

(Research Article)

ISSN: 0975-8232



INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 29 September, 2011; received in revised form 13 January, 2012; accepted 30 January, 2012

ASSESSMENT OF COMPLIANCE TO TREATMENT AMONG AMBULATORY ASTHMATIC PATIENTS IN A SECONDARY HEALTH CARE FACILITY IN NIGERIA

A. A. Obasan, S. J. Showande* and T. O. Fakeye

Department of Clinical Pharmacy and Pharmacy Administration, Faculty of Pharmacy, University of Ibadan, Nigeria

ABSTRACT

Keywords: Compliance, Asthmatic patients, Pill count, Self report, Peak Expiratory Flow Rate

Correspondence to Author:

S. J. Showande

Department of Clinical Pharmacy and Pharmacy Administration, Faculty of Pharmacy, University of Ibadan, Nigeria This study assessed the level of compliance using three different methods: pill count, self report and peak expiratory flow rate, in asthmatic patients attending a secondary health care facility. Self report (using a pre-tested structured questionnaire), peak expiratory flow rate and pill count were used to assess patient's compliance and identify the factors which may be responsible for non compliance. Measurement of peak expiratory flow rate and the pill count were done at two different occasions. The data obtained was analysed using descriptive statistics. The study showed that the patients were prescribed a range of one to four drugs: 54% (3 drugs), 32% (2 drugs), 8% (4 drugs) and 2% (1 drug). The levels of compliance were 86.57% for self report and 83.56% for pill count (p > 0.05). Reasons given for non compliance were: apparent wellness (33.31%), forgetfulness (26.67%), cost of drugs (6.67%), dysphagia (6.67%), presence of non-disturbing symptoms (6.67%), side effects (6.67%), ignorance/fear of addiction (6.67%), perceived lack of benefit from treatment (6.67%), and lethargy towards chronic medication (6.67%). However, there was a significant difference in the readings of the peak expiratory flow rate measured at two different occasions (p < 0.05). The study showed no significant difference in the methods used to assess the level of compliance. Non compliance can be overcome by proper education of patients on the importance of complying with the administration of medication and proper usage of metered dose devices.

INTRODUCTION: Asthma is a reactive and sometimes reversible airway disease with attacks occurring episodically with varied intensity ¹. Despite the various forms of treatment/management that are available, ranging from oral medications to parenteral medications, asthma morbidity is still considerable ² and poor management has been associated with impaired quality of life ^{3, 4}. According to World Health Organisation (WHO) estimates, 300 million people suffer from asthma and 255,000 people died of asthma

in 2005 ⁵. Over 80% of asthma deaths occur in low and lower-middle income countries ⁵. The disease may be under-diagnosed and under-treated, creating a substantial burden to individuals and families and possibly restricting individuals' activities for a lifetime.

Compliance has been defined as the extent to which a patient's behaviour coincides with the medical or health advice given ⁶ and noncompliance is not only costly in terms of time, money and resources, but can

also be detrimental to the health care giver-patient relationship ⁷. Assessment of compliance in asthmatic patients and those with chronic diseases is attended with a lot of difficulties ⁷. WHO reported that 50% of patients from developed countries with chronic diseases do not use their medications as recommended ^{7, 8}. Compliance rate in asthma ranges from 30% to 92% worldwide ⁹⁻¹⁵.

Compliance failure with the treatment regimen may also result in loss of treatment efficacy or over-dosagerelated side effects and may lead to the administration of further medication and the involvement of the patient in unnecessary diagnostic procedure or hospitalization ⁶. Different methods of measuring compliance include self report using Morisky scale, clinical assessment, pill count, administrative pharmacy refill data, biological markers and electronic monitoring system such as Medication Event Monitoring System, MEMS. Different combinations of these methods have been found advisable for validating compliance ¹⁶⁻¹⁹.

Compliance with chronic diseases is usually found to be comparatively low ²⁰. There is a dearth of studies on compliance in asthmatic patients in Nigeria. This study was done to evaluate compliance among asthma patients in a selected secondary healthcare facility in south-western Nigeria using a combination of self report, pill count and peak expiratory flow measurement.

METHODS: Ethical approval was obtained from the local research ethics committee of the General Hospital at Ogun state in Southwest Nigeria. The importance of the study was explained to each patient/caregiver in English or Yoruba language, the local dialect. Written informed consent was obtained from each participant.

Study Setting: The outpatient clinic of a secondary health care facility in a south western state of Nigeria was used for this study.

Inclusion Criteria: Patients who had been diagnosed with asthma, on medications for a period of not less than one month, older than five years of age and were willing to take part in the study were recruited into the study. For children less than eighteen years old, the

consent of the caregiver who was usually a parent or an older sibling/guardian was sought and obtained.

Exclusion Criteria: Patients who were less than five years of age, those on admission or those who were recently diagnosed of the ailment for a period of less than a month were not recruited for this study.

Instrument of Study: To assess the level of compliance among the fifty patients who were enrolled for the study, three methods were used. These included a pretested self-administered questionnaire which was used to gather baseline information in order to assess patient's compliance and identify the factors which may be responsible for non compliance. Other methods include measurement of the peak expiratory flow rate of each patient after filling the questionnaire which was repeated after two weeks. The pill count method was carried out by noting the number of tablets (pills) of each drug the patient should use until the next appointment. The remaining number of tablets for each medication was also noted after two weeks.

Peak Expiratory Flow rate (PEF) of the patients was obtained using the peak flow meter (Micro Peak MPE 7200, Micro Medical UK). The reading was taken thrice with the highest reading taken as the patient's best PEF. The same process was repeated after two weeks and compared with the first reading. The compliance rate was calculated from the data obtained from the pill counts using the following equation:

Compliance rate = {Number of pills used / Number of pills expected to have been taken} X 100......(1)

Where:

Number of pills used = Number of pills dispensed -Number of pills remaining at the next visit......(2)

Data Analysis: The data obtained from the questionnaire were subjected to descriptive statistical analysis using the SPSS windows version 15 to evaluate the distribution of respondent's opinion. The number of patients with improved PEF (higher PEF reading) at the second reading was compared with those whose PEF reading did not improve (lower or same PEF reading).

RESULTS: Fifty patients were enrolled for the study. All completed the self report questionnaire, while majority participated in the pill count and measurement of the Peak Expiratory Flow rate (PEF). From the fifty respondents, 36 (72%) were female and 14 (28%) male. The age distribution showed that 28 (56%) and 14 (28%) were in the age range 20-60years (this age bracket represent the working-class group as shown by the occupational distribution) and > 60years respectively. Twenty two (44%) had tertiary education (**Table 1**).

Seven (14%) have had asthma since preschool age (0-5years), 4 (8%) have had it since school age (6-12years), 8 (16%) as teenager / adolescent (13 -19years), 23 (46%) as adults (20 - 60years) while 3 (6%) > sixty-one years. Two patients (4%) could not remember the exact time they were diagnosed. About half, 26 (52%) of these respondents experienced symptoms of the disease for the very first time less than 10years prior to the study while 19 (38%) had the symptoms 11-40 years before the study. However five (10%) of the patient cannot remember the first time they experienced the symptoms of the disease. Most of these patients 34 (68%) went to the hospital with the first experience of the ailment while others 16 (32%) self medicated or used herbal medicines on the advice of relatives or guardians.

TABLE 1: DEMOGRAPHIC DATA	OF THE RESPONDENTS
TABLE I. BEINGGRATHIC DATA	

DEMOGRAPHIC DATA OF THE RESPONDENTS		
DEWIOGRAPHIC VARIABLES		FREQUENCY (%)
AGE	6 – 12 years	2 (4%)
	13 - !9 years	6 (12%)
	20 – 60 years	28 (56%)
	61 years and above	14 (28%)
SEX	Male	14 (28%)
	Female	36 (72%)
	Married	25 (50%)
MARITAL STATUS	Single	20 (40%)
	Widowed	5 (10%)
EDUCATIONAL LEVEL	No formal education	2 (4%)
	Primary education	9 (18%)
	Secondary education	16 (32%)
	Tertiary education	22 (44%)
OCCUPATION	Student	18 (36%)
	Civil Servant	8 (16%)
	Trader	9 (18%)
	Pensioneer	8 (16%)
	Professional	4 (8%)
	Artisan	1 (2%)
	Farmer	2 (4%)

The major symptoms experienced by the patients in different combinations were: breathlessness 43 (86%), cough 39 (78%), dyspnea 32 (64%), wheezing 30(60%), tightness of chest 17(34%) Others included tiredness 3 (6%), catarrh 2 (4%), chest pain 2 (4%), sweating 2 (4%), palpitation 1 (2%) and dizziness 1 (2%). The precipitating factors of the disease as experienced by the respondents in different combinations were dust 35 (70%), process of frying food with oil 28 (56%), smoke fumes 15 (30%), humidity/rain 14 (28%), stress 8 (16%), certain food items such as spicy food, bread etc 4 (8%), cold drink 2 (4%) use of insecticide 1 (2%) and freshly cut grass 1 (2%).

The study showed that the patients were prescribed a range of one to four drugs; with 27 (54%) on three drugs, 17(32%) on two drugs, and 4(8%) on four drugs while 1(2%) of the patient was on one drug. Thirty four (68%) failed to take their drugs regularly according to instructions, the reasons given for this in different combinations were: apparent wellness 16 (33.31%); forgetfulness 13 (26.67%); cost of drugs 3 (6.67%); dysphagia 3 (6.67%); presence of non-disturbing symptoms 3 (6.67%); side effects 3 (6.67%) such as tremor due to salbutamol; ignorance/fear of addiction 3 (6.67%); perceived lack of benefit from treatment 3 (6.67%), and tiredness of having been on medication for long 3 (6.67%).

About 27 (54.55%) of the patients, who reported missing their medication, took the missed dose(s) as soon as they remembered while others 23(45.45%) reported taking the next dose at the scheduled time.

From the self-report, patients who were on 24 hourly daily dosage of medications had a compliance rate of 91.60% \pm 7.71 compared to those who were on 8 hourly daily dosage who had a compliance rate of 78.79% \pm 7.02 as shown in **Table 2**.

The pill count method showed that the different drugs used in the management of asthma in the secondary health care institution had average compliance rate ranging from 82.14% to 100% as shown in **Table 3**. Also, there was a significant difference in the expiratory flow rate (PEF) measured at the commencement of the study and after two weeks (p < 0.05).

TABLE 2: COMPLIANCE BASED ON FREQUENCY OF DOS	ΔGF
TABLE 2. CONTRIANCE DASED ON TREQUENCE OF DOS	AOL

TABLE 2. COMILIANCE BASED ON THE QUELTET OF BOSAGE			
FREQUENCY OF	NON-COMPLIANCE	COMPLIANCE	Ī
DOSAGE	(MEAN % ± SD)	(MEAN % ± SD)	
24 HOURLY DOSAGES	8.40 ± 7.71	91.60 ± 7.71	
12 HOURLY DOSAGES	16.97 ± 11.36	83.03 ± 11.36	
EIGHT HOURLY DOSAGES	21.21 ± 7.02	78.79 ± 7.02	
SD: standard doviation			

SD: standard deviation

TABLE 3: MEDICATION COMPLIANCE

MEDICATION	% NON-COMPLIANCE	% COMPLIANCE
Salbutamol inhaler	17.58	82.42
Aminophylline tablets	17.35	82.65
Prednisolone tablets	15.73	84.27
Asmanol F [®] tablets	0	100
Franol [®] tablets	11.91	88.09
Seretide inhaler	16.07	83.93
Salbutamol tablets	17.86	82.14

Asmanol F[°]: theophylline, ephedrine and chlorpheniramine; Franol[°]: theophylline and ephedrine; Seretide[°]: salmeterol and fluticasone

DISCUSSION: Majority of the patients who took part in this study were literate with about three quarters having a minimum of secondary school education. This level of education possibly made them aware of the consequences of not taking their medications regularly.

In this study, there was no significant association between age or gender and compliance; this has been reported in a previous study ²⁰. This is consistent with other studies which found out that non-compliance in adult with chronic diseases is not consistently dependent on age and gender ²¹⁻²³. Though, our findings seems to be in agreement with Hayes' study ²¹, other studies found out that compliant behaviour is dependent upon several interacting variables and that the likely type of non-compliant patients are: women (especially mothers of high parity) ^{24, 25}, the very young ²⁶, adolescents ²⁴, the elderly ²⁶⁻²⁷, non-Caucasian races ²⁸, social classes ^{26, 29}, low income groups ³⁰ and the unemployed ⁷. These conflicting results have been found to be due to the different methods of assessments used in the various studies ⁷.

Age distribution revealed that majority of the patients were adults within the age bracket of 20-60 years and most of the patients in this age group were workingclass individuals. However, 10% of the respondents gave financial reasons for stopping their medication which may imply that other patients' non-compliance may not be due to financial reasons. Majority of the patients interviewed in this study had been living with asthma for up to ten years. They were likely to be conversant with the symptoms, medications used for treatment when there is an exacerbation and the precipitating factors that may be responsible. Asthma is a chronic disease that sometimes shows periods of remission or even asymptomatic obstruction. The chronic nature of the disease might have a negative impact on compliance ¹⁰. Earlier research has shown that with time, people with asthma or allergies tend to dissociate themselves from the prescribed treatment, and this may invariably impact on compliance ³¹.

The study revealed that apparent wellness and forgetfulness were the major factors affecting compliance among these patients. Other factors mentioned by the patients were cost of drugs, dysphagia, few symptoms, side effects, nonchalant attitude about prescription, perceived lack of benefit from treatment, and lethargy towards chronic medication. Studies ³²⁻³⁴ found out that forgetfulness is the most common cause of non-compliance in hypertension and asthma. According to these studies, the chronic nature of the illness and the daily administration of medications may greatly concern the patient resulting in a repression of desire to follow plan.

Being ill is a cause for concern and having to take a drug is a constant reminder of illness. Hectic lifestyle and irregular schedules also raise the risk of patients forgetting to take their medications. Since, asthma is a chronic condition in which attack is intermittent and occur for a while, depending on the level, extent and duration of exposure to precipitating factors (and some other factors), there is a great tendency for such a patient to forget taking his or her pill as symptoms of the condition wax and wane. This makes compliance difficult to sustain, as the patient may remain asymptomatic for a long time ³².

Some patients reported that they developed tremor to salbutamol, which made them stop the medication. Butler *et al.*, 2004 ³⁵, found out that if symptoms or side effects interfere with daily activities or social skills, compliance might diminish ³⁵. If patients are properly counselled on the magnitude of expected side effects from their medications it may limit the rate of non

compliance in asthmatic patients. Cost of drugs has been found to also serve as an obstacle to compliance ¹³. In this study, 3(6.67%) of the patients complained that their medications were expensive and that sometimes they were financially incapacitated to purchase their medications. There may be various ways this could have a negative effect on compliance as reported in some studies ^{35, 36}.

Patient experiencing financial hardship may find it difficult to spend money on a medication particularly if it does not result in an immediate change in health status or the benefit of the medication is not properly understood. Others may not use a particular medication because of the cost, resulting in the usage of drugs with lower cost which might not be as effective. Prior studies ^{13, 35, 36} found that non-adherence might be due to financial concerns as the cost of medical care rises or may be related to perceived financial distress by the patients rather than an actual cost of the medications or the source of payment.

Ignorance was observed to be one of the factors encouraging non-compliance. Some patients who were placed on inhalers, refused to use it because of the fear that they might become addicted to it especially if it is needed during acute exacerbation and if it is unavailable, they may die. Fear of becoming dependent on treatment is another reason that is commonly cited to explain noncompliant behaviour ³⁷⁻ ³⁹. Some also believed that the inhalers are meant for those whose conditions are life threatening and will not want to get to that stage. This observation is supported by the findings of another study ⁴⁰ where some patients expressed feelings of guilt having to take medication regularly, whereas others see it as a social stigma.

The pharmacists can play a large role educating patients on the basic facts of asthma especially the role of medications (especially the distinction between quick relief and long term control medications), skills for proper inhaler use with or without a spacer, use of peak flow meter for monitoring and self assessment in the management of the disease. Also, the pharmacist should educate patients on environmental control measures, and appropriate use of rescue plans and medications. The result from pill count method showed that the compliance rate ranged from 82% to 100% with an average compliance of 83.67% (16.33% noncompliance rate). Average compliance rate ranking according to dosing frequency was 24hr > 12hr > 8hr showing that the higher the frequency of daily dosage the lower the compliance rate. In one study ⁴¹ the compliance levels achieved with twice daily as opposed to three times daily regimens were found to drop as compared with our findings which was 82% and 78% for twice and thrice daily dosing respectively.

The result for this study was higher but it may be connected with the methods used for the assessment which were self report questionnaires, daily diary reports and electronic monitors in children with cystic fibrosis. Though, compliance has been shown to drop sharply as the number of drugs taken daily increases ⁴²⁻⁴³, increasing the number of prescribed drugs may not always result in poor compliance ⁴⁴.

For example, a patient on three or more drugs which has to be taken once a day may be more compliant than a patient who is on one drug but has to take it three times daily. It is evident that the frequency of daily dosage has more effect on compliance rate than the number of drugs the patient is using ⁴⁴. The duration of treatment is also important with treatment extending beyond five days being particularly affected by poor compliance ⁴⁵⁻⁴⁶ such as we have in chronic diseases. As expected the highest levels of compliance are achieved when the drug is administered parenterally for a short period ¹¹.

The result of the clinical response in which peak flow meter was used to measure the peak expiratory flow rate indicated a significant difference between the initial PEF and those carried out after the usage of the medications. This method may however not be able to determine the extent to which the patient has complied with his medication accurately, despite this; it has helped to confirm some measure of compliance which may however not be quantifiable.

Comparison of the three methods of assessing compliance showed that self-report has a higher average compliance rate of 86.57% compared to 83.56% calculated for pill count method. This study was limited by the fact that the compliance rate using the peak flow meter monitoring could not be calculated since the readings were only taken twice and not repeatedly for a considerable length of time. Also, compliance could not be calculated for medications taken "as needed" including short time metered dose inhalers. The pill count method also is limited by the fact that it cannot verify that a dose removed from the container was actually consumed, or that it was consumed at the correct time.

In this study, the pill count confirmed non compliance as given by self report in this group of asthmatic patients. Higher compliance rate calculated for selfreport might be due to vulnerability of the method to reporting bias, problems with recalls and exaggeration of compliance by patients. This result is consistent with study conducted by Quittner *et al.*, 2000⁴¹.

As good as multi-method measure of compliance is, there are some limitations noted: first, although multimethod measure of compliance is ideal, different measurement methods use different time scale. For example, pill count can be calculated over the entire monitoring period while self-report measures average compliance over a relatively unspecified period. The time interval differences make comparison across measurement method difficult to interpret. Secondly, the methods do not account for whether the medication was actually taken by the patient.

CONCLUSION: The reasons given for non-compliance in this study such as cost of medication, forgetfulness, ignorance, social stigma, side effect of medications, apparent wellness, perceived lack of benefit from medications and been on the same medication for a long time- were detected using the self report method of evaluating compliance. Though the compliance rate from this method was higher than that reported by the pill count method, both methods complimented each other. The Peak Flow Meter readings showed an improvement which indicated compliance with medications on the part of the patient though the rate of compliance could not be ascertained. The reasons given for non compliance in the group of patients' studied could be overcome with proper and detailed education as majority of them are as a result of ignorance or inadequate information. If this is done, the level of compliance among asthmatic patients may improve.

REFERENCES:

- Creer TL, Renne CM, Chai H. The application of behavioural techniques to childhood asthma. In D.C Russo & Varni JW (Eds). Behavioural paediatrics: Research and Practice. 1982. 27-66. New York, New York. Plenum.
- Thoonen BPA, Schermer TRJ, Boom G, Molema J, Folgering H, Akkermans RP *et al.* Self-management of asthma in general practice, asthma control and quality of life: a randomised controlled trial. Thorax. 2003; 58 (1):30–36
- Juniper EF, Guyatt GH, Epstein RS, Jaeschke R, and Hiller TK. Evaluation of impairment of health related quality of life in asthma: development of a questionnaire for use in clinical trials. Thorax. 1992; 47 (2):76–83.
- 4. Juniper EF, Guyatt GH, Ferrie PJ, Griffith LE. Measuring quality of life in asthma. Am Rev Respir Dis. 1993; 147 (4):832–8.
- http://www.who.int/respiratory/asthma/en/ (accessed on 5th January, 2011)
- 6. Neville R. Getting patients to take their drugs. MIMS Magazine; 1987: 22-24.
- 7. Susan G. A review of the factors associated with patient compliance and the taking of prescribed medicines. British Journal of General Practice. 1990. 40, 114-116.
- 8. World Health Organization. Adherence to long-term therapies: evidence for action. Geneva: WHO, 2003.
- 9. Bander B, Milgrom H, Rand C. Non-adherence in asthmatic patients: is there a solution to the problem. Ann Allergy Asthma Immunol. 1997. 79:177–85.
- Verschelden P, Cartier A, L'Archevêque J, Trudeau C, Malo JL. Compliance with and accuracy of daily self-assessment of peak expiratory flows (PEF) in asthmatic subjects over a three month period. Eur Respir J. 1996, 9, 880–885
- 11. Colcher JS, Bass JW. Penicillin treatment of streptococcal pharyngitis: a comparison of schedules and the role of specific counselling. JAMA 1972: 222: 457.
- Palen JV, Klein JJ, Rovers MM. Compliance with inhaled medication and self-treatment guidelines following a selfmanagement programme in adult asthmatics. Eur Respir J. 1997. 10: 652–657.
- 13. Petkova V. Physicians, pharmacists and patients' compliance with chronic treatment in Bulgaria. Pharmacoepidemiol Drug Saf. 2006; 15(8):607-12.
- 14. Petkova V, Dimitrova Z. Asthma, drug medication and noncompliance. Boll Chim Farm. 2002; 141(5):355-6.
- Chung KF & Naya I. Compliance with an oral asthma medication: a pilot study using an electronic monitoring device. Respiratory Medicine. 2000. 94(9): 852-858.
- Hughes DA, Cowell W, Koncz T, Cramer J. Methods for considering medication compliance and persistence in pharmaco-economic evaluations. Value in Health (Published online: 22-May-2007)
- Spilker B. Methods of assessing and improving compliance in clinical trials. In: Cramer JA, Spilker B, eds. Patient compliance in medical practice and clinical trials. New York: Raven Press. 1991:37-56
- Liu H, Golin CE, Miller LG, Hays RD, Beck CK, Sanandaji S, *et al*. A comparison study of multiple measures of adherence to HIV protease inhibitors. Ann Intern Med 2001; 134:968-77. [Erratum, Ann Intern Med. 2002; 136:175.]
- 19. Turner BJ, Hecht FM. Improving on a coin toss to predict patient adherence to medications. Ann Intern Med 2001; 134:1004-6.
- Sabate E (ed): "Adherence to Long Term Therapy: Evidence for Action" World Health Organisation. Geneva, 2003. 212. ISBN 92-4-154599-2 [1] 2003

- 21. Hayes-Baulista DE. Modifying the treatment; patient compliance, patient control and medical care. Soc Sci Med. 1976; 10: 233-238
- 22. Balkrishnan R. Predictors of medication adherence in the elderly. Clin Ther. 1998; 20:764-71.
- Stone V E, Hogan JW. Schuman P, Rompalo A M, Howard AA, Korkontzelou C *et al*. Antiretroviral regimen complexity, self reported adherence, and HIV patients' understanding of their regimens: survey of women in the HER Study. J Acquir Immune Defic Syndr 2001; 28 (2):124-31
- Becker MH, Maiman LA. Socio-behavioural determinants of compliance with health and medical care recommendations. Med Care. 1975; 13: 10-24.
- 25. Porter AMW. Drug defaulting in a general practice. Br Med J. 1969; 1: 218-222.
- 26. Blackwell B. Patient compliance. N Engl J Med 1973; 289: 249.
- Gryfe CI, Gryfe BM. Drug therapy of the aged: the problem of compliance and the roles of physicians and pharmacists. J Am Geriatr Soc. 1984; 32: 301-307.
- 28. Chapman SF. Psychotropic drug use in the elderly. Public ignorance or indifference? Med J Aust. 1976; 2: 62-64.
- 29. Gilbert JR, Evans CE, Haynes RB, Tugwell P. Protecting compliance with a regime of digoxin therapy in family practice. Can Med Assoc J. 1980; 123: 119-122.
- Baekeland F, Lundwall L. Dropping out of treatment: a critical review. Psychol Bull. 1975; 82: 738-783.
- Hanson SM. Refusing to be ill: A longitudinal study of patients relationship with the asthma/allergy: Medical dissertations (in Swedish) Gothenburg University. 1955.
- Maijtas J and Liscakova A. Medication compliance patterns in population with antihypertensive treatment. Bratislavia: Faculty of Pharmacy, Comenius University. 2003.
- Ulrik CS, Lange P, Plaschke PP, Backer V, Søes-Petersen U, Harving H. The quality of asthma treatment in Denmark. How far are we--and how far are our patients? Ugeskr Laeger. 2008; 170(4):230-4.
- Walewski KM, Cicutto L, D'Urzo AD, Heslegrave RJ, Chapman KR. Evaluation of a questionnaire to assess compliance with anti-asthma medications. J Asthma. 2004; 41(1):77-83.
- 35. Butler JA, Roderick P, Mullee M, Mason JC, Peveler RC. Frequency and impact of nonadherence to

immunosuppressants after renal transplantation: a systematic review. Transplantation. 2004. 77 (5) 769-776

- Balkrishnan R, Rajagopalan R, Fabian T, Camacho MS, Sally A. Huston MS, et al. Predictors of medication adherence and associated health care costs in an older population with type 2 diabetes mellitus: A longitudinal cohort study. Clinical Therapeutics, 2003. (25) 11: 2958-2971
- 37. Prien RF, Cathy EM. Long-term maintenance drug therapy and the current effective illnesses: current status and issues. Diseases of the Nervous System. 1977; 38: 991.
- 38. Stimpson GB. Obeying doctors orders: a view from the other side. Soc Sci Med. 1974; 8: 97.
- 39. Evans L, Spelman N. Problem of non-compliance with drug therapy. Drugs. 1983; 25: 63-76.
- 40. Kutay Demirkan. Asthma In: Textbook of therapeutics, Drug and Disease management. Hefindale and Gourley. 1996. 721-262
- Quittner AL, Espelage DL, Levers-Landis C, Drotar D. Measuring adherence to medical treatments in childhood chronic illness. Considering multiple methods and sources of information. Journal of clinical and Psychology in medical Settings. 2000. 7 (1), 41-54
- 42. Reasner CA, Goke B. Overcoming the barriers to effective glycemic control for type 2 diabetes. Br J Diabetes Vasc Dis. 2002; 2:290-5.
- Blandford L, Dans PE, Ober JD, Wheelock C. Analyzing variations in medication compliance related to individual drug, drug class, and prescribing physician. J Managed Care Pharm. 1999; 5:47-5
- 44. Seth AE, Douglas KM, Robert SW, Edward S, Thomas RP. The Effect of Prescribed Daily Dose Frequency on Patient Medication Compliance. Arch Intern Med. 1990; 150(9):1881-1884.
- Carey RM, Reid RA, Ayers CR, Lynch SS, McLain WL, Vaughan ED. The Charlottesville blood pressure survey. The value of repeated blood pressure measurements. JAMA 1976; 236 (7): 847-851.
- Mohoer D, Wallin DG, Dreyfuss EG. Studies in the home treatment of streptococcal disease. Failure of patients to take penicillin by mouth as prescribed. N Engl J Med. 1955; 252: 1116.
