



Assessment of therapeutic compliance and its associated factors in tunisian adult asthmatic patients

Évaluation de l'observance thérapeutique et de ses facteurs associés chez l'adulte asthmatique tunisien

Haifa Zaibi, Asma Allouche, Emna Ben Jemia, Hend Ouertani, Meriem Ferchichi, Jihen Ben Amar, Hichem Aouina
Service de pneumologie, Hôpital Charles Nicolle Tunis / Université Tunis El Manar / Faculté de médecine de Tunis

ABSTRACT

Introduction: Despite therapeutic advances, morbidity attributed to asthma continues to increase. This seems partly to be due to poor adherence. Aim: To assess therapeutic adherence and the association between poor compliance and asthma control.

Methods: We carried out a descriptive cross-sectional study on a sample of 150 asthmatics, followed in the pneumology department of Charles Nicolle hospital for more than 6 months. The survey took place over 1 month. The 4-item Morisky questionnaire (MMAS-4) was used to assess adherence to therapy.

Results: Our patients had a median age of 44.2 years and a sex ratio of 0.47. Asthma was severe in 48% of cases and poorly controlled in 34% of cases. Adherence was poor in 66% of patients. Factors significantly associated with adherence were education level ($p=0.02$), socio-economic status ($p=0.01$), treatment cost ($p=0.02$), its availability ($p=0.04$) and its free cost ($p=0.001$), consultation waiting time ($p=0.03$) and knowledge on asthma ($p=0.04$).

We retained in multivariate analysis two factors determining therapeutic adherence, which are socio-economic status (OR = 2.02 ; [1.2-6.26]) and participation in the therapeutic choice (OR = 1.2 ; 95% CI [2.02-4.25]).

Conclusions: It appears that medication adherence is widely influenced by socio-economic status. So, improving these conditions would guarantee better treatment compliance.

Keywords: Asthma - Therapeutic compliance - Control.

RÉSUMÉ

Introduction : Malgré les progrès thérapeutiques, la morbidité attribuée à l'asthme continue d'augmenter. Cela semble être en partie dû à la mauvaise observance thérapeutique.

Objectif : Évaluer l'observance thérapeutique et ses facteurs associés, et d'étudier l'association entre l'observance et le contrôle de l'asthme.

Méthodes : Nous avons mené une étude transversale descriptive sur un échantillon de 150 asthmatiques, suivis dans le service de pneumologie de l'hôpital Charles Nicolle pendant plus de 6 mois. L'enquête s'est déroulée sur 1 mois. Le questionnaire de Morisky à 4 items (MMAS-4) a été utilisé pour évaluer l'adhésion au traitement.

Résultats : Nos patients avaient un âge médian de 44,2 ans et un sex ratio de 0,47. L'asthme était sévère dans 48% des cas et mal contrôlé dans 34% des cas. L'observance était mauvaise chez 66% des patients. Les facteurs significativement associés à l'observance étaient le niveau d'éducation ($p=0,02$), le statut socio-économique ($p=0,01$), le coût du traitement ($p=0,02$), sa disponibilité ($p=0,04$) et sa gratuité ($p=0,001$), le temps d'attente aux consultations ($p=0,03$) et les connaissances sur l'asthme ($p=0,04$). L'analyse multivariée avait retenu deux facteurs déterminant l'adhésion thérapeutique, qui sont le statut socio-économique (OR = 2,02 ; [1,2-6,26]) et la participation au choix thérapeutique (OR = 1,2 ; IC95% [2,02-4,25]).

Conclusions : Il semble que l'observance thérapeutique soit largement influencée par le statut socio-économique. Ainsi, l'amélioration de ces conditions garantirait une meilleure observance du traitement.

Mot clés : Asthme - Observance thérapeutique - Contrôle

Correspondance

Haifa Zaibi

Service de pneumologie, Hôpital Charles Nicolle Tunis / Université Tunis El Manar / Faculté de médecine de Tunis

Email : haifa.zaibi@yahoo.fr

INTRODUCTION

Asthma is a chronic inflammatory disease of the bronchi which represents a major public health problem in the world since it affects more than 5% of the world population, or approximately 300 million people. It is responsible for 250,000 deaths per year (1). According to WHO estimates, the prevalence of asthma will increase by 100 million by 2025. It will result in 27,000 deaths by 2030 (2).

In Tunisia, according to studies, the prevalence of asthma varies between 4 and 6% (3, 4).

Over last years, significant progress has been made in the etiologic and therapeutic approach of asthma. However, the prevalence and the morbidity and mortality due to this disease are increasing worldwide (5). The climbing morbidity and mortality associated to asthma may be partly attached to therapy adherence.

Indeed, life quality of asthma patients benefits greatly from better treatment compliance since poor compliance is a factor of poor disease control leading to increase exacerbations, emergency visits and professional absenteeism. Poor therapy adherence is also responsible for three squares of the total cost of the disease (6).

The level of compliance varies widely, ranging from 18 to 60%. It depends on studies, measurement tools and scores used to assess it (7). Tunisian data on this subject are scarce.

We then proposed to conduct this study to assess therapeutic adherence, its associated factors and its association with asthma control.

METHODS

This was a descriptive and cross study, conducted over a period of one month from 15 March to 15 April 2019, in the pulmonology department of the Charles Nicolle hospital of Tunis.

We included 150 patients aged 18 or more. They were followed up for asthma since at least 6 months. An oral consent was obtained by all patients.

Data collect was done through face to face questionnaires. We used pre-established questionnaires, the Morisky questionnaire (MMAS) (8) and the ACT score (9).

We used the Morisky questionnaire composed of 4 items to which patient answered with " yes " or " no ". Patient was

considered as " observing " if his score is 0, and " poorly observing " if his score is greater than or equal to 1 (10).

To assess asthma control over the past 4 weeks, we relied on:

- The asthma control criteria of the GINA 2018 that are based on the daytime symptoms, the need for reliever, symptoms night and activity limitation. The control is optimal when said all criteria are met, partial when one or two criteria are present and uncontrolled when three criteria or more are present (11).

-The ACT score (Asthma Control Test) defines the asthma as totally controlled if the score is between 20 and 25, partially controlled for a score between 19 and 15 and not controlled for a score lower than 15 (9).

The asthma severity has been retrospectively defined as the minimum level of treatment necessary to achieve and maintain control of the asthmatic disease over several months (11).

The socio-economic status was assessed according to 2 factors: level of studies and social security. Three levels have been defined in table 1.

Table 1. Classification of Socioeconomic Status

	Level of studies	Social security
Good socioeconomic status	Secondary / higher education	With
Avredge socioeconomic status	Secondary / higher education	Without
	Primary education / unschooled	With
Poor socioeconomic status	Primary education / unschooled	Without

The therapeutic regimens were defined according to the options proposed by the GINA 2018 (11). Prescribed molecules were the inhaled corticosteroid, beta 2 adrenergic, xanthic base, anti-leukotriene and anti-cholinergic. Inhaled devices used were the spray, diskus, turbuhaler, breezhaler and respimat.

Data were entered and analyzed using SPSS version 23 software.

In analytic study, Student's T test and ANOVA test were used for comparison of means. For comparison of percentages, we used chi-square test, and in case of invalidity of this test by the two-tailed Fisher test.

Correlation study was carried out by the Pearson or Spearman test according to variables normality.

Logistic regression analysis was performed to study

independent factors influencing therapeutic adherence and to evaluate independent association between poor compliance and asthma control.

In all the statistical tests, the significance level was set at 0.05.

RESULTS

Patients and asthma characteristics:

Recruited patients were aged between 18 and 78 years, with a mean age of 44.2 ± 5 years. Their sex ratio was 0.47 with 102 women and 48 men.

Three quarters of patients (74.4%) benefit from social security. Forty percent of patients had a poor socioeconomic status.

Asthma caused professional absenteeism at least once a year in 33% of patients.

Active smoking was found in 40 patients (27%). Co-morbidities were found in 76 (51%) of patients dominated by obesity (52%), Gastroesophageal Reflux (33.3%), hypertension (24.6%), and diabetes (18.6 %). Obstructive Sleep Apnea was noted in 26 patients (17.3%).

Atopy was present in most of our patients dominated by rhinitis (83%) and conjunctivitis (42%).

The average duration of asthma at the surveytime was 13.2 ± 10.05 years [4-42]. Asthma duration exceeded 13 years in 102 patients.

Only 16% of patients know the pathophysiology of asthma, 56% know the exacerbating factors, and 43% know the potential treatments side effects.

Asthma was mild in 11 patients (7%), moderate in 73 patients (48%) and severe in 66 patients (44%).

Asthma was controlled in 42.7% of patients and uncontrolled in 34% of patients.

During the year preceding the survey, 108 patients (72%) presented at least one exacerbation during the previous year. A quarter of patients (25.6%) had been hospitalized in a pneumology department for exacerbation moderate to severe. Five patients were transferred to intensive care.

Based on the therapeutic step-by-step approach of the 2018 GINA recommendations, approximately half of the patients (48.6%) were classified as step 3. About a half of patients (44.6%) were taking two molecules. One molecule was prescribed in 46

patients (30.6%), it was an inhaled corticosteroid. Twenty nine patients (19.3) were taking 3 types of drugs.

Eighty-eight patients (62%) participated in the choice of their treatment according to its availability at the hospital. One hundred and two patients (68%) participated in the choice of their inhalation devices, after having offered them the device and explained to them how to use it. The spray was the device used by 56% of the patients, followed by the breezhaler (21%), the diskus (15%), the turbuhaler (6%) and the respimat (2%).

Assessment of therapeutic compliance

Asthma patients were seen at the outpatient clinic for a check-up every 1 to 6 months according to asthma control. The average annual number of consultations was 2.23 per year [1-10]. Among our asthmatics, 12.3% consulted only after exacerbations, and 119 (79.3%) had regular follow-up visits.

According to the MMAS score, 70% of patients (n=105) were poorly adherent to their treatment. Most patients (96%) stopped their treatment when symptoms improved (Tables 2 and 3).

Table 2. Therapeutic compliance of asthmatics by MMAS score

MMAS score	Effective	Percentage(%)
3 or 4	99	66
1 or 2	6	4
0	45	30

Table 3. Distribution according to MMAS items

MMAS Items	Effective	Percentage
Do you ever forget to take your treatment ?	86	81.2%
Do you find yourself not being careful about the days you take your treatment ?	74	70.4%
If you sometimes feel less well while taking your treatment, do you stop taking it ?	34	32.3%
When you feel better, do you ever stop taking your treatment ?	92	87.6 %

Factors associated with poor treatment adherence (Tables 4 and 5)

Demographic factors (age, gender, and marital status), as well as level of education and occupation, did not influence treatment adherence. Likewise, adherence was not related to smoking or co-morbidities.

However, patients with good to moderate socioeconomic conditions were more compliant.

Asthma age, severity and control did not influence the treatment compliance.

Contrary to the therapeutic burden, which reduced adherence to treatment, the acceptable cost of disease-modifying treatment, its availability at the pharmacy and free treatment, significantly increased therapeutic adherence. However, neither the regimen nor the type of inhalation device influenced.

Knowledge of the pathophysiology of asthma, treatment indications and its potential side effects significantly influenced the compliance level.

In adherent patients, the wait time for the outpatient clinic was shorter and it was easier to get an appointment. Also patients who participated in the choice of treatment and inhalation device were more compliant.

Univariate analysis of the factors influencing asthmatics therapy adherence are summarized in table 4.

Table 4. Factors influencing the asthmatics therapeutic adherence in univariate analysis

Factors	P
Socio-economic level	0.01
Cost of treatment	0.02
Availability of treatment at pharmacies	0.04
Free treatment	0.001
Therapeutic load	0.005
Waiting time for consultation	0.03
Ease of getting an appointment	0.01
Participation in the therapeutic choice	0.01
Participation in the choice of device	0.04
Verification of therapeutic adherence	0.05
Knowledge of the disease	0.04
Knowledge of drug indications	0.01
Knowledge of side effects	0.02

In multivariate analysis, only the socio-economic conditions (OR = 2.02 ; 95% CI [1.2 to 6.26]) and participation in the therapeutic choice (OR = 4.2 , 95% CI [2.02 to 6.25]) were predictive of treatment adherence (Table 5) .

Table 5. Factors influencing the asthmatics therapeutic adherence in multivariate analysis

	OR	95% CI	P
Socio-economic status	2.02	1.2-6.26	0.002
Participation in the therapeutic choice	4.2	2.02-6.25	0.003

Impact of compliance on asthma control

Adherent patients had better controlled asthma ($p=0.001$) and fewer annual exacerbations ($p=0.01$) with less scholar and professional absenteeism ($p=0.002$).

Also, Morisky score was negatively correlated with ATC ($p<0.0001$, $r=-0.6$) and positively correlated with annual exacerbation rate ($p<0.0001$, $r=0.5$), annual hospitalization rate ($p=0.001$, $r=0.2$) and absenteeism ($p<0.0001$, $r=0.3$).

DISCUSSION

Our study aimed to assess therapeutic adherence in asthmatics, to study the factors that influence it, and its impact on asthma control.

To meet these objectives, we conducted a cross-sectional study on a population of 150 asthmatics aged more than 18 years, free of any psychiatric illness followed in pneumology consultation of the hospital Charles Nicolle for more than 6 months.

More than half of our patients (66%) were poorly compliant with an MMS score at 3 or 4.

In univariate analysis, factors significantly associated with therapeutic compliance were educational level secondary or higher ($p=0.02$), average to good SES ($p=0.01$), acceptable cost ($p = 0.02$), availability ($p=0.04$), free ($p=0.001$) and low treatment load ($p=0.005$) , short waiting time for consultation ($p=0.03$) and ease of obtaining an appointment ($p=0.01$) .

Similarly, treatment compliance was better in patients who know the asthma pathophysiology ($p=0.04$), exacerbation factors ($p=0.05$), indications ($p=0.01$) and side effects of treatment ($p=0.02$).

Multivariate analysis retained only two predictive factors of treatment adherence, socioeconomic status (OR = 2.02 ; 95% CI [1.2-6.26]) and participation in the choice of treatment (OR = 1.2. ; 95% CI [2.02-4.25]) .

It is clear also from our study that 77.8% of compliant patients had controlled asthma (vs 27.8% ; $p=0.01$). These patients had fewer annual exacerbations (0.6 vs 1.8 ; $p=0.01$) with less absenteeism (1 vs 2.9 ; $p=0.002$).

First, limits of this study were essentially methodological. It was a transversal study, which will not allow us to confirm the cause and effect relationship between the variables. Also, our study was based, for the evaluation of therapeutic

compliance, on an indirect method, which is a subjective method, often source of compliance overestimation.

Furthermore, the strengths of this study were the innovation in terms of the therapeutic adherence areas studied. In fact, in the literature, most studies have looked at medication adherence. In our own, we assessed, in addition to medication adherence, follow-up adherence, as well as asthmatics' knowledge of their disease and treatment. All these elements are, of course, the main targets of therapeutic education and improvement of adherence (5).

In asthma, adherence is evaluated by various direct and indirect methods. Biological assay is the only direct method that seems to accurately reflect therapeutic adherence (12). This method is however expensive, invasive, and limited in asthma by the low number of dosable substances.

The most widely used indirect method is the adherence measurement questionnaires. It focuses on compliance, knowledge of the disease and the use of medications.

Despite their simplicity and low cost, these approaches have the drawback of overestimating compliance. There is no standardized questionnaire validated in French or Arabic that can be used to assess therapeutic adherence in asthma in clinical practice (13).

In our study, adherence to drug treatment has been evaluated by the score of MMAS, this is the most used score in the literature. MMAS-4, proposed by Morisky et al., is composed of 4 questions. Its sensibility seems very good (81%) but its specificity is moderate (44%) (14).

Although this score has not been validated in asthma, we have chosen to use it, for its ease of use in practice, especially since it is the most widely used score for assessing compliance in asthma (14).

Based on the Morisky score, in our study, 2/3 (n=105) of patients were poorly compliant to their treatment (70%). Our results agreed with other Tunisian studies. In their cross-sectional study conducted in 2018 about 202 asthmatics, Belloumi et al had found a score of Morisky from 1 to 4 in 59% of patients (15). Similarly, in a prospective study conducted on 45 asthma patients in the Hedi Chekir hospital in Sfax in 2015, the observance was considered good in only 35% of cases according to the questionnaire Morisky (16).

In our study, 79.3% of patients respected the regularity

in the follow-up and 12.3% consulted only after the exacerbations. These figures are close to those of Fauroux (17), who, in 50 asthmatic children, found regularity in the follow-up of 86%.

Regarding the causes of poor adherence, we have demonstrated in our study that most of patients (96%) stopped their treatment when symptoms improved, or for fear of side effects (91%), for lack of understanding of the therapeutic modalities (85%) or for lack of means (82%) .

Cochrane had proved in his study that in 68% of non-observant asthmatics, non-compliance was unintentional, related to the patient's incomprehension of the therapeutic regimen, due to its complexity, or due to the insufficient explanation from the physician in 48% of cases (18).

In our study, the socio-economic status was positively associated with the adherence of asthma patient to his treatment ($p = 0.01$). This recalls the results reported by Barr (19) and Schultz (20), which concluded that the poor socio-economic conditions and the low level of education decrease treatment compliance in children.

In fact, in our study, the acceptable cost of therapies ($p = 0.02$), its availability at the pharmacy ($p = 0.04$) and its free cost (0.001) significantly influence therapeutic adherence.

In addition, in most studies, the increase in the number of molecules prescribed on a prescription impairs compliance. According to Fauroux, compliance becomes low beyond 3 drugs prescribed (17).

According to Wade and al, the therapeutic compliance appeared to be affected by the relationship doctor-patient, but also by patient satisfaction with the quality of reception. Thus, an excessive waiting time, the multiplicity of attending physicians and the lack of clarity in the doctor-patient communication conditioned therapeutic compliance (21). This was confirmed in our study, where the reduced waiting time for consultation ($p = 0.03$) and the ease of making an appointment ($p = 0.01$) were significantly associated with better treatment adherence.

Of course, the effectiveness of the treatment is conditioned by the knowledge that the patient must have about the disease, whether it is its pathophysiology, its exacerbation factors, the indications of the drugs and their adverse effects (17).

In our study, only 16% of patients recognize asthma as a chronic inflammatory disease with paroxysmal bronchoconstriction, 56% know the exacerbations factors,

45.3% distinguished the basic treatment from the relievers, and 43% were aware of the potential side effects.

In our study, we also noted that 43.3% of patients were aware of the adverse effects of their treatment. In the study of Fauroux, nearly half of the patients were not aware of the side effects of β_2 agonists and inhaled corticosteroids (17).

The patients who know the adverse effects of their drugs observed better in our study ($p = 0.02$).

Concerning asthma control, Sulaiman et al had revealed the association between poor inhaler adherence and poor asthma control (22). This agreed with our study where compliant patients had fewer annual exacerbations with less school and work absenteeism.

Also, our results agreed with Tunisian studies such as that of Mjid et al, where compliant patients had a better controlled asthma (23).

CONCLUSION

Despite it is a key element in the asthma management, therapeutic adherence remains insufficient in Tunisian asthmatic patients. This insufficiency seems to be directly linked to lack of therapeutic education. In fact, programs of therapeutic education, through asthma schools, have proven to be effective in other countries in reducing morbidity of asthma. Given these findings, the creation of an asthma school in Tunisia seems to be essential to guarantee better compliance and control of asthma.

However, in the current context of our country, the challenge is to overcome the socio-economic difficulties and compensate the lack of healthcare access and medications cost and availability.

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