Factors Affecting Adherence of Patients with Bronchial Asthma and Chronic Obstructive Pulmonary Disease to Inhaled Therapy

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Abstract

Background:adherence to medication is a growing issue and there aremany factors affecting adherence in bronchial asthma and COPD.

Objectives: This study was designed to determine the factors affectingadherence to inhalation therapy in asthma and chronic obstructivepulmonary disease.

Patients and Methods*:* The present study included 300 patients (164males and 136 females and 156 COPD and 144 asthma also 189 werealready on inhaler therapy and 111 were naive(no previous inhaler)whoattended Sohag university hospital (inpatient department and outpatientclinic of chest diseases)during the period from April 2016 to May 2017using morisky questionnaire to determine factors affecting adherence toinhaled therapy.

Results*:* 300 patients 164cases (54.67%) were males and 136 cases(45.73)were female, Good adherence to inhaled therapy was observed in 124 (35.3%) patients and both intermediate and good adherence was observed in 227 (64.6%) patients. Most of the naive patients were poor adherent to inhaled therapy.There was no relationship between demographic data and adherence in asthmatic patients. However, there was significant relation between adherence and socioeconomic status and residence in COPD patients. Patients with bronchial asthma had better adherence to inhaled therapy than patients with COPD, However good adherence was frequently encountered in patients with COPD who had 2-4 emergency visits in the last year. Good adherence was observed frequently in patients who had ENT diseases as comorbidity, while poor adherence was observed frequently in patients who had cardiac disease. Good adherence was frequently encountered among asthmatic patients whoused inhaler twice daily, who used drugs its onset of action 5- 20 minutes, whoused aerolizer and turbohaler devices and who used budesonide and budesonide/formetrol. Good adherence was frequently encountered among patients with COPD who used inhaler twice daily, who used aerolizer and handihaler devices and who used formetrol and tiotropium

Conclusion*:* This study confirmed that many factors affect adherence toinhaled therapy,so the interventions to maintain adherence contain fivecategories should be joint together(patient related factors, condition related factors, drug related factors, healthcare system related and socioeconomic status)to improve adherence and thus quality of life.

Key Words*:* COPD, bronchial asthma, adherence, inhaled therapy.

INTRODUCTION

Asthma and chronic obstructive pulmonary disease (COPD)are two of the leading causes of morbidity, mortality and economic burden worldwide.Approximately 235 million people are thought to suffer from asthma globally,and 65millionare affected by moderate-to-severe COPDestimates that chronic respiratory diseases represent 5% of total disease burden and 8.3% of chronic disease burden worldwide, accounting for more than 4 million deaths each year.COPD is expected to be the third leading cause of mortality by 2030, The burden of chronic respiratory diseases has major adverse effects on the quality of life and ability of affected individuals. Indeed, asthma and COPD are ranked 22nd and 10th, respectively, in terms of the leading causes of disease burden when assessed using disability-adjusted life years **(world health organization (WHO, 2007)**.Adherence to medication is a crucial part of patient care and indispensable for reaching clinical goals. The WHO, in its 2003 report on medication adherence, states that "increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment" **(Sabat´e, 2003)**. By opposition, non adherence leads to poor clinical outcomes, increase in morbidity and death rates, and unnecessary healthcare expenditure **(Brown and Bussell, 2011)**.

While non communicable and mental illnesses are expected to exceed 65% of the global burden of disease in 2020, approximately 50%–60% of patients are non adherent to the medicine that they have been prescribed, especially those suffering from chronic diseases **(Lavsa et al., 2011)**.

The aim of the study:was to identify the factors that contribute to adherence to inhaled therapy in patientswith bronchial asthma and COPD and to improve treatment outcome in thosepatients.

Patients and Method: This prospective study of factors affecting adherence of patients with bronchial asthma and chronic obstructive pulmonary disease to inhaled therapy was carried out on 300 patients (164 males and 136 females and 156 COPD and 144 asthma also 189 were already on inhaler therapy and 111 were naive (no previous inhaler) who attended Sohag university hospital (inpatient department and outpatient clinic of chest diseases)during the period from April 2016 to May 2017. Patients included in the study were already diagnosed to have COPD or Bronchial asthma based on GOLD and GINA criteria **(GOLD and GINA, 2017).** The study was approved by the local ethics committee of sohag university hospital and a written informed consent was obtained from every patient included in the study.

The current prescribed medications for asthma and COPD were identified for all included patients. Respiratory medications included long-acting β2-agonists(LABA), inhaled corticosteroids, combined LABA/ inhaled corticosteroids, combined LABA and long acting anticholinergics, short-acting anticholinergics, short-acting β2-agonists, long-acting anticholinergics, combined anticholinergics/short-acting β2-agonists.Most patients were on combination therapy. All participants were interviewed and detailed medical history taking as well as thorough clinical examination, plain chest

radiography, and spirometry were recorded.

Lung function: Prebronchodilator and postbronchodilator reversibilitytests were performed according to the standard practice. Forced expiratory in the first second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, with the highest valuesrecorded and severity of COPD was assessed according to GOLD guidelines (Stage I: mild COPD, FEV1 > 80.0% predicted; Stage II: moderate COPD, 50.0%≤ FEV1<80.0% predicted; Stage III: severe COPD, 30.0%≤ FEV1<50.0%; Stage IV: very severe COPD, FEV1 <30.0%, or FEV1 <50.0% predicted with respiratory failure **(GOLD, 2011).**

Medication adherence: Medication adherence was tested using the Morisky Questionnaire (the modified version with 3 specific questions on inhaled therapy) **(Morisky et al., 1986)**on patients already on treatment, and using another Questionnaire to estimate the compliance of patients who newly starting inhaler therapy**(Rotter , 1979)**The modified version of morisky scale is an seven-itemquestionnaire with yes/no questions . On the basis ofthe scoring system , adherence wasrated as follows: good adherence (score: 0-1), moderateadherence (score: 2-4), and poor adherence (score:5-7).

Statistical analysis: Data was analyzed using STATA intercooled version 14.2. Quantitative data was represented as mean, standard deviation, median and range. Data was analyzed using student t-test to compare means of two groups and ANOVA for comparison of the means of three groups. When the data was not normally distributed Kruskal Wallis test for comparison of three or more groups and Mann-Whitney test was used to compare two groups. Qualitative data was presented as number and percentage and compared using either Chi square test or fisher exact test. Graphs were produced by using Excel or STATA program. P value was considered significant if it was less than 0.05.

Results

Variables	Asthma	COPD	P value
Age/year Mean ± SD Median (range)	39.22±13.51 40 (12-70)	63.01±10.58 61 (35-95)	<0.0001
GenderMales Females	41 (28.47%) 103 (71.53%)	123 (78.85%) 33 (21.15%)	<0.0001
Residence Rural Urban	58 (40.28%) 86 (59.72%)	95 (60.90%) 61 (39.10%)	<0.0001
BMIMean ± SD Median (range)	27.02±4.86 25.55(19.6-43.5)	24.94±3.73 24.3(16-47.6)	<0.0001
Educational level Illiterate Primary Secondary Graduate Postgraduate	 65 (45.14%) 25 (17.36%) 43 (29.86%) 5 (3.47%) 6 (4.17%)	 134 (85.90%) 12 (7.69%) 6 (3.85%) 1 (0.64%) 3 (1.92%)	<0.0001
Socioeconomic status Low Middle High	 10 (6.94%) 129 (89.58%) 5 (3.47%)	 27 (17.31%) 125 (80.13%) 4 (2.56%)	0.02
Smoking status Non Ex-smoker Stop smoking Current smoker	 130 (90.28%) 8 (5.55%) 3 (2.1%) 3 (2.1%)	 35 (22.4%) 83 (53.2%) 16 (10.3%) 22 (14.1%)	<0.001
Smoking index Mild Moderate Heavy	2 (20%) 1 (10%) 7 (70%)	79 (77.5%) 2 (2%) 21 (20.5%)	<0.001
Total number for SI	10	102	

SI: smoking index

Table (1) Comparison between patients with asthma (n=144) and COPD (n=156) according to demographic data and smoking history

Table (1)shows that by comparing patients with bronchial asthma and patients with COPD in the studied population, there were statistically significant differences as regard age, gender, residence, body mass index, educational level, socioeconomic status p= (<0.0001 ,<0.0001, <0.0001, <0.0001, <0.0001, 0.02) respectively ,where older age, male gender, rural residence, low BMI, low educational level, low socioeconomic status were more frequent in COPD patients

As regard smoking history in the studied population table(2) shows that COPD patients were more frequently heavy smokers in comparison with asthmatic patients (p=<0.0001).

Parameter	Asthma N (%)	COPD N (%)	Total N (%)
One inhaler			
-Naive patients	**56**	**55**	**111 (44.58%)**
-Patients on treatment	**70**	**68**	**138 (55.42%)**
Total	**126**	**123**	**249 (100%)**
Two inhaler			
-Naive patients	**0**	**0**	**0 (0%)**
- Patients on treatment	**20**	**31**	**51(100%)**
Total	**20**	**31**	**51 (100%)**

Table(2)Distribution of the studied population according to number of inhaler and start of use of inhaler (N=300)

Table (2)shows thedistribution of the studied population according to number of inhaler and start of use of inhaler. Among the studied population, there were 249 (83%) patients used one inhaler, out of them 111 patients were naive(as regard use of inhaler) and 138 patients were already using inhaler treatment ; and 51(17%) patients used two inhaler all of them were already using inhaler treatment.

Pattern	Naive patients N (%)	Patients already on treatment*N (%)	Total	P value
Good	25	99	124 (35.32%)	
Intermediate	0	103	103 (29.34%)	0.00
Poor	86	38	124 (35.32%)	
Total	111	240	351(100%)	

Table(3) Pattern of adherence in the studied population

Table (3) shows pattern of adherence in the studied population. Out of the studied population, there were124 (35.32%) patients had good adherence to inhaled therapy, out of them 25 were naive patients and 99 patients were already on treatment . Out of the studied population , there were 103(29.34%) patients had intermediate adherence all of them were patients already on treatment as there is no intermediate score in the questionnaire of the naive patients , also there were124 (35.32%) patients had poor adherent, Out of them 86 were naive patients and 38 patients were already on treatment.

Variables	Asthma	COPD	Total	P value
Frequency of inhaler administration				
Once	3 (2.7%)	33 (25.4%)	36 (15%)	
Twice	83 (75.5%)	83 (63.8%)	166 (69.2%)	<0.001
on need	24 (21.8%)	14 (63.8%)	38 (15.8%)	
Onset of action of inhaler				
5 minutes	36 (32.7%)	69 (53.1%)	105 (43.7%)	
20 minutes	2 (1.9%)	1 (0.8%)	3 (1.3%)	<0.001
5-20 minutes	36 (32.7%)	11 (8.4%)	47 (19.6%)	
30 minutes	36 (32.7%)	49 (37.7%)	85 (35.4%)	
Type of device				
Aerolizer	37 (33.6%)	66 (50.8%)	103 (42.9%)	
MDI	23 (20.9%)	16 (12.3%)	39 (16.3%)	
Turbohaler	38 (34.6%)	12 (9.2%)	50 (20.8%)	<0.001
Handihaler	2 (1.8%)	20 (15.4%)	22 (9.2%)	
Diskus	7 (6.4%)	6 (4.6%)	13 (5.4%)	
Breezhaler	1 (0.9%)	9 (6.9%)	10 (4.2%)	
Respimat	0 (0.0%)	1 (0.8%)	1 (0.4%)	
Evohaler	2 (1.8%)	0 (0.0%)	2 (0.8%)	
Type of drug				
Budesonide	27 (24.5%)	17 (13.1%)	44 (18.3%)	
Formetrol	11 (10.0%)	49 (37.7%)	60 (25%)	
Salbutamol	23 (20.9%)	13 (10.0%)	36 (15%)	
Budesonide formetrol	37 (33.6%)	12 (9.2%)	49 (20.4%)	
Fluticasone salmetrol	8 (7.4%)	6 (4.6%)	14 (5.8%)	<0.001
Glycopyrinum bromide	1 (0.9%)	5 (3.8%)	6 (2.5%)	
Tiotropium	2 (1.8%)	21 (16.2%)	23 (9.6%)	
Ipratropium	1 (0.9%)	1 (0.8%)	2 (0.8%)	
Formetrolbeclomethasone	0 (0.0%)	2 (1.5%)	2 (0.8%)	
Indicatrol	0 (0.0%)	1 (0.8%)	1 (0.4%)	
Indicatrolglycopyrinum	0 (0.0%)	3 (2.3%)	3 (1.3%)	

N.B:Number of drug used more than patients as some patients use more than one drug **MDI**:meterd dose inhale

Table (4): Comparison between patients with asthma and COPD according to medications

Table (4) shows comparison between patients with asthma and COPD according to medications. As regard frequency of administration of inhaler, it was found that both asthma and COPD patients were frequently using the inhaler twice daily and patients with COPD preferred to use the once daily inhaler more frequently than asthmatic patients, also asthmatic patients used the on need more frequently than COPD patients and this was statistically significant(p=<0.001).As regard onset of action of inhaler, it was found that the inhaler that of 5 minutes of onset of action was frequently used by both asthma and COPD patients (n=105) patients than other types of inhalers and this was statistically significant(p=<0.001).As regard type of device, it was found that aerolizer , MDI, turbohaler and handihaler were frequently used by both asthma and COPD in order (103, 39,50 ,22) patients than other types of devices and this was statistically significant(p=<0.001).As regard type of drug, it was found that budesonide, formetrol,

salbutamol and budesonide formetrol were frequently used by both asthma and COPD in order (44, 60,36,49) patients than other types of drugs and this was statistically significant(p=<0.001).

Variables	Good	Intermediate	Poor	Total	P value
Age/year					
Mean ± SD	43.82 ±13.501	42.61 ±13.05	37.56 ±15.84	41.86±14.06	0.082
Median (range)	46 (16-70)	45 (13-67)	34 (14-70)	42 (13-70)	
Gender:					
Males	12 (26.7%)	9 (23.7%)	11 (40.7%)	32 (29.1%)	0.295
Females	33 (73.3%)	29 (76.3%)	16 (59.3%)	78 (70.9%)	
Residence:					
Rural	19 (42.2%)	13 (34.2%)	11 (40.7%)	43 (39.1%)	0.742
Urban	26 (57.8%)	25 (65.8%)	16 (59.3%)	67 (60.9%)	
Educational level					
Illiterate	24 (53.3%)	20 (52.6%)	11 (40.7%)	55 (50%)	0.563
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 status					
Low	0 (0.0%)	2 (5.3%)	2 (7.4%)	4 (3.6%)	0.05
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					
Non	42 (93.3%)	34 (89.5%)	21 (77.8%)	97 (88.2%)	0.289
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					
Mild	1 (50%)	0 (0.0%)	2(40%)	3 (37.5%)	
Moderate	0 (0.0%)	0 (0.0%)	1 (20%)	1 (12.5%)	0.797
Heavy	1 (50%)	1 (100%)	2 (40%)	4 (50%)	

Table(5)Relation between demographic data and adherence pattern in asthmatic patients already on therapy (n=110):

Table (5) shows relation between demographic data and adherence in asthmatic patients already on inhaler therapy. therewas no statistically significant relationship as regard age (p=0.08),gender (p=0.29),residence (p=.074),educational level (p=0.56) ,socioeconomic status (p=0.05),smoking status (p=0.28) and smoking index(p=0.79). However good adherence was frequently encountered with older age, female gender, urban residence, illiterate educational level and non smoking status

Variables	Good	Intermediate	Poor	Total	P value
Age/year					
Mean ± SD	60.89 ±9.56	62.42±11.93	66.25±10.95	62.48±11.07	0.198
Median (range)	61 (35-78)	60 (35-89)	65 (49-85)	61 (35-89)	
Gender: Males	40 (88.9%)	55 (84.6%)	13 (65%)	108 (83.1%)	
Females	5 (11.1%)	10 (15.4%)	7 (35%)	22 (16.9%)	0.054
Residence					
Rural	32 (71.1%)	37 (56.9%)	14 (70%)	83 (63.8%)	0.258
Urban	13 (28.9%)	28 (43.1%)	6 (30%)	47 (36.2%)	
Educational level					
Illiterate					
Primary	31 (68.9%)	54 (83.1%)	18 (90%)	103 (79.2%)	0.266
Secondary	5 (11.1%)	7 (10.8%)	2 (10%)	14 (10.8%)	
Graduate	4 (8.9%)	3 (4.6%)	0 (0.0%)	7 (5.4%)	
Postgraduate	2 (4.4%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	
	3 (6.7%)	1 (1. 5%)	0 (0.0%)	4 (3.1%)	
Socioeconomic status					
Low	12 (26.7%)	7 (10.8%)	4 (20%)	23 (17.7%)	0.009
Middle	29 (64.4%)	58 (89.2%)	16 (80%)	103 (79.2%)	
High	4 (8.9%)	0 (0.0%)	0 (0.0%)	4 (3.1%)	
Smoking status					
Non	6 (13.3%)	11 (16.9%)	7 (35%)	24 (18.4%)	
Ex-smoker	29(64.4%)	46 (70.8%)	7 (35%)	82 (63.1%)	0.07
Stop smoking	6 (13.3%)	3 (4.6%)	2 (10%)	11 (8.5%)	
Current smoker	4 (8.9%)	5 (7.7%)	4 (20%)	13 (10%)	
Smoking index					
Mild	17 (58.7%)	38 (79.2%)	10 (90.9%)	65 (73.9%)	
Moderate	3(10.3%)	0 (0.0%)	0 (0.0%)	3 (3.4%)	0.05
Heavy	9 (31%)	10 (20.8%)	1 (9.1%)	20 (22.7%)	

Table(6)Relation between demographic data and adherence pattern in COPD patients already on therapy (n=130)

Table (6)shows the relation between demographic data and adherence pattern in COPD patients already on treatment. It was found that there was statistically significant relationship (p=0.009) between adherence and socioeconomic status, but there was no statistically significant relationship as regard other demographic data as regard age (p=.19), gender (p=0.054), residence (p=.25), educational level (p=.26), and smoking status (p=.07). However good adherence was frequently encountered with younger age, male gender, rural residence, illiterate educational level and Ex-smoker smoking status .

Variables	Good	Poor	Total	P value
Age/year Mean ± SD Median (range)	67.44 ±7.09 65 (57-80)	63.33±9.95 62 (45-95)	64 ±9.61 65 (45-95)	0.234
GenderMales Females	6 (66.7%) 3 (33.3%)	33 (71.7%) 13 (28.3%)	39 (70.9%) 16 (29.1%)	0.71
Residence Rural Urban	1 (11.1%) 8 (88.9%)	29 (63%) 17(37%)	30 (54.5%) 25 (45.5%)	0.008
Educational level Illiterate Primary Secondary Postgraduate	 8 (88.9%) 0 (0.0%) 0 (0.0%) 1 (11.1%)	 44 (95.6%) 1 (2.2%) 1 (2.2%) 0 (0.0%)	 52 (94.5%) 1 (1.8%) 1 (1.8%) 1 (1.8%)	0.136
Socioeconomic status Low Middle High	 1 (11.1%) 7 (77.8%) 1 (11.1%)	 9 (19.6%) 37 (80.4%) 0 (0.0%)	 10 (18.2%) 44 (80%) 1 (1.8%)	0.067
Smoking status Non Ex-smoker Stop smoking Current smoker	 3 (33.3%) 2(22.3%) 3 (33.3%) 1 (11.1%)	 13 (28.3%) 19 (41.3%) 4 (8.7%) 10 (21.7%)	 16 (29.1%) 21 (38.2%) 7 (12.7%) 11 (20%)	0.187

Table (7): Relation between demographic data and adherence pattern in COPD naïve patients (N=55)

Table (7) shows the relation between demographic data and adherence pattern in COPD naive patients .It was found that there was statistically significant relationship as regard residence (p=.008), But no statistically significant relationship as regard other demographic data , as regard age (p=0.23), gender (p=0.71) ,educational level (p=0.136),socioeconomic status (p=.06),smoking status(p=0.187),smoking index(p=.07). However, good adherence was frequently encountered with older age, male gender, illiterate educational level .

Parameter	Type of disease		Total	P-value
	Asthma	COPD		
Good	**70 (42.2%)**	**54 (29.2%)**	**124 (35.3%)**	**0.013**
Intermediate	**38 (22.9%)**	**65 (35.1%)**	**103 (29.4%)**	
Poor	**58 (34.9%)**	**66 (35.7%)**	**124 (35.3%)**	
Total	**166 (100%)**	**185 (100%)**	**351 (100%)**	

Table(8)Relation between adherence pattern and type of disease (351)

Table (8) shows the relation between adherence pattern and type of disease. Among asthma patients, 70 (42.2%) had good adherence, 38 (22.9%) had intermediate adherence, 58 (34.9%) had poor adherence. Among patients with COPD patients, 54 (29.2%) had good adherence, 65 (35.1%) had intermediate adherence, 66 (35.7%) had poor adherence.

It was found that there was statistically significant relationship between adherence pattern and type of disease (p=0.013).

Variables	Good	Intermediate	Poor	Total	P value
Duration of disease/ year Mean ± SD Median (range)	12.48 ±11.08 10 (1-50)	12.76±6.53 13 (2-35)	13.55 ±5.63 15 (4-20)	12.79 ±8.24 11.5 (1-50)	0.13
Number of emergency visit in the last year < 2 visits 2-4 visits	33(73.3%) 12(26.7%)	58 (89.2%) 7(10.8%)	19 (95%) 1(5%)	110(84.6%) 20(15.4%)	0.028

Table (9)Relation between disease characteristics and adherence pattern in COPD patients already on therapy

Table (9) shows the relation between disease characteristics and adherence in COPD patients already on therapy. It was found that there was statistically significant relationship between adherence and number of emergency visit (p=0.02) but there is no statistically significant relationship between adherence and duration of disease (p=0.13).

Parameter	Adherence			Total	P-value
	Good	Intermediate	Poor		
D.M No Yes	102 (82.3%) 22 (17.7%)	90 (87.4%) 13 (12.6%)	110 (88.7%) 14 (11.3%)	302 (86%) 49 (14%)	0.306
HTN No Yes	93 (75%) 31 (25%)	82 (79.6%) 21 (20.4%)	95 (76.6%) 29 (23.4%)	270 (76.9%) 81 (23.1%)	0.71
ENT diseases No Yes	91 (73.4%) 33 (26.6%)	89 (86.4%) 14 (13.6%)	94 (75.8%) 30 (24.2%)	274 (78.1%) 77 (21.9%)	0.046*
GIT diseases No Yes	110 (88.7%) 14 (11.3%)	92 (89.3%) 11 (10.7%)	115 (92.7%) 9 (7.3%)	317 (90.3%) 34 (9.7%)	0.518
Cardiac diseases No Yes	107 (86.3%) 17 (13.7%)	75 (72.8%) 28 (27.2%)	94 (75.8%) 30 (24.2%)	276 (78.6%) 75 (21.4%)	0.03*
Renal diseases No Yes	119 (96%) 5 (4%)	102 (99%) 1 (1%)	119 (96%) 5 (4%)	340 (96.9%) 11 (3.1%)	0.325
Eye diseases No Yes	113(91.1%) 11 (8.9%)	99 (96.1%) 4 (3.9%)	118 (95.2%) 6 (4.8%)	330 (94%) 21 (6%)	0.231
Thyroid diseases No Yes	120 (96.8%) 4 (3.2%)	103 (100%) 0 (0.0%)	122 (98.4%) 2 (1.6%)	345 (98.3%) 6 (1.7%)	0.174
OSANo Yes	124 (100%) 0 (0.0%)	103 (100%) 0 (0.0%)	122 (98.4%) 2 (1.6%)	349 (99.4%) 2 (0.6%)	0.159
Vascular diseases No Yes	124 (100%) 0 (0.0%)	101(98.1%) 2 (1.9%)	124 (100%) 0 (0.0%)	349 (99.4%) 2 (0.6%)	0.089
Scoliosis: No Yes	123 (99.2%) 26 (0.8%)	102 (99%) 1 (1%)	124 (100%) 0 (0.0%)	349 (99.4%) 2 (0.6%)	0.57
Allergic dermatitis No Yes	124 (100%) 0 (0.0%)	103 (100%) 0 (0.0%)	123 (99.2%) 26 (0.8%)	350 (99.7%) 1 (0.3%)	0.399
Rheumatoid arthritis No Yes	123 (99.2%) 26 (0.8%)	103 (100%) 0 (0.0%)	124 (100%) 0 (0.0%)	350 (99.7%) 1 (0.3%)	0.399
CVS stroke No Yes	124 (100%) 0 (0.0%)	102 (99%) 1 (1%)	122 (98.4%) 2 (1.6%)	348 (99.1%) 3 (0.9%)	0.382

DM: diabetes mellitus **HTN**: hyupertension**OSA:** obstructive sleep apnea **CVS:**cerbrovascular stroke

Table (10): Relation between adherence pattern and comorbidities.

Table (10) shows the relation between adherence and comorbidities. It is found that there was statistically significant relation between poor adherence to inhaler therapy and patients who had cardiac patients (p=0.03) and significant relation between good adherence and patients who had ENT diseases (p=0.04). There were no statistically significant relations between adherence to inhaler therapy and other comorbidities as D.M (p=0.30), hypertension (p=0.71),GIT diseases (p=0.51), renal disease (p=0.325), eye disease (p=0.231), thyroid disease (p=0.174), obstructive sleep apnea (p=0.159), vascular disease (p=0.08), allergic dermatitis (p=0.39), rheumatoid arthritis (p=0.39) nor neurological disease (p=0.38).

Variables	Good	Intermediate	Poor	Total	P value
Frequency of inhaler administration					
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%)	<0.001
Onset of action of inhaler					
<5-20 minutes	13 (28.9%)	19 (50%)	4 (14.8%)	36 (32.7%)	
5 minutes	13 (28.9%)	8 (21.1%)	15 (55.6%)	36 (32.7%)	0.002
20 minutes	0 (0.0%)	0 (0.0%)	2 (7.4%)	2 (1.9%)	
30 minutes	19 (42.2%)	11 (28.9%)	6 (22.2%)	36 (32.7%)	
Type of device					
Aerolizer	20 (44.5%)	13 (34.2%)	4 (14.8%)	37 (33.6%)	
pMDI	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%)	0.001
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					
Budesonide	15 (33.4%)	9 (23.8%)	3 (11.1%)	27 (24.5%)	
Formetrol	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	13 (28.9%)	19 (50%)	5 (18.5%)	37 (33.6%)	0.001
formetrol	6 (13.3%)	1 (2.6%)	1 (3.7%)	8 (7.3%)	
Fluticasone	0 (0.0%)	0 (0.0%)	1 (3.7%)	1 (0.9%)	
salmetrol	0 (0.0%)	1 (2.6%)	1 (3.7%)	2 (1.8%)	
Glycopyrinum bromide	0 (0.0%)	0 (0.0%)	1 (3.7%)	1 (0.9%)	
Tiotropium					
Ipratropium					

N.B: Number of drug used more than patients as some patients use more than one drug **MDI:** metered dose inhaler

Table(11)Relation between drug characteristics and adherence pattern in asthmatic patients already on therapy (n=110)

Table (11) show the relation between drug characteristics and adherence in asthmatic patients already on therapy. It was found that there was statistically significant relationship between adherence pattern and 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 minutes, who used Aerolizer and turbohaler, who used budesonide/ formetrol and budesonide

Variables	Good	Intermediate	Poor	Total	P value
Frequency of inhaler administration					
Once	11(24.4%)	18 (27.7%)	4 (20%)	33 (25.4%)	0.003
Twice	29 (64.5%)	45 (69.2%)	9 (45%)	83 (63.8%)	
on need	5 (11.1%)	2 (3.1%)	7 (35%)	14 (10.8%)	
Onset of action of inhaler					
<5-20 minutes	5 (11.1%)	6 (9.2%)	0(0.0%)	11 (8.4%)	0.622
5 minutes	23 (51.1%)	35 (53.9%)	11 (55%)	69 (53.1%)	
20 minutes	1 (2.2%)	0(0.0%)	0(0.0%)	1(0.8%)	
30 minutes	16 (35.6%)	24 (36.9%)	9 (45%)	49 (37.7%)	
Type of device					
Aerolizer	25 (55.6%)	35 (53.8%)	6 (30%)	66 (50.8%)	0.008
MDI	6 (13.3%)	2 (3.1%)	8 (40%)	16 (12.3%)	
Turbohaler	5 (11.1%)	7 (10.9%)	0(0.0%)	12 (9.2%)	
Handihaler	5 (11.1%)	11 (16.9%)	4 (20%)	20 (15.4%)	
Diskus	1 (2.2%)	3 (4.6%)	2 (10%)	6 (4.6%)	
Breezhaler	3 (6.7%)	6 (9.2%)	0(0.0%)	9 (6.9%)	
Respimat	0(0.0%)	1 (1.5%)	0(0.0%)	1 (0.8%)	
Type of drug					
Budesonide	8 (17.8%)	6 (9.2%)	3 (15%)	17 (13.1%)	0.034
Formetrol	17 (37.8%)	29 (44.6%)	3 (15%)	49 (37.7%)	
Salbutamol	4 (8.9%)	2 (3.1%)	7 (35%)	13 (10%)	
Budesonide formetrol	5 (11.1%)	7 (10.8%)	0(0.0%)	12 (9.2%)	
Fluticasone salmetrol	1 (2.2%)	3 (4.6%)	2 (10%)	6 (4.6%)	
Glycopyrinum bromide	2 (4.4%)	3 (4.6%)	0(0.0%)	5 (3.8%)	
Tiotropium	5 (11.1%)	12 (18.5%)	4 (20%)	21 (16.2%)	
Ipratropium	1 (2.2%)	0(0.0%)	0(0.0%)	1(0.8%)	
Formetrolbeclomethason	1 (2.2%)	0(0.0%)	1 (5%)	2(1.5%)	
e	0(0.0%)	1 (1.5%)	0(0.0%)	1 (0.8%)	
Indicatrol	1 (2.2%)	2 (3.1%)	0(0.0%)	3 (2.3%)	
Indicatrolglycopyrinum					

Table(12)Relation between drug characteristics and adherence pattern in COPD patientsalready on therapy (n=130)

Table (12) show the relation between drug characteristics and adherence pattern in COPD patients already on therapy. It was found that there was statistically significant relationship between adherence pattern and frequency of administration, type of device, type of drug with p=(0.003, 0.008, 0.034) respectively. But there was no statistically significant relationship between adherence and onset of action (p=0.62). It was found that

good adherence frequently encountered among patients who used inhaler twice daily, who used Aerolizer and handihaler and who used formetrol and tiotropium.

Discussion

Non-adherence to medications is considered as one of the largest drug related issues**,** So our study focused on factors affecting adherence.

In our study we found that by comparing patients with bronchial asthma and patients with COPD, there were statistically significant differences as regard age, gender, residence, body mass index, educational level, socioeconomic status, where older age, male gender, rural residence, low BMI, low educational level, low socioeconomic status were more frequent in COPD patients

In our study we found that, Among the studied population poor adherence was observed in 124 (35.3%) and both intermediate and good adherence was observed in 227 (64.6%) and this result is comparable with WHO 2003 report which recorded that treatment compliance in chronic disease was 50% . also this result matches with the results of the study of **(Rifaat et al., 2013)** who found thatadherence among asthmatic patients was 49%. and this may be a reflection of the fact that most of their patients has significant asthma and followed up in tertiary centers rather than primary centers.

As there are patients already on inhaled therapy, also there are patients who use their inhaler therapy for the first time and each group has their own characteristics which should be searched for with their relation to adherence to inhaler therapy, so that the current study showed that out of the studied population the naive patients were 111 and most of them were poor adherent which was statistically significant and this result agrees with the results of , Latty et al studied adherence to asthma inhalers and leukotriene receptor antagonists in childern and found that 12-month persistence rates were lower in new medications users (1.5%–6%) than in chronic medication users (27%–44%) **(Latty et al., 2008).** This suggests that perhaps, after years of suffering from asthma, patients may be more likely to accept and follow prescribed treatment regimens **(Jin et al., 2008).** Also good adherence with patients already on therapy resulted from more confidence of inhaler device, less fear, greater sense of security and trusting in the treatment option than naive patients **(Braido et al., 2013).**

In this study, there was no statistically significant relation between gender and adherence in asthmatic patients already on therapy, our observation is consistent with another review that concluded that gender has not been found to influence compliance **(Senior et al., 2004).** Gender may not be a good predictor of non-compliance because of inconsistent conclusions**(Vic et al., 2004).** However in our study good adherence was frequently encountered in female gender which matches with other studies which concluded that, female patients were found to have better compliance**(Choi-Kwo et al., 2005)** while some studies suggested otherwise **(Hertz et al., 2005).**

As regard COPD patients already on therapy we found in our study that there was statistically significant relation between adherence to inhaler therapy and socioeconomic status, where good adherence was significantly encountered with low socioeconomic status in

comparison with other socioeconomic status; this observation is in consistence with that of **Agh et al**. who showed that patients adhered to treatment poorly when they had several drugs prescribed, but the price of the drugs did not influence their attitude to treatment **(Agh T et al., 2011).**

In our study we found that there was no significant relation between adherence to inhaler therapy and disease characteristics in both asthma and COPD apart from COPD patients on therapy , good adherence was encountered in patients who had 2-4 emergency visits in the last year, it was statistically significant this can be explained by the patients need more physician visits to receive more information about treatment adherence and inhaler technique ;our observation agrees with a study of Dimatteo whose Study of how well patients retain health information suggest that immediately after an office visit, they recall <50% of the information conveyed by the physician**(Dimatteo., 1991).**

We also found in our study that there was statistically significant relation between adherence to inhaler therapy and patients with cardiac diseases (p=0.03) where the patients who had cardiac disease express poor adherence because those receive a lot of medications as non adherence to treatment may be caused by a lot of medications which agrees with a study of **(Restrepo et al., 2008).** Also there was significant relation between adherence and patients who had ENT diseases (p=.04) where the patients who had ENT problems were good adherent because those patients mostly had allergic rhinitis and receive inhalers and they usually know that the two diseases has the same pathology and same treatment.

As regard frequency of administration of inhaler in our study we found that both asthma and COPD patients were frequently using the inhaler twice daily and patients with COPD preferred to use the once daily inhaler more frequently than asthmatic patients and this relation was statistically significant. This result agrees with a study of **(Sanduzzi et al., 2014)**which showed thatthe percentage of compliant COPD patients drops from 43% with a once daily medication to 23% with a therapy requiring 4 administrations per day.

As regard onset of action of inhaler, we found in our study that the inhaler of 5 minutes of onset of action was frequently used by both asthma and COPD patients (number =105) patients than other types of inhalers and this was statistically significant, this result due to asthma and COPD patients almost always complaining and need rescue bronchodilators medications which rapidly acting.

As regard the type of devices and the type of drugs used in the studied population, we found that COPD patients preferred to use aerolizer ,handihaler (single-dose DPI) and breezhaler (a low-resistance, single-dose DPI) than asthmatics who preferred to use turbohaler. We found also that budesonide and budesonide/formetrol were used more frequently in asthmatic patients while formetrol, glycopyrinum bromide and tiotropium were used more frequently in COPD patients and this was statistically significant. This observation is consistent with that of sanduzzi et al who find that COPD patients preferred to use DPI more frequently than other types of inhaler devices (**Sanduzzi et al., 2014)**.

In the present study we found that there was statistically significant relationship

between good adherence and the use of inhaler twice daily in asthmatic patients in comparison with the use of on need inhaler which disagrees with other studies of secondary non-adherence (rates of medication use) showed that long-term rates of adherence to preventive therapies (e.g. controller or preventer medications) among adult patients were low **(Spector et al., 1986)** suggesting while patients tend to under-use controller or maintenance therapies, symptom-relieving drugs such as bronchodilators are often overused.

In the current study we found that asthmatic patients who used inhaled medications of onset of action of 5- 20 minutes were good adherent to inhaled therapy and this was statistically significant, this result can be explained by that large number of our studied population used the formetrol/ budesonide combination as this combination is usually prescribed freely in our hospital. And this result agrees with a previous study of **(Sanduzzi et al., 2014)** which showed that the perception of the product delivering its action rapidly may lead the patient to continue taking the therapy on a daily basis among this drug the available ones (budesonide and budesonide formetrol).

In our study we found that there was statistically significant relationship between good adherence and the use of budesonide/ formetrol and budesonide in asthmatic patients in comparison with the use of salbutamol . This observation agrees with that of Axelsson et al. who found better adherence to ICS/LABA compared to ICS and/or LABA and/or SABA**)(Axelsson et al., 2009)**.

In our study there was statistically significant relationship between good adherence and the use of turbohaler and aerolizer in asthmatic patients in comparison with the use of PMDI. Our study result agrees with a previous study of**(Friedman et al., 2010)** whichfound thatusing dry-powder inhalers (DPIs) versus metered-dose inhalers (MDIs) was linked to adherence in this study results.

In the present study we found that there was statistically significant relationship between good adherence and the use of inhaler twice daily in patients with COPD in comparison with the use of on need inhaler, which disagrees with the study of **(Sanduzzi et al., 2014)** which showed that the higher is the number of administrations, the lower the adherence to the medical therapy. The percentage of compliant COPD patients drops from 43% with a once daily medication to 23% with a therapy requiring 4 administrations per day **(Toy et al., 2011).** our explanation is that COPD patients always has persistent symptoms which need preventer medications regularly unlike asthmatic patients who use rescue medication on attacks.

In our study we found that there was no statistically significant relationship between adherence and onset of action of inhaler therapy in COPD patients.

In our study we found that there was statistically significant relationship between good adherence and the use of formetrol and tiotropium in patients with COPD in comparison with the use of salbutamol. Our study result agrees with a previous study of **(Halpin et al., 2016)** whichfound that tiotropium associated with longer time to first exacerbation event and fewer exacerbations compared with other lines of treatment because patient feel better when used it and experienced less exacerbations also using once daily.

In our study there was statistically significant relationship between good

adherence and the use of aerolizer and handihaler in patients with COPD in comparison with the use of PMDI. Our explanation is that it is easy to be applied and no need to coordinate actuation and inhalation, which is required with a pMDI, portable and compact and many of them are multi-dose, Some are single-dose with doses kept separately in sealed packages. For the treatment of COPD, the most commonly used and preferred inhalers are DPI (dry powder inhalers**).** Also our study result agrees with the study of **(Anderson., 2006)** which showed that in the most severe stages of the disease, the inhaler may fail to activate due to an inappropriate peak inspiratory flow, which would prevent an effective dose of drug from reaching the lungs **(Hill and Slater., 1998).**

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