelines we assessed the patients for daytime symptoms, nocturnal symptoms, limitation of activity, need for relievers, and lung function test.Controlled patients have none of the above with normal function test, partially controlled have one of them with PEFR below 80%, anduncontrolled patients have three or more symptoms. Statistical analysis was performed using (SPSS) 16 for Windows software.Student's "t" test, ANOVA test andSimple Pearson's correlation were used as they needed. P-value was considered significant when it is below 0.05. The approval of the ethical committee of Royal Medical Services was achieved in order to conduct this study.

Results

A total of 110 asthmatic patients, of them 50(45%) males and 60(55%) females, were included in this study. The mean age of study sample was 42.1+ 17.7, range13-65 years.53 (48%) patients were adherent to ICS, 10(9%) patients have controlled, 65(59%) partially controlled, and 35(32%) patients have

Table1. Basic components of asthma education program

1•Asthma is a chronic but reversible disease.

2-Airway inflammation and hyper responsiveness is the main issue in the pathogenesis of bronchial asthma.

3. Good adherence to prescribed medication including ICS in addition to proper technique are most important tools in relieving symptoms and consequently improving quality of life .

4-Making asthma more controlled, this will lead to decreased cost of therapy and less disease complication.

5. Asthma is diagnoseddepending on symptoms (cough, wheezes, and dyspnoea), signs (wheezes), and improvement of pulmonary test after inhalers.

6. Types of drugs available for the treatment of asthma (LABA, ICS,MDI,DPI, combined inhalers, oral drugs, etc), and the role of relievers and preventer.

7. Steroid inhalers have the advantageous role as they are effective management with minimal systemic side effects.Many misconceptions about this drug must be removed.

8. Factors that may improve the asthma control includes avoidance of triggers (dusts, infections, drugs), and adopting healthy life style (stop smoking, balanced diet, sport).

9•Promptrecognition and adequate treatment ofCrisis are vital issues.

Table 2. Items of the Modified Morisky Scale

Items	Response format
Do you sometimes forget to take your [health concern] pills?	Yes or No
For reasons other than forgetting, over the last two weeks, did you miss at any days to take any of your [health concern] medicine?	Yes or No
, Do you sometimes forget to take your medicinewith you in case of travel or being out of home? [health concern]	Yes or No
Did you take your [health concern] medicine yesterday?	Yes or No
When you feel like your [health concern] is under control, do you sometimes stop taking your medicine?	Yes or No
Do you ever feel hassled about sticking to your [health concern] treatment plan?	Yes or No
How often do you have difficulty remembering to take all your medications?	Never/Rarely, Once in a while, Sometimes, Usually, All the time

. The scores of the Modified Morisky scale are categorized as low compliers (<6), medium compliers (=6) and high compliers (=7).

Table 3. Sociodemographic data of the study population

Data	N (%)
Sex	
Male	50 (45)
Female	60(55)
Residence	
Urban	62 (56)
Rural	64(44)
Level of education	
University and postgraduate	45 (41)
primary and secondary school	55(50)
Illiterate	10 (9)
Control level	
Controlled	10 (9)
partially controlled	65 (59)
uncontrolled	35 (32)
Adherence to ICS	
Adherent	53 (48)
not adherent	57 (52)
asthma education	
present	80 (72)
absent	30 (28)
Age (mean ± SD) years	42.1 ± 17.7

Table 4. Relation between level of asthma control and adherence to ICS.

Adherence to ICS	Control level			p Value
	uncontrolled	Partial control	Full control	
	N35 (%)	N65 (%)	N10 (%)	
Adherent	10 (29)	33 (51)	10(100%)	0.006
Not adherent	25 (71)	32 (49)	0	
Total	35 (100%)	65(100%)	10(100%)	

Table 5. Relation between sociodemographic factorsand adherence to ICS.

	Patients not adherent to ICS (N = 57) N (%)	Patient adherent to ICS (N = 53) N (%)	p Value
Sex Male (N = 50) Female(N = 60)	30 (60) 38 (64)	20 (40) 22 (36)	0.18
Residence Urban (N = 65) Rural (N = 55)	34 (52) 25 (45)	31 (48) 30 (55)	0.15
Level of education University and postgraduate (N =45) primary and secondary (N = 55) Illiterate) (N = 10)	20 (44) 25 (45) 7 (70)	25 (56) 30 (55) 3 (30)	0.045
Age (mean ± SD) years	40.2 ± 13.642	48.6 ± 15.5	0.02

Table 6. Relation between asthma education and adherence to ICS.

Adherence to ICS	Asthma education		P Value
	Yes	NO	
Adherent, N (%)	49 (61%)	4 (13%)	0.002
Non adherent, N (%)	31 (39%)	26 (87%)	
Total, N (%)	80 (100%)	30 (100%)	

Table 7.Comparison between adherence in different combinations of ICS and LABA.

Methods of ICS administration	Adherence to ICS		P Value
	Adherent (No = 53)	Not adherent (No = 57)	
Group 1: (no-60) users of ICS and LABA in the same device	41 (68%)	19 (32%)	0.002
Group 2: (25,100%) users of ICS and LABA in 2 separate devices	8 (32%)	17 (68%)	
Group 3: (25,100%) users of ICS alone or plus oral LABA	4 (16%)	21 (84%)	

International journal of Medical Investigation

Table 8. Relation between adherence and type of ICS.

Type of ICS	Adherence N (%)	NonadherenceN (%)	P value
DPI (N41)	28 (68%)	13 (32%)	0.009
MDI (N 69)	25 (32%)	44 (68%)	0.005

uncontrolled asthma. Other social, demographic, and basic clinical data of the studied population are demonstrated in Table 3. The data of the study suggests that adherent patients have a significantly higher level of asthma control than nonadherent patients- p value 0.006(table 4).Furthermore, such factors as older age, level of education (table 5), asthma education (table6), using ICS with inhaled LABA in the same device(table 7), and using DPI in opposite to MDI (table 8), showed significant effect in promoting adherence to prescribed ICS, P-value< 0.05. On other hand, other factors such as sex and residence did not show any significant effect on adherence, p-value >0, 05(table 3).

Discussion
Up to our best knowledge adherence of asthmatic patients to treatment was scarcely investigated in Jordan. This study was held in order to open the eyes on this important aspect of medicine and possibly to preclude for further investigations in other regions of Jordan. This study highlights the importance of such factors as level of education and asthma education in adherence to ICS and consequently in the level of asthma control. Other factors which were found to be involved in adherence were older age, using DPI, and using ICS with LABA by the same device.
Our study showed that adherence was prevalent in 48% of our patient and that controlled asthma is significantly more prevalent in adherent patients than in nonadherent.These data are in agreement with observations of other studies in this regard(11).
Reviewing the literature, some studies showed significant relation between adherence and asthma education but not with educational level (12).
Other investigations showed that patient were morecompliant to treatment when they used DPI instead of MDI and when they use ICS combined with LABA in the same device than in separate devices (13, 14).These data are in agreement with our study. In agreement with some studies (14) and disagreement with other (15, 16), our study suggest

that older age, but not gender and residence, play a role in promoting adherence to ICS therapy.
This study suggests that most important factors that modulate the adherence are correctable. In this regard it is important to establish national programs to improve the level of health knowledge in general population and in asthma patients partly, in addition to the use of combined inhalers with less frequent doses and more simple use.
This study hassome limitations. Among these limitations the relatively small number of study population and that it is a single hospital study.

Conclusion
Incompliance with ICS and consequently uncontrolled symptoms are prevalent in asthmatic patients and we still stay far away from the ideal level in this regard. National efforts are mandatory to overcome this situation. Among the factors that can promote adherence to treatment in asthmatic patients are the intensification of asthma education, increase the educational level in general, and simplification of inhaler devices. Further multicenter investigations are strongly needed.

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