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Original Research

Assessing adherence to medications: Is there a difference between a subjective method and an objective method, or between using them concurrently?

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Abstract

Background: Patients' adherence to medication can be assessed by several subjective or objective methods. The Global Initiative for Asthma (GINA) has recommended the use of both measures simultaneously. **Objective:** To assess patients' adherence to medication using a subjective or an objective method separately, and via using a combination of both methods. As well as identifying the degree of agreement between the two methods. **Methods:** Participants who met the study inclusion criteria completed the Adherence to Asthma Medication Questionnaire (AAMQ). A retrospective audit was conducted in order to extract pharmacy refill records for the previous twelve months. The patients' pharmacy refill records were expressed using the Medication Possession Ratio (MPR). Data were analyzed using the Statistical Package for Social Science. The degree of agreement was determined by Cohen's kappa coefficient (κ). **Results:** In terms of the difference in the ability of each method to identify non-adherent patients, a higher percentage of non-adherent patients were identified using the self-reported AAMQ (61.4%) compared to the pharmacy refill records (34.3%). When both methods, in combination, were used to assess adherence, the percentage of non-adherent patients was 80.0%, which is higher than each method when used separately. Twenty percent of the patients were considered adherent on both assessment methods, while 15.7% were considered non-adherent via both methods. Consequently, the AAMQ and pharmacy refill records agreed on 35.7% of the patients. The degree of agreement analysis showed a low correlation between the two methods. **Conclusion:** The combination strategy resulted in a higher percentage of non-adherent patients, compared to using a subjective (the AAMQ) or an objective (the pharmacy refill records) method. The GINA guideline proposition may be supported by the present study's findings.

Keywords: asthma; adherence to medication; questionnaire; pharmacy refill records

INTRODUCTION

Asthma is a chronic respiratory disease experienced by over 334 million individuals worldwide, it is characterized by wheezing, coughing, chest tightness, and breathing difficulties.[1,2] It is crucial to distinguish between severe asthma and uncontrolled asthma in order to determine the most appropriate intervention.[1] Improper inhaler technique and non-adherence to medications lead to uncontrolled asthma, thus, it is essential to assess the patient's adherence to medication.[3] Although adherence has received considerable attention in the literature, it is still considered a significant challenge to the healthcare system.[4,5]

Adherence is defined as the degree to which patients take medications as prescribed by the healthcare team, taking into consideration the amount of the dose, the frequency, and the correct time of each medication.[6] Adherence consists of three phases; initiation (the first time a patient takes the prescribed medication), implementation (the degree to which a patient actually follows the recommended dosing regimen), and discontinuation (the act of skipping the next dose to be taken and stopping all subsequent doses).[7] Adherence rates to asthma medications range from 14% to 50%.[8] Poor asthma control, increased hospitalizations, higher expenses, and higher mortality rates are all consequences of inadequate inhaler adherence, particularly in low- and middle-income countries.[9]

Patients' adherence to medication has been assessed using a variety of *direct* methods such as biological markers and observational measures and *indirect* methods such as questionnaires, pharmacy refill records, therapist evaluation, pill count, and electronic monitoring systems.[10,11] None of these methods has been nominated as a gold standard method

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in assessing the patient's adherence to medication.[12] The used methods to assess adherence are divided into *subjective* (e.g., questionnaires) and *objective* (e.g., pharmacy records) measures. The most reliable measure is the objective measure using the electronic monitoring devices (smart-inhalers).[13] However, this method is expensive, requires technical support, and the use of these devices is impractical in clinical practice.[11] In contrast, questionnaires are considered the most preferred used method due to their simplicity, ease of administration, and flexibility to accommodate various conditions. Moreover, questionnaires are able to predict patterns of non-adherence, patient perception towards medication and treatment regimen, and identify barriers to adherence.[11] Another widely used method to assess adherence to medications is to conduct a retrospective review of pharmacy refill records. It is a valid and suitable method that was used in several studies.[14-16] Furthermore, pharmacy refill records can be easily accessed electronically from the pharmacy, it is also a simple and low-cost method with acceptable reliability.[11]

The GINA has recommended the use of both measures simultaneously in order to assess patient adherence to medication.[17] However, there is limited clinical data that supported this combined approach. In view of the above, this study came to assess adherence to medication using three different methods: first, by using a subjective measure (the Adherence to Asthma Medication Questionnaire (AAMQ)), secondly, by using an objective measure1 (pharmacy refill records), and lastly by using a combination of both methods. The study also aimed to assess the degree of agreement between the two methods.

METHODS

Study design and inclusion criteria

A cross-sectional study (April 2020) and a retrospective review of pharmacy refill records (April 2019-April 2020) were conducted to address the study's objectives. To be eligible for the study, a patient had to have their asthma diagnosed by a specialist, currently prescribed regular inhaled corticosteroids for at least six months, over the age of 18, and be able to manage their medications themselves. These criteria were set to ensure the completeness of the pharmacy prescription records regarding medication use and adherence. Patients who met the inclusion criteria were approached by the researcher (RN) and invited to participate in the study.

Sampling method

The participants were recruited through a face-to-face approach using a convenience sampling method while they were waiting in the clinic to see their respiratory specialist. All participants were approached using the same standardized introduction script, which included explaining the study's objectives and what would be expected of them if they participated. Participants consenting to participate were then requested to sign the study's informed consent form and complete the AAMQ. The demographic information form (age, gender, marital status, living place, education, employment, and smoking status) was completed by all participants.

Adherence was measured for each patient using the three methods. Firstly, subjectively via the published and validated AAMQ, secondly, objectively via the pharmacy refill records, and thirdly, via using both methods simultaneously.

The subjective method (Adherence to Asthma Medication Questionnaire)

The AAMQ is a valid and reliable questionnaire designed to assess asthmatic patients' adherence to their medications. The AAMQ was developed via following a three phase pre-designed approach (extensive review of the literature, applying the Delphi technique, and pilot testing). It was validated using subjective and objective measures.[18] The AAMQ is a 13-item questionnaire with a scoring range of 13 to 65. The AAMQ has 5 possible scores for each item (Always (1), Often (2), Sometimes (3), Rarely (4), and Never (5)), with "Always" representing the worst possible score, and "Never" representing the best possible score.

The survey was administered in Arabic. Translation and back translation of the survey was conducted to ensure the accuracy of the translation. Qualified experts with many years of experience in translation did the translation.

The objective method (pharmacy refill records)

A retrospective audit of pharmacy refill records was conducted by the research team. Once the participants completed the AAMQ, one of the study researchers (RN) extracted their pharmacy refill records for the previous twelve months from the pharmacy. The drug names, the fill dates, directions for use, and the quantities supplied were all noted by the research team for each patient.

The patients' pharmacy refill records were expressed using the MPR, which is defined as the percentage of time a patient has access to his/her medication/s. It was calculated as a percentage by dividing the number of days at which the medication was supplied by the total number of days (from the first day of dispensing the medication to the last day in a particular predefined period).[6,10] If the patient dispensed the medication, the research team assumed that he/she has consumed it. The refill criteria for good adherence was set to be 75%, which presupposes that the patient took his/her monthly prescription from the pharmacy at least nine times during the past twelve-month study period. thus, patients were deemed non-adherent if their pharmacy refill was less than 75%.

Statistical analysis

Statistical analysis was performed with v.24 of the Statistical Package for the Social Sciences (SPSS-IBM; Chicago, IL, USA). The overall percentage of agreement between the two methods was determined by constructing a 2x2 table. The degree of agreement was determined by Cohen's kappa coefficient (κ).[19,20]

RESULTS

A total of 70 patients with asthma were recruited for this study. The participants' age ranged from 15 to 85 years old, with a mean age of 51.12 (SD= 15.34), of whom 65.7% were females. Table 1 shows the demographic data for the study participants.

Table 1. Demographic characteristics of the study participants (n= 70)

Parameter	n (%)
Gender	
• Male	24 (34.3%)
• Female	46 (65.7%)
Marital Status	
• Married	45 (64.3%)
• Single	17 (24.3%)
• Divorced	3 (4.3%)
• Widowed	5 (7.1%)
Living place	
• Amman (the Capital)	41 (58.6%)
• Other cities	29 (41.4%)
Educational level	
• Primary education	13 (18.5%)
• Secondary education	24 (34.3%)
• College	16 (22.9%)
• Bachelor's degree	17 (24.3%)
Employment	
• Employed	18 (25.7%)
• Retired	22 (31.4%)
• Student	4 (5.7%)
• Unemployed	26 (37.2%)
Smoking status	
• Smoker	18 (25.7%)
• Non-smoker	52 (74.3%)

The subjective method (Adherence to Asthma Medication Questionnaire)

Table 2 shows patients' self-reported adherence to their medications using the AAMQ, and the mean score for each item. The lowest mean was observed in item 6 (mean= 2.11) *"I stop taking my medication when I am feeling well"* followed by item 3 (mean= 2.19) *"I alter the dose (use less or more than the prescribed dose)"*, as more than 40.0% of the participants answered these two items with *"Often"*.

According to the AAMQ interpretation, a patient's adherence to asthma medication must be categorized into one of the following categories: poor adherence (total score= 13-29), moderate adherence (total score= 30-47), and excellent adherence (total score= 48-65). Fifteen participants (21.4%) were found to have poor adherence, 28 participants (40.0%) had moderate adherence, and 27 (38.6%) participants had excellent adherence to medications.

The objective method (pharmacy refill records)

The most prescribed medications among the participants were generally Asthalin inhaler® 200 metered doses bottle (salbutamol), Combivent® unit dose vials 2.5ml (ipratropium bromide and salbutamol sulphate), Pulmicrort® 0.5mg/ml nebulizer 2ml unit dose (budesonide), Symbicort turbuhaler® 60 doses (budesonide and formoterol), Seretide diskus® 50/250mcg 60 doses (50 micrograms salmeterol and 250 micrograms fluticasone propionate), cortisone nasal spray, Ramitin® 10mg tablets (loratadine), Omcet® 10mg tablets (cetirizine hydrochloride), Spiriva respimat® 2.5mcg solution for inhaler (tiotropium bromide monohydrate), Seebri breezhaler® 50mcg (glycopyrronium bromide), Duphalac syrup® 300Mls (lactulose solution), Ramlac syrup® 300ml (lactulose), Nocuf syrup® 120ml (natural herbs), vitamin D3® 50,000 IU per capsule, vitamin B12 Depot® 1mg/ml, Diusemide® 40mg tablets (furosemide), Salisal® 100mg tablet (acetylsalicylic acid), and Atorvast® 200mg tablets (atorvastatin).

According to the predefined refill threshold, which indicated that the patient took his/her monthly prescription at least nine times during the past twelve months, 46 out of the 70 patients (65.7%) were shown to be adherent to their asthma medications, whereas 34.3% (n= 24)were non-adherent.

Comparison between the AAMQ and the pharmacy records adherence assessment methods

To simplify the comparison between the methods, the AAMQ scores were divided into dichotomous data (adherent or non-adherent patient). Patients who scored ≤ 47 on the AAMQ were deemed non-adherent, whereas those who scored 48 or higher were considered adherent. Thus, 43 patients (61.4%) were found non-adherent, while 27 patients (38.6%) were found adherent to their asthma medication.

In terms of the difference in the ability of each method to identify non-adherent patients, higher percentages of non-adherent patients were identified using the self-reported AAMQ (61.4%) compared to the pharmacy refill records (34.3%).

Table 3 shows the difference between the AAMQ and the pharmacy records in assessing adherence and identifying non-adherent patients.

As shown in Table 3, 14 patients (20.0%) have an AAMQ score higher than 47 and a pharmacy refill record higher than 75%, thus, were considered adherent on both assessment methods. On the other hand, 15.7% were considered non-adherent via both methods. Consequently, the AAMQ and pharmacy refill records agreed on 25 patients (35.7%).

When both methods, in combination, were used to assess adherence, the percentage of non-adherent patients was 80.0%, which is higher than each method when used separately.

The degree of agreement which was determined using Cohen's kappa coefficient (κ) showed a low correlation (p= 0.200) between the two methods.

DISCUSSION

The main objective of the current study was to explore how two different adherence assessment methods; the AAMQ, and examining the patients' pharmacy records perform when assessing adherence, considering the overall agreement

Table 2. Patient (n= 70) self-reported adherence to their medications using the Adherence to Asthma Medication Questionnaire (AAMQ)

AAMQ items	**Always (1)** n (%)	**Often (2)** n (%)	**Sometimes (3)** n (%)	**Rarely (4)** n (%)	**Never (5)** n (%)	**Mean** (SD)
1. I think I do not need my medication	14 (20.0)	11 (15.7)	8 (11.4)	9 (12.9)	28 (40.0)	3.37 (1.61)
2. I think my medication is not effective	8 (11.4)	19 (27.1)	13 (18.6)	23 (32.9)	7 (10.0)	3.03 (1.22)
3. I alter the dose (use less or more than the prescribed dose)	19 (27.1)	30 (42.9)	12 (17.1)	7 (10.0)	2 (2.9)	2.19 (1.04)
4. I stop taking my medication out of fear of potential side effects	12 (17.1)	10 (14.3)	15 (21.4)	10 (14.3)	23 (32.9)	3.31 (1.50)
5. I do not take my medication because I dislike using corticosteroids	14 (20.0)	11 (15.7)	8 (11.4)	18 (25.7)	19 (27.1)	3.24 (1.51)
6. I stop taking my medication when I am feeling well	20 (28.6)	29 (41.4)	15 (21.4)	5 (7.1)	1 (1.4)	2.11 (0.96)
7. I take my medication only when I feel breathless	17 (24.3)	14 (20.0)	23 (32.9)	10 (14.3)	6 (8.6)	2.63 (1.42)
8. I stop taking my medication because I have multiple medications to take	9 (12.9)	16 (22.9)	15 (21.4)	14 (20.0)	16 (22.9)	3.17 (1.36)
9. I forget taking my medication	16 (22.9)	8 (11.4)	13 (18.6)	11 (15.7)	22 (31.4)	3.21 (1.56)
10. I cannot afford my medication	11 (15.7)	13 (18.6)	12 (17.1)	15 (21.4)	19 (27.1)	3.26 (1.44)
11. I stop taking my inhaler because I did not understand my doctor/pharmacist instructions on how to use it	18 (25.7)	8 (11.4)	11 (15.7)	11 (15.7)	22 (31.4)	3.16 (1.60)
12. I do not take my inhaler as I find it difficult to use it	15 (21.4)	9 (12.9)	13 (18.6)	13 (18.6)	20 (28.6)	3.20 (1.52)
13. I stop taking my inhaler because I am afraid of becoming addicted to it	13 (18.6)	9 (12.9)	7 (10.0)	11 (15.7)	30 (42.9)	3.51 (1.59)

Table 3. Comparison of medication adherence between the two methods among the study participants (n= 70)

	AAMQ	
Pharmacy Records	Adherent patient, n (%)	Non-adherent patient, n (%)
Adherent patient, n (%)	14 (20.0%)	32 (45.7%)
Non-adherent patient, n (%)	13 (18.6%)	11 (15.7%)

between the two methods, and whether a combination of the two different methods would provide a more accurate assessment. Results showed that although the AAMQ and the pharmacy records adherence methods were successful in identifying non-adherent patients, 20.0% of the patients were considered adherent on both assessment methods, while 15.7% were considered non-adherent via both methods. Consequently, the AAMQ and pharmacy refill records agreed on 35.7% of the patients.

Successful control of asthma depends on patients' adherence to their medications. Various methods have been used to assess adherence and each method has a distinct combination of strengths and weaknesses. The electronic monitoring devices have been seen by some as the gold standard, however; this method is costly and challenging to use in clinical settings.[10] Questionnaires and pharmacy refill records are often used in clinical practice because they are more convenient, practical, and noninvasive.[21] Self-reported questionnaires are generally fast, easy to use, and able to provide adequate information regarding patients' adherence to medications behavior, such as patterns of medication use and patient perception of appropriate use. Many studies have assessed the usefulness of these questionnaires in measuring adherence and many others have documented the ability of the self-reported questionnaire in identifying adherence problems.[18,22-26] On the other hand, some studies supported the use of pharmacy refill records to assess patients' adherence to medications.[27,28]

The GINA recommended the use of both measures simultaneously in order to assess patient's adherence to medication.[17] Nevertheless, there is not much clinical evidence to back up this combination strategy. In the current study, when the combination strategy was used, a higher percentage (80.0%) of non-adherent patients were identified, compared to using the AAMQ (61.4%) or the pharmacy records (34.3%), separately. Therefore, the GINA guideline proposition may be supported by the present study's findings.

In the current study, a higher percentage of non-adherent patients were identified through the self-reported AAMQ compared to the pharmacy refill records; this result can be explained by the fact that some patients take their asthma medications from the pharmacy but do not use it. Interestingly, the ability of the AAMQ to provide sufficient information regarding the patient's pattern of non-adherence can also be used to explain this result.[11] Taking a more profound look at the AAMQ scores reveals that the lowest mean was observed in 'item 6' followed by 'item 3', since a high percentage of the participants reported altering the dose or stopping to use the medication when feeling well by answering "*Often*". As described when developing and validating the AAMQ, 'items 6' and 'item 3' represent intentional non-adherence which is defined as deliberate non-adherence associated with patients' beliefs,[11] accordingly, in the current study, some patients may take their asthma medications from the pharmacy, however, they stop using it when feeling well as proposed in 'item 6' or they may alter the dose by using less or more than the prescribed dose as suggested in 'item 3'.

A previous study also found a low agreement between the self-reported questionnaire and the pharmacy refill records.[21] The reason behind this low agreement, as explained by the authors, was the different concepts these two methods utilized; classifying patients as adherent or non-adherent was based on different defining characteristics. Moreover, the time period was different among the two measures.[21] The previous finding is consistent with the findings of this study. On the other hand, other studies demonstrated a moderate correlation between self-reported questionnaires and pharmacy refill records.[29]

A recent study was conducted in 2019 by Plaza et al. to identify non-adherent patients with asthma or chronic obstructive pulmonary disease using, firstly, the published and validated Test of Adherence to Inhaler (TAI) questionnaire, secondly, the pharmacy refill records, and thirdly, both methods simultaneously. More than 800 patients were included in the study, about 58.0% of the participants were non-adherent according to the TAI, whereas around 29.0% were classified as non-adherent patients according to the pharmacy refill records. When both methods were applied simultaneously, the percentage of non-adherent patients increased to reach 64.6%. The study also aimed to assess the degree of concordance between the TAI and pharmacy refill records; a weak concordance between the two methods was found (Cohen's kappa= 0.205).[15] The previous study's findings come in line with the current study since a higher percentage of non-adherent patients was identified when both methods were used, furthermore, a low agreement was observed between the two methods in both studies. Thus, the same outcomes were found when the GINA recommendation to use both measures simultaneously was evaluated across two different populations.

Indeed, both methods agreed on 35.7% of the participants; however, it is worth highlighting that this low agreement strengthens the utility of the combined strategy, as proposed by GINA, for the reason that each method assesses a unique component of adherence. However, these components are complementary. Moreover, utilizing multiple methods in assessing patient's adherence enables the power of the first method to make up for the weakness of the second method, and vice versa.[30]

Limitations of this study include the fact that it was conducted in one public educational hospital in the capital of Amman, which may not be representative of the situation in other hospitals in the country, thus, this can limit the generalizability of the study. Another limitation of the current study that also can limit the generalizability, is the study sample size. Moreover, pharmacy refill records provide indirect evidence about prescription fulfillment; however, it does not conclude that the patient took the medication.

CONCLUSION

The combination strategy resulted in a higher percentage of non-adherent patients, compared to using a subjective or an objective method. utilizing multiple methods in assessing patient's adherence enables the power of the first method to make up for the weakness of the second method, and vice versa. The GINA guideline proposition may be supported by the present study's findings.

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CONFLICTS OF INTEREST

The authors declare no relevant conflicts of interest or financial relationships.

ETHICS APPROVAL

Ethical approval for this study was obtained from the Faculty of Pharmacy, Applied Science Private University (Approval Number: 2019-PHA-13).

SPECIFIC CONTRIBUTIONS OF EACH CONTRIBUTOR TO THE PAPER

All authors were involved in all parts of the study and manuscript preparation including literature search, study design, analysis of data, manuscript preparation, and review of the manuscript.

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