Drug-related factors affecting medication adherence among Egyptian asthma patients

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Abstract
Background: The aim of this study is to evaluate adherence to inhaler therapy in asthmatic patients and examine drug-related factors affecting medication adherence among Egyptian asthma patients. The study was carried out among 110 clinically diagnosed asthma patients attending at a university hospital, Sohag, Egypt. Inhaler criteria and adherence were evaluated by a standardized tool “Morisky Medication Adherence Scale (MMAS), 2008.”

Results: The study revealed that out of 110 patients, 42.2% had a high level, 22.9% had medium level, and 34.9% had a low level of medication adherence. There was no relationship between demographic data and medication adherence in asthmatic patients. However, good adherence was frequently encountered among asthmatic patients who used inhaler twice daily, who used drugs its onset of action 5-20 min, who used aerolizer and turbo haler devices, and who used budesonide and budesonide/formoterol.

Conclusions: Poor adherence to inhaler therapy is high in patients with bronchial asthma attending Sohag University Hospital in Upper Egypt. There was a strong relationship between inhaled drug criteria and degree of adherence in asthmatic patients.

Background
Poor adherence to inhaler therapy in patients with bronchial asthma increases mortality, morbidity, and hospital visits [1, 2]. Increasing medication adherence is important to increase the benefits of inhaled treatment. So, assessment of the level of adherence to the inhaler therapy in asthmatic patients becomes essential in daily practice [2].

By opposition, poor adherence leads to poor clinical outcomes, an increase in morbidity and mortality, and unnecessary healthcare expenses [3]. Few studies have assessed adherence to asthma medications in Egypt. We aimed to evaluate adherence to inhaled therapy in asthmatic patients and to examine drug-related factors affecting medication adherence.

Methods
Study subjects and design
A descriptive cross-sectional study design was used, and 110 asthma patients were selected from the inpatient department and outpatient clinic of chest diseases, Sohag University Hospitals. Before the data collection, this study was approved by the ethical committee of Sohag University Hospitals and an informed consent was taken from the patients.

After taking informed consent from the patients, the informations regarding age, sex, literacy, residence, occupation, smoking habits, socioeconomic status, comorbidities, date of diagnosis of asthma, and pulmonary function tests were recorded.
Inhaler use
Further questions related to the currently prescribed aerosol therapy for asthma-like number of medications prescribed per day, type of device, type of drug, onset of action of inhaler, and frequency of administration of inhaler.

The current prescribed medications for asthma were identified for all included patients: inhaled steroids (ICS), long-acting β2-agonists (LABA), combined LABA/ICS, short-acting β2-agonists, short-acting anticholinergics, and long-acting anticholinergics. Most patients were on combination therapy.

Level of adherence
Level of adherence was examined by the eight-item Morisky Medication Adherence Scale (MMAS-8) [4]. According to MMAS-8, the level of adherence was high adherence (score, 8), moderate adherence (score, 6 to < 8), and low adherence (score, < 6). Patients with low or moderate level of adherence were considered non-adherent.

Statistical analysis
SPSS version 20 (SPSS Inc., Chicago, IL, USA) was used, and data is presented as mean ± standard deviations. To compare between groups, $\chi^2$ test and the ANOVA test were used. $P$ value of ≤ 0.05 was considered significant.

Results
The clinical data of studied patients are depicted in Table 1. A total of 110 included in the study. The age of patients was 39.22 ± 13.51 years. Most of the patients were females (69/41; 62.72%). Fifty percent of patients are illiterate. The most commonly used inhaled therapy in asthma patients is presented in Table 1.

As regard frequency of administration of inhaler, it was found that asthma patients were frequently using the inhaler twice daily; also, asthmatic patients used the on need more frequently. As regard the onset of action of inhaler, it was found that the inhaler of 5 min of onset of action was frequently used by asthma patients than other types of inhalers. As regard type of device, it was found that aerolizer, metered-dose inhaler (MDI), turbo halers, and hand halers were

| Table 1 Patients with asthma according to medications |
|--------------------------------------------------------|
| Variables                                             | Asthma |
| Frequency of administration of inhaler                |       |
| Once                                                  | 3 (2.7%) |
| Twice                                                 | 83 (75.5%) |
| On need                                               | 24 (21.8%) |
| Onset of action of inhaler                            |       |
| 5 min                                                 | 36 (32.7%) |
| 20 min                                                | 2 (1.9%) |
| 5-20 min                                              | 36 (32.7%) |
| 30 min                                                | 36 (32.7%) |
| Type of device                                        |       |
| Aerolizer                                             | 37 (33.6%) |
| MDI                                                   | 23 (20.9%) |
| Turbolser                                             | 38 (34.6%) |
| Handihaler                                            | 2 (1.8%) |
| Diskus                                                | 7 (6.4%) |
| Brezhsalier                                           | 1 (0.9%) |
| Evohaler                                              | 2 (1.8%) |
| Type of drug                                          |       |
| Budesonide                                            | 27 (24.5%) |
| Formoterol                                            | 11 (10.0%) |
| Salbutamol                                            | 23 (20.9%) |
| Budesonide/formoterol                                 | 37 (33.6%) |
| Fluticasone/salmelrot                                 | 8 (7.4%) |
| Glycopyrinum bromide                                   | 1 (0.9%) |
| Tiotropium                                            | 2 (1.8%) |
| Ipratropium                                           | 1 (0.9%) |

MDI metered-dose inhaler

![Fig. 1 Level of adherence among patients with bronchial asthma](image)
Table 2: Relation between demographic data and adherence pattern in asthmatic patients already on therapy (n = 110)

| Variables               | Good | Intermediate | Poor | Total          | P value |
|-------------------------|------|--------------|------|----------------|---------|
| Age/year                | 43.82 ± 13.501 | 42.61 ± 13.05 | 37.56 ± 15.84 | 41.86 ± 14.06 | 0.082   |
| Gender                  |      |              |      |                | 0.295   |
| Males                   | 12 (26.7%) | 9 (23.7%)    | 11 (40.7%) | 32 (29.1%)     |         |
| Females                 | 33 (73.3%) | 29 (76.3%)   | 16 (59.3%) | 78 (70.9%)     |         |
| Residence               |      |              |      |                | 0.742   |
| Rural                   | 19 (42.2%) | 13 (34.2%)   | 11 (40.7%) | 43 (39.1%)     |         |
| Urban                   | 26 (57.8%) | 25 (65.8%)   | 16 (59.3%) | 67 (60.9%)     |         |
| Educational level       |      |              |      |                | 0.563   |
| Illiterate              | 24 (53.3%) | 20 (52.6%)   | 11 (40.7%) | 55 (50%)       |         |
| Primary                 | 6 (13.3%)  | 8 (21.1%)    | 4 (14.8%)  | 18 (16.4%)     |         |
| Secondary               | 14 (31.1%) | 9 (23.7%)    | 9 (33.3%)  | 32 (29.1%)     |         |
| Graduate                | 0 (0.0%)   | 1 (2.6%)     | 1 (3.7%)   | 2 (1.8%)       |         |
| Postgraduate            | 1 (2.2%)   | 0 (0.0%)     | 2 (7.4%)   | 3 (2.7%)       |         |
| Socioeconomic           |      |              |      |                | 0.05    |
| Low                     | 0 (0.0%)   | 2 (5.3%)     | 2 (7.4%)   | 4 (3.6%)       |         |
| Middle                  | 45 (100%)  | 36 (94.7%)   | 23 (85.2%) | 104 (94.5%)    |         |
| High                    | 0 (0.0%)   | 0 (0.0%)     | 2 (7.4%)   | 2 (1.8%)       |         |
| Smoking status          |      |              |      |                | 0.289   |
| Non                     | 42 (93.3%) | 34 (89.5%)   | 21 (77.8%) | 97 (88.2%)     |         |
| Ex-smoker               | 3 (6.7%)   | 3 (7.9%)     | 3 (11.1%)  | 9 (8.2%)       |         |
| Stop smoking            | 0 (0.0%)   | 1 (2.6%)     | 2 (7.4%)   | 3 (2.7%)       |         |
| Current smoker          | 0 (0.0%)   | 0 (0.0%)     | 1 (3.7%)   | 1 (0.9%)       |         |
| Smoking index           |      |              |      |                | 0.797   |
| Mild                    | 1 (50%)    | 0 (0.0%)     | 2 (40%)    | 3 (37.5%)      |         |
| Moderate                | 0 (0.0%)   | 0 (0.0%)     | 1 (20%)    | 1 (12.5%)      |         |
| Heavy                   | 1 (50%)    | 1 (100%)     | 2 (40%)    | 4 (50%)        |         |
| Degree of asthma        |      |              |      |                | 0.082   |
| Intermittent            | 32 (45.7%) | 8 (21.1%)    | 21 (36.2%) | 61 (36.7%)     |         |
| Mild persistent         | 4 (5.7%)   | 9 (23.7%)    | 10 (17.2%) | 23 (13.9%)     |         |
| Moderate persistent     | 25 (35.7%) | 15 (39.5%)   | 21 (36.2%) | 61 (36.7%)     |         |
| Severe persistent       | 9 (12.9%)  | 6 (15.8%)    | 6 (10.3%)  | 21 (12.7%)     |         |
| Duration of disease     | 14.49 ± 9.36| 11.74 ± 8.45| 10.83 ± 10.32| 12.64 ± 10 | 0.097   |
| No. of emergency visit/last year | | | | | 0.231 |
| 1 visits                | 35 (77.8%) | 34 (89.5%)   | 19 (70.4%) | 88 (80%)       |         |
| 2-4 visits              | 7 (15.6%)  | 4 (10.5%)    | 7 (25.9%)  | 18 (16.4%)     |         |
| > 4 visits              | 3 (6.7%)   | 0 (0.0%)     | 1 (3.7%)   | 4 (3.6%)       |         |
| No. of comorbidities    |      |              |      |                | 0.153   |
| 1 comorbidities         | 27 (32.53%)| 31 (37.34%)  | 25 (30.13%)| 83 (75.45%)    |         |
| ≥ 2 comorbidities       | 11 (40.74%)| 9 (33.33%)   | 7 (25.93%) | 27 (24.55%)    |         |
frequently used by asthma in order than other types of devices. As regard type of drug, it was found that budesonide, formoterol, salbutamol, and budesonide/formoterol were frequently used by asthma in order than other types of drugs.

The different categories of adherence are shown in Fig. 1. A total of 42.2% of patients had good adherence, 22.9% intermediate adherence, and 34.9% poor adherence.

Table 2 shows the relation between demographic data and adherence in asthmatic patients already on inhaler therapy. No significant relationship between demographic data and medication adherence was found in asthmatic patients (P > 0.05).

The relation between drug characteristics and adherence patterns in asthma patients already on therapy is shown in Table 3 (Fig. 2 a-d). Adherence pattern was significantly associated with frequency of administration, onset of action, type of device, type of drug with P = (0.001, 0.002, 0.001, 0.001) respectively. It was found that good adherence frequently encountered among patients who used inhaler twice daily, who used drugs its onset of action < 5-20 min, who used aerolizer and turbo haler, and who used budesonide/formoterol and budesonide only.

**Discussion**

Poor adherence was associated with poor clinical outcomes among asthma patients. So that our study aimed at determining factors affecting inhaled therapy adherence in asthma patients using the MMAS-8 [5, 6].

The study was conducted in 110 asthma patients among which 69 were female and the other 41 were male. The mean age was of 39.22 ± 13.51 years. A total of 52.72% came from urban area, 86.36% had middle socioeconomic class, and 50% was illiterate. The duration of asthma was 11.21 ± 8.91 years. More than half (75.45%) of the patients had one comorbidity.

| Variables                      | Good     | Intermediate | Poor    | Total  | P value |
|--------------------------------|----------|--------------|---------|--------|---------|
| **Frequency of inhaler administration** |          |              |         |        | < 0.001 |
| Once                           | 0 (0.0%) | 2 (5.3%)     | 1 (3.7%)| 3 (2.7%)|         |
| Twice                          | 40 (88.9%) | 32 (84.2%) | 11 (40.7%) | 83 (75.5%) |         |
| On need                        | 5 (11.1%) | 4 (10.5%) | 15 (55.6%) | 24 (21.8%) |         |
| **Onset of action of inhaler**  |          |              |         |        | 0.002   |
| < 5-20 min                     | 13 (28.9%) | 19 (50%)   | 4 (14.8%) | 36 (32.7%) |         |
| 5 min                          | 13 (28.9%) | 8 (21.1%)  | 15 (55.6%) | 36 (32.7%) |         |
| 20 min                         | 0 (0.0%)  | 0 (0.0%)   | 2 (7.4%)  | 2 (1.9%)  |         |
| 30 min                         | 19 (42.2%) | 11 (28.9%) | 6 (22.2%) | 36 (32.7%) |         |
| **Type of device**             |          |              |         |        | 0.001   |
| Aerolizer                      | 20 (44.5%) | 13 (34.2%) | 4 (14.8%) | 37 (33.6%) |         |
| MDI                            | 5 (11.1%)  | 4 (10.6%)  | 14 (51.9%) | 23 (20.9%) |         |
| Turbohaler                     | 14 (31.1%) | 19 (50.0%) | 5 (18.5%) | 38 (34.5%) |         |
| Handihaler                     | 0 (0.0%)  | 1 (2.6%)   | 1 (3.7%)  | 2 (1.8%)  |         |
| Diskus                         | 4 (8.9%)  | 1 (2.6%)   | 2 (7.4%)  | 7 (6.4%)  |         |
| Breezhaler                     | 0 (0.0%)  | 0 (0.0%)   | 1 (3.7%)  | 1 (0.9%)  |         |
| Evohaler                       | 2 (4.4%)  | 0 (0.0%)   | 0 (0.0%)  | 2 (1.8%)  |         |
| **Type of drug**               |          |              |         |        | 0.001   |
| Budesonide                     | 15 (33.4%) | 9 (23.8%)  | 3 (11.1%) | 27 (24.5%) |         |
| Formoterol                     | 6 (13.3%)  | 4 (10.5%)  | 1 (3.7%)  | 11 (10%)  |         |
| Salbutamol                     | 5 (11.1%)  | 4 (10.5%)  | 14 (51.9%) | 23 (20.9%) |         |
| Budesonide/formoterol          | 13 (28.9%) | 19 (50%)   | 5 (18.5%) | 37 (33.6%) |         |
| Fluticasone/salmeterol         | 6 (13.3%)  | 1 (2.6%)   | 1 (3.7%)  | 8 (7.3%)  |         |
| Glycopyrinnur                   | 0 (0.0%)  | 0 (0.0%)   | 1 (3.7%)  | 1 (0.9%)  |         |
| Tiotropium                     | 0 (0.0%)  | 1 (2.6%)   | 1 (3.7%)  | 2 (1.8%)  |         |
| Ipratropium                    | 0 (0.0%)  | 0 (0.0%)   | 1 (3.7%)  | 1 (0.9%)  |         |

_N.B number of drug used more than patients as some patients use more than one drug, MDI metered-dose inhaler_
Among the studied population, poor adherence was observed in 34.9%, 22.9% intermediate adherence, and 42.2% of patients had good adherence. This result matches with the results of those who found that adherence among asthmatic patients was 49% [7, 8]. These results show that many patients with bronchial asthma are not adherent to their inhaled therapy. A previous study shows that inhaled therapy adherence is worse than other medications in asthmatic patients [9–12]. In other studies, medication adherence rates have consistently been shown to be 30–40% and may increase as high as 70% among asthma patients [9, 13–16]. This discrepancy in findings may be due to the difference in knowledge regarding asthma among participants, the use of different questionnaires, and the inclusion of different groups of the sample population in the study.

In this study, none of the sociodemographic information (such as age, gender, place of residence, educational status, comorbidity, severity of symptoms, and smoking habit) were associated with patients’ level of medication adherence. Consistent to these findings, Senior et al. showed that patients’ level of medication adherence was not associated with sociodemographic and clinical variables (age, gender, marital status, and place of residence, education, type of occupation and current smoking status, and severity of asthma [17]. However, these findings are contradictory with other studies [18]. The difference in findings might be due to the inclusion of patients of different duration of disease, different study designs, and use of different validated questionnaires in the studies.

As regard frequency of administration of inhaler in our study, we found that 75.5% preferred twice-daily therapy, 2.7% preferred once daily, and 21.8% used inhaler on need. There was a statistically significant association between good adherence and the use of inhaler twice daily in asthmatic patients in comparison with the use of on-need inhaler. However, this result is not comparable with Venables et al. [19]. Other studies found that adherence in asthmatic patients were unrelated to frequent uses of inhaler therapy [20–22]. Others observed that reliever inhalers were frequently used in asthmatic patients [23, 24].

As regard onset of action of inhaler, we found that the inhaler of 5–20 min of onset of action was frequently used by patients than other types of inhalers and this was statistically significant, this result due to asthma patients almost always complaining and need rescue bronchodilators medications which are rapidly acting, also, the drug-delivering its action.
rapidly lead the patient to continue taking the drug daily [25].

In our study, there was a statistically significant association between adherence and the use of turbohaler and aerolizer in asthmatic patients in comparison with the use of MDI. Our study result agrees with a previous study, which found that using dry-powder inhalers (DPIs) versus metered-dose inhalers (MDIs) was associated to adherence [26].

Moreover, a significant relationship was found between good adherence and budesonide/formoterol and budesonide in asthmatic patients in comparison with the use of salbutamol. This observation agrees with that of Axellson et al. [27] and Stempel et al. [28].

Conclusion
Adherence to inhaler therapy is low in Egyptian asthmatics. Type of device, type of drug, onset of action of inhaler, and frequency of administration of inhaler significantly affect medication adherence in asthma patients.

Abbreviations
ICS: Inhaled steroids; LABA: Long-acting β2-agonists; MMAS-8: Eight-item Morisky Medication Adherence Scale; SPSS: Statistical Package for the Social Sciences; MDI: Metered-dose inhaler; DPIs: Dry-powder inhalers

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Authors’ contributions
Abdellah Hamed, Kamal Atta, and Khaled Fwazy put the design of the work, interpreted the data, writing the manuscript, and revised it. Esraa Ameen performed the procedure, data acquisition, analysis, and a contributor in writing the manuscript. All authors have read and approved the final manuscript.

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Availability of data and materials
The datasets used during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
Before the data collection, this study was approved by the ethical committee of Sohag University Hospitals and an informed consent was taken from the patients.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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