



Evaluation of the clinical pharmacist role in improving clinical outcomes in patients with lower urinary tract symptoms due to benign prostatic hyperplasia

Mera Ababneh¹ · Duaa Shamieh¹ · Saddam Al Demour² · Abeer Rababa'h¹

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Abstract

Background Lower urinary tract symptoms due to benign prostatic hyperplasia set restriction to patients' daily life activities and decrease their quality of life. Adherence to medications is considered a core element to improve patients' clinical outcomes. **Objective** To evaluate the role of clinical pharmacist in improving adherence to medication, reducing severity of symptoms, and improving quality of life in this group of patients. **Setting** The study was conducted in urology outpatients' clinics in Amman, Jordan. **Methods** This was a prospective randomized controlled trial, patients were randomly allocated into intervention group or control group. Patients in the intervention group were offered a pharmaceutical care service and patients in the control group received regular healthcare provided by urologist and then followed for 1 month. **Main outcome measures** Morisky Medication Adherence Score and International Prostate Symptom Score. **Results** Among 209 patients completed the study, 105 were in the intervention group and 104 in the control group. By the end of the study, 91.4% of the intervention group patients became adherent to their medication compared to 72.1% in the control group ($p < 0.0001$). At follow up, the severity of the symptoms to calculated score was lower in the intervention group (mean 15.6 ± 5.69) compared to control group (mean 13.9 ± 5.43) ($p < 0.0001$). The quality of life score were better in the intervention group compared to the control group at follow-up ($p < 0.0001$). **Conclusion** The current findings indicate that implementing clinical pharmacy services can positively increase the level of adherence to medications. This was accompanied by modest improvement in the severity of urinary symptoms in benign prostatic hyperplasia and in quality of life for patients. Hence, clinical pharmacy services could provide beneficence in outpatient setting.

Keywords Adherence · BPH · Clinical pharmacist · IPSS score · Jordan · LUTS · Pharmaceutical care

Impact on practice

- The implementation of clinical pharmacist services to patients with lower urinary tract symptoms due to benign prostatic hyperplasia is feasible in an outpatient setting.
- Clinical pharmacist counseling and education improves medication adherence in patients with lower urinary tract symptoms due to benign prostatic hyperplasia.
- Patients' medication adherence may have a role in improving clinical outcomes in patients with benign prostatic hyperplasia.
- Longer duration of follow-up and larger sample size are recommended for future studies into the effect of clinical pharmacy services.

✉ Mera Ababneh
mababneh@just.edu.jo

¹ Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan University of Science and Technology, P.O. Box 3030, Irbid 22110, Jordan

² Department of Urology/Special Surgery, Faculty of Medicine, University of Jordan, Amman, Jordan

Introduction

Benign prostatic hyperplasia (BPH) is a histopathological disease that is manifested by lower urinary tract symptoms (LUTS) such as poor flow, frequency, urgency, nocturia, dribbling and incomplete voiding [1–3]. The lifetime

prevalence of LUTS suggestive of BPH was reported to be 26.2% [4]. The prevalence of moderate to severe LUTS is increasing with age as it affects 8% of men 40–49 year-old, 50% in men 60–69 years old and 80% in men ≥ 90 years [5].

The main treatment goal for LUTS due to BPH is to decrease bothersome symptoms, modify the progression of the diseases and prevent long-term complications [6–8]. Therapeutic plan to manage LUTS due to BPH is usually guided by the severity of the symptoms, degree of inconvenience and patient's preference [8]. Medical therapy include; α -adrenergic antagonists, 5 α -reductase inhibitors, and anticholinergic agents [8–11]. Previous investigations reported low adherence to medications in patients with LUTS due to BPH, especially in patients on combination therapy [12–14]. Moreover, adherence to medication therapy was found to have considerable impact on BPH progression in this group of patients [12]. Hence, implementing pharmaceutical service by clinical pharmacist may leads to improve disease control, ensure patient compliance, and improve patient outcomes.

Aim of the study

The aim of this study was to assess the role of the clinical pharmacist in improving the level of medication adherence, severity of urinary symptoms and its effect on quality of life in patients with LUTS due to BPH.

Ethics approval

The study protocol got ethical approval by Jordan University of Science and Technology Institutional Review Board committee and the Ministry of Health of Research on Human Committee (no. 160087). A signed informed consent form was obtained for each patient and patients' were interviewed privately to obtain necessary information for the study.

Methods

Study design and subjects

This was a prospective, randomized controlled clinical trial conducted in Urology Outpatients' Clinics. Patients were screened for eligibility during routine visit to the urology clinic; eligible patients were offered to participate in the study. Patients who fulfilled the eligibility criteria were randomly allocated into two groups; intervention and control group with a 1:1 ratio by using randomization scheme generated by randomization software. The following were the inclusion criteria: Adult patients aged over 45 years, patients diagnosed with BPH and complain from LUTS and patient is taking at

least one medication prescribed as a treatment for LUTS for at least 6 months. On the other hand, patients with history of prostate cancer, previous prostate removal surgery, use of medications known to affect urination such as antihistamine, phenothiazines, tricyclic antidepressant, and anticholinergic agents and patients with liver or renal disease were excluded.

Study outcomes measurements

Medication adherence was measured through Morisky Medication Adherence Scale (MMAS-8) which was measured in both groups at baseline and follow-up [15–17]. The MMAS-8 is an eight-item questionnaire designed to measure medication adherence. It is composed of seven Yes/No questions. The wording of six items was reversed to avoid the "yes-saying" bias, while one item was not reversed to ensure participants will consider the contents of questions in their responses. The eighth question uses a 5-point Likert scale. The total scale has a range of 0 to 8 with scores of 8 indicating high adherence, 7 or 6 indicating medium adherence, and < 6 indicating low adherence. In this study, patients with MMAS-8 score of 8 were considered adherent and those with MMAS-8 score ≤ 7 were considered non-adherent.

One of the main outcomes of this study was to assess LUTS due to BPH and levels of patients' quality of life by using the International Prostate Symptoms Score (IPSS). IPSS is one of the most beneficial tools to determine the level of prostate symptoms control in a practical way [18, 19]. The IPSS is based on the answers to eight questions, seven regarding urinary symptoms and one question related to the patient's quality of life (QoL). For the symptom questions, the patient is allowed to choose one out of six answers indicating increasing severity of the particular symptom. The answers scale range from (0 to 5) with 0 representing no symptoms at all and 5 representing the most symptomatic disease, giving an overall maximum possible score of 35. The answers to the quality of life question are scored on a scale of 1 to 6 [5]. Quality of life, as perceived by the patient, is assessed using only a single question. The answer to this question range from "delighted" to "terrible" or 0 to 6, and it serves as a valuable starting point for a doctor–patient conversation. Further, IPSS scores can be categorized into 3 groups: mild (0–7), moderate [8–19], and severe (20–35). IPSS is considered the official symptoms assessment tool for patients suffering from BPH by the International Scientific Committee (ISC) and the American Urological Association (AUA) measurement committee [18].

Study procedure

The main procedure in this trial was the pharmaceutical care provided for patients according to randomization scheme by trained clinical pharmacist. The recruited patients were randomly assigned to receive either an intervention in which

patients received a pharmaceutical care provided by clinical pharmacist or assigned to be a control in which patients received regular physician care by urologist. The intervention group patients received the following pharmaceutical care: (1) Education about nature and clinical presentation of BPH; (2) types of medications usually prescribed for this disease; (3) the importance of medication adherence and its effect on symptoms control; (4) recommendations for diet and lifestyle modifications that would have a significant effect in improving symptoms. A diet modification to include plenty of fresh fruits and vegetable, reduction of high-fat foods, regular physical exercise, weight loss and smoking cessation. The pharmacist also made sure to explain to the patient the association between stopping medication and worsening of symptoms they endured. In addition to the verbal communication with patients, written information (educational brochure) was given to patients by the end of session. On the other hand, patients in the control group received regular health care evaluation by physician in the clinic and seen by clinical pharmacist for data collection purposes only. Also, the time spent with patients in the intervention group took about 20 min while patients in the control group had 10 min with the clinical pharmacy for data collection. Four weeks after the first visit, patients' IPSS, MMAS-8 were assessed again for both groups.

To maintain our ethical role as healthcare providers, at the end of the study, patients in both groups were provided with the educational material verbally or in a brochure.

Statistical analysis

Continuous variables were presented as mean \pm standard deviation (SD) while categorical variables were presented as numbers and percent. Within each group, data at baseline and follow-up were compared using McNemar's test for categorical variables and Wilcoxon signed rank test for continuous variables. Control and intervention groups were compared at baseline and follow-up were compared using ANOVA, Chi square test or Fisher exact test; depending on type of data.

All tests were two-sided, and statistical significance was set at p value ≤ 0.05 . The analysis was carried out using SPSS version 22.

Results

A total of 220 eligible patients were enrolled and followed during this period. The 220 patients were randomized into an intervention group ($n = 110$) and control group ($n = 110$). Of the 220 patients 5 were dropped out from the intervention group and 6 patients dropped out from the control group ending up with 209 patients.

The study population age ranged between 50 and 85 years. Most patients from both groups presented with moderate

symptoms of the disease. There were no significant differences in all baseline demographics and clinical data between intervention and control groups. Patients' baseline demographic and characteristic details are shown in Table 1. All patients were on α -adrenergic antagonists, while 54 patients were in combination therapy with 5 α -reductase therapy.

Table 1 Baseline demographic and characteristic details of included patients ($n = 209$)

Patient characteristics	Intervention group ($n = 105$) n (%)	Control group ($n = 104$) n (%)	p value
Age (years)			
Mean \pm SD [§]	68.5 \pm 7.7	67.24 \pm 8.52	0.2681**
Marital status			
Married	95 (90.5)	93 (89.4)	0.8001*
Widowed/ divorced	10 (9.5)	11 (10.6)	
Level of education			
Illiterate	13 (12.4)	18 (17.3)	0.1589*
Primary/second- ary	64 (61)	69 (66.4)	
Diploma/bachelor/ higher education	28 (26.6)	17 (16.3)	
Tobacco use			
Non smoker	82 (78)	70 (67.3)	0.1782*
Former smoker	7 (6.7)	13 (12.5)	
Current smoker	16 (15.3)	21 (20.2)	
Water pipe use			
Non smoker	93 (88.6)	98 (94.2)	0.342***
Former smoker	9 (8.6)	5 (4.8)	
Current smoker	3 (2.8)	1 (1)	
History of hypertension			
No	55 (52.4)	55 (52.9)	0.8832*
Yes	50 (47.6)	49 (27.1)	
History of DM			
No	75 (71.4)	67 (64.4)	0.2779*
Yes	30 (28.6)	37 (35.6)	
History of MI			
No	88 (83.8)	85 (55.8)	0.6907*
Yes	17 (16.2)	19 (18.2)	
History of dyslipidemia			
No	87 (82.9)	88 (84.6)	0.7305*
Yes	18 (17.1)	16 (15.4)	
History of heart failure			
No	98 (93.3)	92 (88.5)	0.2182*
Yes	7 (6.7)	12 (11.5)	
Use of 5- α reductase inhibitor			
No	76 (72.4)	79 (76)	0.5542*
Yes	29 (27.6)	25 (24)	

*Data analyzed using Chi square test, **data analyzed using t-test

***Data analyzed using Fisher test, [§]SD, Standard Deviation

Table 2 Comparison between level of adherence to medication based on (MMAS-8) between intervention and control group at baseline and follow-up

	Baseline			Follow up		
	Intervention** n (%)	Control n (%)	<i>p</i> value*	Intervention [†] n (%)	Control n (%)	<i>p</i> value*
Adherent	73 (69.5)	75 (72.1)	0.6803	96 (81.4)	75 (72.1)	<0.0001*
Non adherent	32 (30.5)	29 (27.9)		9 (8.6)	29 (27.9)	

*Fisher exact test, **McNemar's test for within group analysis ($p=0.7235$), [†]McNemar's test for within group analysis ($p<0.0001$). Use of the ©MMAS is protected by US copyright and registered trademark laws. Permission for use is required. A license agreement is available from: Donald E. Morisky, MMAR LLC, 294 Lindura Court, Las Vegas, NV 89138-4632; dmorisky@gmail.com

Table 3 Comparison of IPSS scores between intervention and control group at baseline and follow-up

IPSS score	Baseline			Follow up*		
	Control	Intervention	<i>p</i> value	Control	Intervention	<i>p</i> value
Mean \pm SD	16.2 \pm 5.4	15.5 \pm 5.6	0.1994	16.7 \pm 6.7	13.9 \pm 5.4	<0.0001

*Within group analysis $p<0.0001$

Regarding medication adherence, data analysis showed that there is no significant difference in adherence level between both groups at baseline ($p=0.6803$). At follow-up, the proportion of patients classified as adherent in the intervention group increased significantly from 69.5% at baseline to 91.4% at follow-up ($p<0.0001$) compared to the control group in which adherence to medication did not change significantly from baseline to follow-up as shown in Table 2. At follow-up, patients in the intervention group were significantly more adherent than patients in the control group ($p<0.0001$).

The current study found significant differences in IPSS score between both groups at 4 weeks follow-up interval. As shown in Table 3 patients in the intervention group had significantly lower mean IPSS score [13.9 ± 5.43] at follow up compared to control group [16.7 ± 6.7]. Further, when patients IPSS scores were categorized into 3 categories (mild, moderate, severe), patients in the intervention group at follow-up had higher proportion of patients in mild and moderate category and lower proportion in the severe category compared to control group ($p<0.0001$) as depicted in Table 4.

Finally, patients' quality of life was evaluated IPSS QoL. At baseline, no statistically significant difference was observed among groups. However, patients in the intervention group had significantly lower quality of life mean [2.2 ± 0.9] compared to controls [2.8 ± 1.1] at follow-up as shown in Table 5 ($p<0.0001$).

Discussion

Various studies in different countries have examined the effect of the level of adherence to medication on the patients' clinical outcomes and consequently their quality of life. Many of these studies have made recommendations for

Table 4 Comparison of IPSS categories between intervention and control group at baseline and follow-up

IPSS category	Baseline n = 104, $p=0.2278$		Follow-up n = 105, $p<0.0001$	
	Control n (%)	Intervention n (%)	Control n (%)	Intervention n (%)
Mild (scores 0–7)	12 (11.5)	5 (4.5)	10 (9.6)	14 (13.3)
Moderate (scores 8–19)	60 (57.7)	71 (67.6)	63 (66.6)	73 (69.6)
Severe (scores 20–35)	32 (30.8)	29 (27.6)	31 (29.8)	18 (17.1)

taking steps toward interventions that improve adherence to medications to achieve the maximum therapeutic outcomes [12, 13]. In the current study, around 75% of patients were adherent to their medication in both groups at baseline. None-adherence to medications occur as a result of poly-pharmacy, multi-daily drug scheduling, and side effects [20].

The present study is a randomized clinical study that evaluated the role of clinical pharmacist intervention in improving the level of adherence to medication, improvement in urinary symptoms and quality of life (using IPSS) in patients with LUTS due to BPH. The present study has shown a significant improvement in the level of adherence to medication in the intervention group. The level of adherence to medication was improved in the intervention group from (69.5%) at baseline to (91.4%) at follow-up based on MMAS-8. On the other hand, adherence was not significantly changed in the control group.

The significance increase in the level of adherence to medications can be related to the intervention performed; patient counseling was done at private setting, one to one, and in simple language. The relation between adherence to medications and symptoms relief were explained clearly to

Table 5 Comparison of IPSS Quality of life scores (QoL) between intervention and control group at baseline and follow-up

IPSS-QoL	Baseline			Follow up*		
	Control	Intervention	<i>p</i> value	Control	Intervention	<i>p</i> value
Mean ± SD	2.7 ± 1.1	2.5 ± 1.1	0.2389	2.8 ± 1.1	2.2 ± 0.9	< 0.0001

*Within group analysis $p < 0.0001$

the patients to encourage their compliance and lastly, patient educational material was provided for each patient to remind them of the information provided in the counseling session.

The results were consistent with other studies which revealed the importance of a pharmacist's role in increasing the level of medication adherence [21, 22]. Ramantha et al. evaluated the effect of a clinical pharmacist's intervention on improving the medication adherence level in hypertensive patients. The results of the study had shown that the group who received the clinical pharmacist intervention became more adherent to medication compared to the control group. Furthermore, the values of blood pressure measurements in the intervention group became more controllable than the measurements in the control group [21]. Lindenmeyer et al. evaluated the effect of the clinical pharmacist intervention in improving the level of medication adherence in diabetic patients with uncontrolled glycemia. The results showed that the pharmacist intervention was successful in increasing the level of adherence to medication and reaching the blood glycaemic control [22].

Another finding in this study was the statistically significant difference in the severity of the LUTS between groups at follow-up, as the intervention group showed change in IPSS scores while the control group did not. This could be—in part—related to the improvement in adherence level. Several studies were consistent with the results of this study. Cindolo et al. [12] studied the association between adherence to medication and its clinical value in improving LUTs. The authors reported a low level of adherence to medication in the study group which was related to the poor clinical outcome. Shortridge et al. [13] evaluated almost 2000 patients with LUTS to study the association between the medication adherence level and the persistence of LUTS associated with BPH. The results showed a high level of adherence to medication which was associated with symptoms improvement. The authors concluded that the sufficient symptoms relief experienced in the study group were enough reason to enhance the patient to tolerate the challenges of remaining adherent to their medication.

This study found that patients who received pharmaceutical interventions had better IPSS QoL mean scores compared to patients in the control group at follow-up. Cindolo et al. [12] result has shown that poor adherence to medications was associated with a poor clinical outcome which had reflected as a poor quality of life for patients.

This study had few limitations. First, we were able to follow-up patients at a single time point (4-week), multiple follow-up points would strengthen our results. Second, following-up with patients by phone had a few barriers, such as lack of eye contact. Third, the tool used for measuring the severity of the symptoms like IPSS is considered a subjective tool, which is highly affected by the nature of the patients and their ability to handle their pain and discomfort. Uroflowmetry to evaluate maximum flow rate may be considered for future studies. Fourth, from an ethical point, the clinical pharmacist answering any questions the control group patients had about their disease and medications they used, may have a role in a biased outcome. Fifth, the physician who worked with the clinical pharmacist became more aware of the importance of informing patients of continuous adherence to the prescribed medication so they can achieve maximum effect of the drug; this may also play a role in a biased outcome. Finally, although a statistically significant difference was observed in the IPSS scores among the two groups, the clinical significance was not sufficient to draw a causal relationship.

Conclusion

The present study evaluated the role of a clinical pharmacist in improving clinical outcomes in patients with LUTS due to BPH. The results shown that a clinical pharmacist intervention has a significant effect in improving the level of adherence to medication. Improvement in adherence could have a possible impact on reducing the severity of the symptoms, and improving patients' quality of life.

The role of the clinical pharmacist was not only advising the patients about the importance of adherence to their medications but to focus on linking the relief of symptoms with the adherence attitude for patients. This study shed the light on the importance of the clinical pharmacist's role in managing patients with LUTS due to BPH.

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Conflicts of interest There are no conflicts of interest to declare.

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