アプライド・セラピューティクス
Vol. 7 No. 2, pp 32-43, 2016

＜一般論文＞

An assessment tool for the intervention by community pharmacists to treat lower urinary tract symptoms: a preliminary study

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Abstract

Background: The prevalence of lower urinary tract symptoms (LUTS) increases with age, and LUTS negatively impact on quality of life (QOL). Many medications can cause LUTS and affect the efficacy of pharmacological treatment of LUTS. Interventions by the pharmacists is necessary for improving clinical management of LUTS.
Methods: An LUTS assessment tool, which evaluates core LUTS score (CLSS), therapeutic outcomes, QOL, and adverse drug events (ADEs), was developed to monitor medication use and ensure that LUTS are treated safely and effectively. Patients were divided into a control group, which received standard care, and an intervention group managed using the assessment tool. Clinical outcomes, CLSS, QOL, and ADEs were compared between the two groups at baseline and at 12 months.
Results: Over the 12-month study period, the intervention by pharmacists using the assessment tool improved the detection of adverse drug reactions in the intervention group compared with that in the control group (P = 0.0345). However, the intervention by pharmacists had little influence on any of the intermediate health outcomes related to LUTS.
Conclusions: The intervention by pharmacists using the assessment tool for LUTS significantly improved the detection of ADEs.

要旨

背景：下部尿路障害は，高齢者に罹患率が高く，QOL に大きな影響を及ぼす. さらに，本疾患を，を引き起こす薬剤（排尿障害原因薬）が多種類存在する. 薬剤師による LUTS 治療への介入が必要である.
方法：下部尿路障害患者の薬学的管理を適切かつ効率的に行うための手段として，症状（主要下部尿路症スコア（CLSS），QOL，服薬状況，副作用の発現状況を経時的に確認できるチェックシート（アセスメントツール）を作成し，排尿障害治療薬を処方された患者を対象とし，アセスメントツールの導入群と対照群による前向き並行群間比較試験を行いその有用性を検討した.
結果・考察：アセスメントツール使用による 1 年間の介入で，副作用の発見回数は，導入群で有意に増加した（P = 0. 0345）. しかし，服薬コンプライアンス，CLSS，QOL は両群で変化が見られなかった.
結論：下部尿路症状アセスメントツールの使用は処方薬の副作用の検出に有用であることが分かった.

Keywords：Lower urinary tract symptoms, community pharmacy, assessment tool

(Received; October 2, 2015, accepted; December 22, 2015)

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Background

The prevalence of urinary incontinence (UI) among adults is rapidly increasing as the global and Japanese populations age [1]. Estimates of the prevalence of UI among residents in nursing home facilities range from 50% to 70% [2]. UI can negatively impact quality of life (QOL) and its costs to society are high [3, 4]. Women are twice as likely as men to suffer from UI. The causes of UI are multifactorial, and the elderly population is particularly susceptible to adverse drug events (ADEs). Therefore, the treatment of UI must be individualized. Many medications, including antihistamines, benzodiazepines, antimuscarinics, anticholinergics, antidepressants, antipsychotics, opioids, and angiotensin-converting enzyme inhibitors, may cause UI [5, 6]. Anticholinergic medications are associated with multiple adverse reactions to which older individuals are particularly susceptible.

The most common cause of UI is disease or dysfunction of the lower urinary tract. Lower urinary tract symptoms (LUTS) can be classified as storage symptoms (urgency, frequency, nocturia, and urgency incontinence), voiding symptoms (bladder emptying, urinary hesitancy, slow or weak urine stream, urinary retention, and dribbling of urine), or mixed urinary symptoms. Storage symptoms tend to be more common among women, whereas voiding symptoms resulting from prostatic enlargement and ensuing bladder outlet obstruction are more common among men.

In our previous study, we found that the use of LUTS-causing prescription drugs correlated with polypharmacy. The ADEs associated with LUTS-causing drugs were highly prevalent in elderly patients. [7]. Thus, pharmacists should be alert to the risk of preventable ADEs in patients with LUTS in daily practice.

Community pharmacists are in an ideal position to provide counseling as they dispense medication, to monitor medications to optimize patient outcomes, and to pass on information to other healthcare professionals when indicated. In addition to their role in the prevention and management of medication errors, ADEs, dose adjustment, and drug interactions, community pharmacy services are beneficial for patients with conditions, such as diabetes or hypertension, which use objective parameters such as blood pressure or glycosylated hemoglobin to assess patient health status [8, 9, 10]. However, most community pharmacists do not have time to perform such specialty services because they spend a majority of their time in a dispensing role [11, 12].

In the present study, we developed an assessment tool comprising the core LUTS score (CLSS) questionnaire for therapeutic monitoring [13], the drug compliance scale (DCS) for evaluation of drug compliance, and a check sheet for ADEs of medications used to treat LUTS. We then investigated the impact and effectiveness of the assessment tool on pharmaceutical intervention for patients with LUTS visiting community pharmacies.

Methods

Assessment questionnaire for patients with LUTS

The assessment questionnaire included items related to patient attributes, therapeutic monitoring, QOL, ADEs, and DCS. The structured questionnaire was administered to all participants during face-to-face interviews conducted by pharmacists. The patient attributes recorded were age, sex, past and/or

present comorbid diseases, risk factors for LUTS, prescribed medications, and over-the-counter (OTC) medication. Three types of the questionnaire for collecting patient information were developed for the management of storage symptoms, voiding symptoms, and mixed urinary dysfunction (supplement 1).

Development of the assessment tool for LUTS

The assessment tool comprised the following three sections: 1. therapeutic monitoring and QOL, 2. ADEs, and 3. drug compliance for the management of storage symptoms, voiding symptoms, and mixed urinary dysfunction. We included a scoring book to more efficiently perform pharmaceutical care in accordance with a time-series change of the score (supplement 2).

1. Therapeutic monitoring

The degree of LUTS was measured using the CLSS questionnaire developed by Homma et al. [11]. The CLSS is a validated questionnaire that assesses the overall range of LUTS in men and women. The questionnaire provides an overall assessment of relevant symptoms, including daytime frequency, nocturia, urgency, urgency incontinence, stress incontinence, slow stream, straining, incomplete emptying, bladder pain, and urethral pain. Scores are marked from 0–3, with 0 indicating no problem and 3 indicating a frequent problem. Patients are asked which single core symptom has the greatest impact on their QOL using a seven-item visual analog scale, with 0 indicating very satisfied and 6 indicating terrible (supplement 3).

2. Adverse drug events

Any adverse reactions of medication for LUTS were identified through the check sheet, which was composed of the listed adverse reactions occurring with a high frequency (supplement 4).

3. Drug Compliance

Patient attitudes toward medication and noncompliance were assessed using DCS, which comprised the following four drug compliance items: (1) I take my medicine as indicated; (2) I decide to miss out on a dose of my medicine; (3) I stop taking my medicine for a while; and (4) I forget to take my medicine [14].

Participants

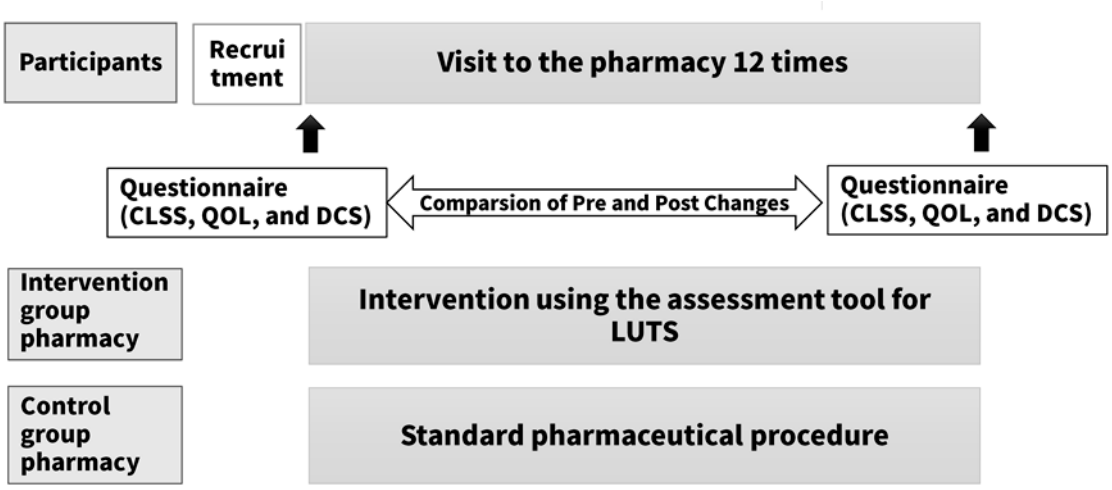
Patients recruited for this study were randomly selected from those visiting the pharmacy located in Ishikawa Prefecture, Japan, between June 1, 2013 and July 31, 2013. Only patients who were prescribed a medication for urinary disturbances for at least 28 days (1 month) were eligible for inclusion. Subjects also had to be over 65 years of age and self-administer medications at home. Patients were excluded if they could not visit the pharmacy 12 times (once a month) during the study period from June 1, 2013 to August 31, 2014. Twelve patients who provided informed consent and agreed to participate in this study were included. Three patients dropped out. The classification of patients with LUTS was determined by the prescribed medications, medical history of the patient, and diagnosis by a general practitioner.

Study design

Six Temari Group pharmacies in Ishikawa Prefecture, Japan, were invited to participate in the study and were randomly divided into a control and intervention group. A director of pharmacy at control group pharmacies applied the standard pharmaceutical procedure for patients with LUTS and a director of pharmacy at intervention group pharmacies utilized the assessment tool for LUTS in their practice.

At the initial visit, individual patient data, including the CLSS and patient attributes, were collected using the assessment questionnaire. In the intervention group, patients met a pharmacist 12 times over the study period to review drug therapy using the assessment tool for LUTS. In the control group, patients also met a pharmacist 12 times for drug therapy review in a standard manner (monitoring therapeutic outcomes and drug-related problems as well as recording the medication history). Data from participants were only collected at the initial visit and final visit 12 months later (Fig. 1).

If any problem related to a prescribed medication and/or patient's medical condition was identified, the pharmacist referred the patient to their general practitioner (GP) for adjustment of pharmacotherapy.



CLSS: Core lower urinary tract symptom score; DCS: Drug compliance scale for evaluation of drug compliance

Fig. 1: Flowchart of study procedures

Outcome measures

Primary outcome measure was changes in CLSS between the first and final (12th) visit to the pharmacy and secondary outcomes included QOL score and DCS. The number of ADEs and referrals to the GP during the observation period were also recorded. The CLSS is corresponded to the scores of corresponding symptoms. All symptom scores of CLSS were significantly increased in symptomatic patients. The clinical significance of the intervention was evaluated as decrease of score of CLSS.

Statistical analysis

Differences between the control and intervention groups in CLSS for therapeutic monitoring, DCS, and the numbers of ADEs were compared using Tukey's test. The Pearson chi-square test was used for categorical data as indicated. Statistical Package for the Social Sciences (SPSS) (ver. 23. IBM, Japan) was used for all analyses and $P < 0.05$ was considered significant.

Ethics statements

This study was approved by the ethics committee of the Faculty of Health Sciences of the University of Kanazawa. All participants signed a written informed consent form and information in the questionnaires was kept anonymous.

Results

Table 1 shows demographic characteristics of the patients according to group allocation. There were no statistically significant differences between the control and intervention groups with respect to these

Table 1: Demographic characteristics of the intervention (n = 11) and control group (n = 8) patients

	Intervention (n = 11)	**Control (n = 8)**	**P value**
Age (mean ± SD)	76 ± 10.68	75 ± 7.07	0.649[a)]
Male (%)	7 (63.6)	3 (25.0)	0.096[b)]
Type of LUTS			
voiding symptoms	7	6	0.870[b)]
storage symptoms	2	1	
mixed urinary symptoms	2	1	

a) Mann-Whitney *U*-test, b) χ^2 test.

variables, including age, symptom type (voiding vs. storage), and gender, although 63.6% of the intervention group were males and 75.5% of the control group were females.

The effect of interventions using the assessment to manage patients with LUTS is shown in Table 2 and Fig. 2. The number of ADEs identified in the intervention group was significantly higher than that in the control group ($P < 0.05$). In the intervention group, CLSS decreased from 7.1 to 6.1 (difference: −1.00 ± 2.49), whereas in the control group, CLSS increased from 7.3 to 7.8 (difference: 0.05 ± 3.59), although the difference was not statistically significant. The change in the QOL score in the intervention and control groups was 0.14 ± 0.95 and −0.17 ± 1.47, respectively. DCS was good in both groups before getting into the study and did not change during study period. The number referrals to the GP did not statistically differ between intervention (0.46 ± 0.21) and control groups (0.38 ± 1.47).

Table 2: Clinical characteristics and outcomes in the intervention and control group patients

	Innervation (n = 11)	**Control (n = 8)**	**P value**
CLSS (Mean ± SD)	−1.00 ± 0.75	0.50 ± 1.27	0.295
QOL score (Mean ± SD)	0.23 ± 0.26	−0.13 ± 0.441	0.478
DCS	0	0	-
Discover the number of times of adverse drug reaction (Mean ± SD)	0.82 ± 0.26	0.13± 0.13	0.050[a)*]
Number of times of doubt reference to general practitioner per patient (Mean ± SD)	0.46 ± 0.36	0.38 ± 0.26	0.872

a) Tukey's test * Significant difference at $P < 0.05$ level.

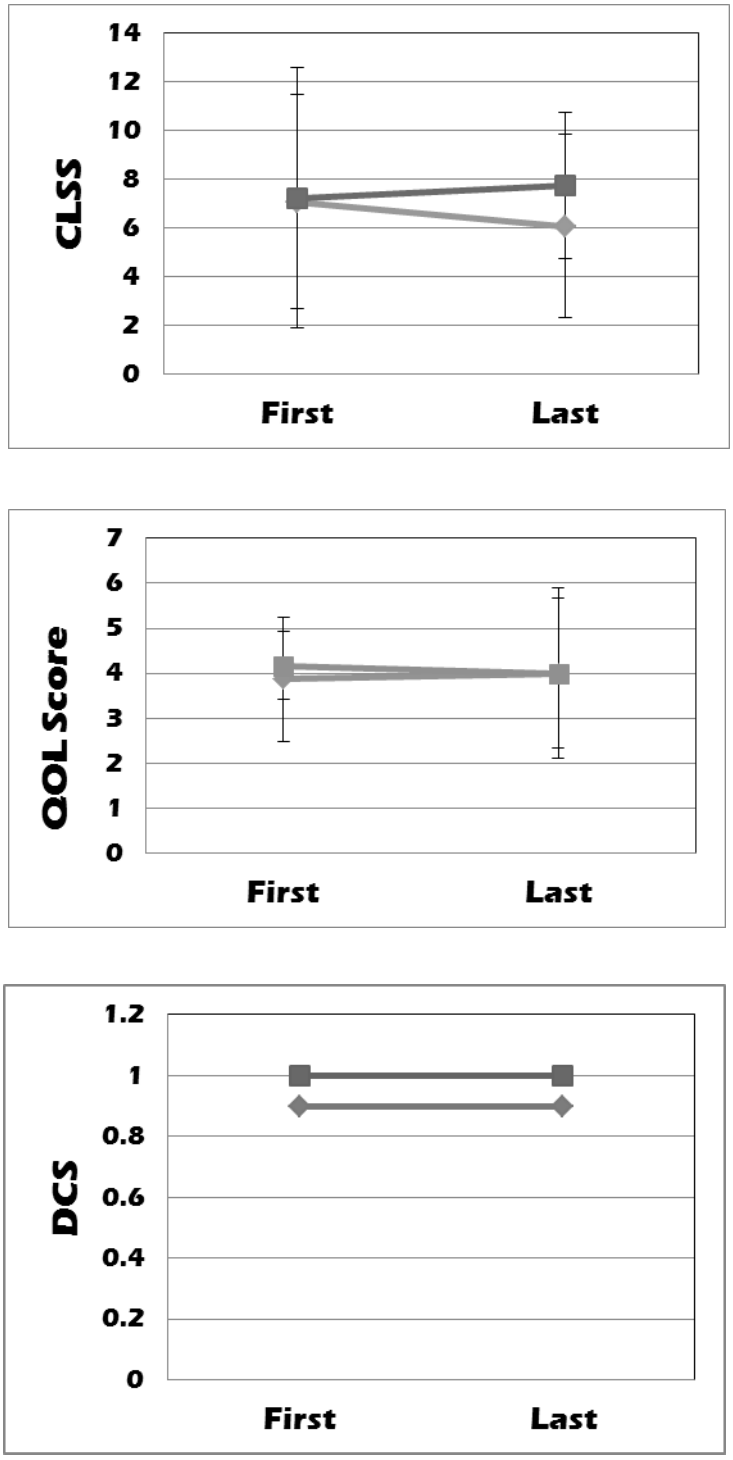


Fig. 2: Pre-Post Changes in CLSS and QOL score

Discussion

In this study, we examined the effect of an assessment tool for the intervention by pharmacists for patient with LUTS. During the study, we observed changes over time in detection of ADEs of medication for LUTS. However, there were no significant differences on CLSS, medication compliance, and QOL between the groups. There was a tendency toward decreased CLSS or improvement in LUTS symptoms in the intervention group. However, the difference was not statistically significant. This could result from a lack of statistical power. Medication compliance of participants in this study was good from the beginning of the study. Therefore, no difference was detected in this measure. Little information is available about the relationship between medication compliance and clinical outcomes for pharmacological treatment of LUTS. Cindolo and colleagues present data stating that adherence to pharmacological therapy for benign prostatic hyperplasia (BPH), one of the causes of LUTS, is low and could affect clinical outcomes [15]. Medication compliance to LUTS may be essential for the effective management of patients with LUTS. Pharmacists play an important role in improving compliance with LUTS medications. Although the detection of ADEs in the intervention group was higher than that in the control group, there no difference in the number of times of doubt reference to GP. The reason is that pharmacists did not provide the ADEs to GP and have limits their interaction with GPs to such activities. There is evidence that greater collaboration between general practitioners and pharmacists can improve patient care. Interprofessional collaboration between GPs and pharmacists must continue to evolve to meet the medication management and healthcare needs of the community. We will develop the collaboration of community pharmacies and GPs in LUTS treatment, with the aim of enhancing patient care.

Our finding of improvements in detection of ADEs by the intervention by pharmacists is consistent with those of other studies [16, 17, and 18]. The pharmacotherapy assessment tool for LUTS presented here is useful to monitor medication use and adverse effects of prescribed medication in an efficient and systematic manner.

There are some limitations to our study. First, the location of the pharmacy and its distance from a clinic is a limitation in terms of patient population and possible collaboration between general practitioners and pharmacists. Second, pharmacists were not equal to in skill of pharmacy practice. However, all pharmacists involved were directors of pharmacy with over 10 years of work experience. The third, we use subjective methods (self-report scales and questionnaires) to measure patient outcomes, which may be subject to bias. However, subjective methods appear reliable and correlate with the clinical state of patients in clinical practice. Finally, there is a chance that researchers who were not blind to the intervention group may have biased the results.

Conclusions

The intervention by pharmacists based on the assessment tool showed a significant positive effect on detection of ADEs but not on medication compliance, treatment satisfaction, and improvement in symptoms. Compared with patients provided with usual care, patients given the intervention had statistically

insignificant but better scores on these outcomes. This finding highlights the important role that pharmacists could play in providing direct patient care in regular pharmacy practice to improve the detection of ADEs.

Lists of Abbreviations

ADEs: adverse drug events
BPH: benign prostatic hyperplasia
CLSS: core lower urinary tract symptom score
DCS: Drug compliance scale
GP: general practitioner
LUTS: lower urinary tract symptoms
QOL: quality of life
UI: urinary incontinence

Acknowledgements

We thank Ms. Mika Shibata for her significant help in the design of the study. The authors would like to thank Enago for the English language review.

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Supplement 1: For storage symptoms

患者基本情報シート（蓄尿障害）

●患者情報

患者ＩＤ		年齢	（　　）歳
		性別	男　・　女
加療中の疾病		介護者の有無	無　・　有（　　）
		キーパーソン	
ADL 状況	自立　・　一部介助　・　全介助		

●排尿障害治療薬

薬剤名（商品名）	服用期間
1	年　月から
2	年　月から
3	年　月から
4	年　月から

●リスク因子

OTC 薬	有	OTC 薬/健康食品	有
牛車腎気丸		ノコギリヤシ	
八味地黄丸（八味丸）		ウワウルシ	
竜胆瀉肝湯		カゴソウ	
六味地黄丸（六味丸）		クランベリー	
五淋散		ペポカボチャ	
清心蓮子飲		イソフラボン	
小建中湯			
桂枝加竜骨牡蠣湯			

●OTC/健康食品

リスク因子	有	リスク因子	有
脳梗塞		認知症	
脳血管障害		前立腺肥大	
パーキンソン		骨盤臓器脱	
脊髄損傷		骨盤内の癌	
その他の神経疾患		下部尿路の手術経験	
糖尿病		うつ病	
膀胱炎		肥満	
尿崩症		多発性硬化症	
その他（　　）		その他（　　）	

●原因薬

薬効分類	一般名	有	薬効分類	一般名	有
認知症治療薬			抗ヒスタミン薬		
経口腸管洗浄剤			悪性腫瘍治療薬		
その他	（　　）（　　）		その他	（　　）（　　）	

Supplement 2: For storage symptoms

Supplement 3: For storage symptoms

お薬の効果の評価シート

この１週間の状態に当てはまる回答を１つだけ選んで、
数字に○をつけてください。

何回くらい、排尿しましたか？			
1	朝起きてから寝るまで	7回以下	0
		8～9回	1
		10～14回	2
		15回以上	3
2	夜寝ている間	0回	0
		1回	1
		2～3回	2
		4回以上	3
以上の症状が、どれくらいの頻度でありましたか？			
3	我慢できないくらい、尿がしたくなる	なし	0
		たまに	1
		ときどき	2
		いつも	3
4	我慢できずに、尿が漏れる	なし	0
		たまに	1
		ときどき	2
		いつも	3
5	セキ・クシャミ・運動のときに、尿が漏れる	なし	0
		たまに	1
		ときどき	2
		いつも	3

以上の症状が、どれくらいの頻度でありましたか？			
6	尿の勢いが弱い	なし	0
		たまに	1
		ときどき	2
		いつも	3
7	尿をするとき、お腹に力を入れる	なし	0
		たまに	1
		ときどき	2
		いつも	3
8	尿をした後に、まだ残っている感じがする	なし	0
		たまに	1
		ときどき	2
		いつも	3
9	膀胱（下腹部）に痛みがある	なし	0
		たまに	1
		ときどき	2
		いつも	3
10	尿道に痛みがある	なし	0
		たまに	1
		ときどき	2
		いつも	3

1	2	3	4	5
朝起きてから、寝るまでの排尿回数	夜寝ている間の排尿回数	我慢できないくらい、尿がいしたくなる	我慢できずに、尿が漏れる	セキ・クシャミ・運動の時に、尿が漏れる
6	7	8	9	10
尿の勢いが弱い	尿をするとき、お腹に力を入れる	尿をした後に、まだ残っている感じがする	膀胱（下腹部）に痛みがある	尿道に痛みがある

１から 10 の症状のうち、困る症状を３つ以内で選んで
番号に○をつけてください。

1	2	3	4	5	6	7	8	9	10	0該当なし

上で選んだ症状うち、最も困る症状の番号に
○をつけてください。（１つだけ）

1	2	3	4	5	6	7	8	9	10	0該当なし

現在の排尿の症状がこのまま変わらずに続くとしたら、
どう思いますか？

0	1	2	3	4	5	6
とても満足	満足	やや満足	どちらでもない	気が重い	いやだ	とてもいやだ

Supplement 4: For storage symptoms