Patient Preference and Adherence Dovepress

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Phytomedicines in Pharmacotherapy of LUTS/BPH – What Do Patients Think?

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Purpose: Lower urinary tract symptoms (LUTS) consist of voiding and storage symptoms. While the therapeutic efficacy of current LUTS medications is limited, and with more than 20% of patients suffering from mixed symptoms, current guidelines offer nothing more than combining monotherapies. An individualized approach is urgently warranted, and phytomedicines have become an integral part of patient-empowerment in therapeutic shared-decision making processes. Therefore, we aimed to investigate patients' preference of phytomedicines and treatment adherence at the dawn of an era leaving α_1-blocker monotherapies behind.

Patients and Methods: A questionnaire was prepared, and patients at our tertiary referral center were given the opportunity to voluntarily participate in our survey. We collected questionnaires from 300 patients during their visits from January 2022 to December 2022.

Results: With 73% (218/300), most of our study cohort had either taken one or more or were currently on prescription medication for LUTS/BPH. Patients were prescribed α_1-blockers (72%), followed by 5α-reductase inhibitors (21%), and phosphodiesterase-5-inhibitor (5%), while antimuscarinics and β_3-agonists were rarely prescribed. However, 41% (89/218) of our patients, who were taking medication for LUTS, had taken or were currently taking phytomedicines, making this the second most common drug class in our patient cohort. Patients scored the efficacy of phytomedicines at a mean in the lower third, but 87% of patients attributed excellent tolerability, and only 9% experienced side effects. While 43% of patients recommended phytomedicines for other patients, two-thirds of patients thought phytomedicines should be covered by statutory health insurance.

Conclusion: We found that phytomedicines were the second most common drug class taken by LUTS patients at our hospital. Reasons may be easy availability as over the counter medication and a superior safety profile with less bothersome side effects than commonly prescribed drug classes. Taken together, phytomedicines may be able to bridge an important gap in LUTS pharmacotherapy to provide sufficient treatment adherence where prescription drug classes fail, and ultimately, adequate improvement of symptoms. However, patients need to be counseled on potentially limited efficacy.

Keywords: urology, phytomedicines, LUTS, BPH, OAB, patient preference, treatment adherence, decision making

Introduction

Lower urinary tract symptoms (LUTS) consist of both voiding and storage symptoms.[1,2] On the one hand, urethral obstruction leads to voiding symptoms, which are most commonly attributed to benign prostatic hyperplasia (BPH), in which hyperplastic growth and increased smooth muscle tone in the hyperplastic prostate may lead to benign prostatic obstruction (BPO).[1,3] On the other hand, spontaneous contractions of the detrusor smooth muscle cause storage symptoms and may present as a direct consequence of BPO, and symptoms are referred to as overactive bladder (OAB).[2,4] There is a considerable proportion of patients suffering from "mixed LUTS", which presents as a combination of voiding and storage symptoms, and in general LUTS affects a large portion of the population worldwide.[1,3] In 2018, an estimated 2.7 billion patients suffered from storage symptoms and 1.1 billion patients suffered

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from voiding symptoms.[5] In LUTS, exaggerated smooth muscle tone and hyperplastic prostate growth are important targets of medical treatment.[1,3,4]

Alpha$_1$-adrenoceptor antagonists (α_1-blockers) for reduction of prostate smooth muscle tone, and 5-AR inhibitors (5-ARI) for reduction of prostate size, represent the current standard-of-care for LUTS/BPH.[1] While α_1-adrenoceptor antagonists improve prostate symptom scores (IPSS) and urinary flow rates (Q_{max}) by no more than 40%, 5-ARI reduce prostate size only up to 25%. However, the side effects of α_1-blockers are particularly bothersome and mostly cardiovascular, including hypotension, dizziness and a tendency to fall, while 5-ARI may lead to bothersome heat waves, loss of libido, or even a combination of sexual dysfunction and depression, subsumed under the term post-finasteride-syndrome.[1,6,7] Medical treatment for LUTS/OAB focuses on muscarinic receptor antagonists for relief of spontaneous bladder contractions.[1,2] While antimuscarinics may improve storage symptoms in up to 65% of patients, side effects include dry mouth, obstipation, tachycardia, and may even lead to cognitive impairment.[8,9] The more recent introduction of β_3-adrenoceptor agonist mirabegron reflects the need for new substance classes for medical therapy of male LUTS.[1,10] However, the specificity of mirabegron for β_3-adrenergic receptors has been increasingly questioned,[11] as the compound antagonizes α_1-adrenoceptors, at least at high concentrations, out of therapeutic range.[11–13] Recently and due to continuous research in the field, urologists have been behind the dogma of α_1-blocker monotherapies and entered an era, which now sees clinical trials focused on combination therapies, reflecting on the increasing amount of patients suffering from mixed LUTS.[1,3] By combining α_1-blockers with muscarinic receptor antagonists, two main pharmacological processes are targeted at once. However, adverse events of both drug classes are potentiated with combined treatment using α_1-blockers and antimuscarinics, with the most common and bothersome side-effects including ejaculation failure and therapy-limiting dry mouth.[14] Thus, respective discontinuation rates of up to 90% due to treatment failure or therapy-limiting side effects highlight the limitations of current pharmacotherapy and may explain patients' desire for over-the-counter (OTC) phytotherapeutic agents.[6,8]

Recently, the European Association of Urology recommended hexane-extracted fruit of *Serenoa repens* (HESr) in their guidelines on management of non-neurogenic male LUTS. Thus, making it the first guideline recommendation of a phytotherapeutic agent for the treatment of LUTS secondary to BPH.[1] Despite previously lacking recommendations, phytotherapeutics are among the most investigated medications for LUTS/BPH in clinical trials, where they provide effective symptom relief for male LUTS.[15,16] Phytotherapeutic agents are part of a growing market with patients seeking alternatives to current standard-of-care treatment. Most phytotherapeutic agents are available without prescription, so that their access does not warrant a urologist's appointment, which can be bothersome and time consuming for patients.[17] While the mechanistic properties of HESr have only recently been revealed,[18] the EAU's 2021 recommendation is the first guideline recommendation of any phytotherapeutic agent and is based on two systematic reviews showing improvement of LUTS similar to that of α_1-blocker tamsulosin and short-term use of 5-ARI finasteride, with considerably less side effects.[15,16]

Thus, we aimed to assess the prevalence of phytotherapeutic agents for LUTS secondary to BPH, and what patients thought in terms of efficacy and safety. For this we developed a questionnaire, which was offered to patients during urology consultation hours for LUTS/BPH at our tertiary referral center. To the best of our knowledge, there is no such survey covering this specific question after the guideline recommendation by the EAU in 2021.

Materials and Methods

Patient Population

In our tertiary referral center, patients were given the opportunity to voluntarily participate in our survey. From January to December 2022 questionnaires were available to all patients presenting at our outpatient clinic for our urology consultation hours for LUTS. Thus, included patients present a highly selective study population. Consultation hours for LUTS patients are offered every Wednesday from 8 a.m. to 2 p.m., with 30-minute appointments for 12–15 patients per week, covering 46 operating weeks of the outpatient office per year. Thus, questionnaires were available to every single patient throughout the sampling period of 1 year upon their first presentation at the outpatient office.

Study Design

Non-random sampling was conducted at our institution's outpatient clinic on multiple occasions from January to December 2022. Patients presenting during urology consultation hours for LUTS/BPH were handed the paper questionnaire with their documents and patient information at the beginning of the visit. The questionnaire was accompanied by a cover sheet explaining the survey. As participation was completely optional, patients were instructed to deposit the filled-out questionnaire in a sealed container at any given time or return the blank questionnaire with their other documents. All data were collected anonymously and cannot be linked to any individual participant in our survey.

Study Tool

As with our previous research on factors influencing patients' choice of urologist,[17,19] we adhered to the article on good practice in the conduct and reporting of survey research by Kelley and colleagues.[20] To collect data from a large patient cohort on the use and impact of phytomedicines in LUTS/BPH, we developed a questionnaire containing 15 different items of interest specifically for this patient survey (Supplementary File 1). Items were designed as closed questions with pre-coded multiple-choice response options, open questions, where the respondents composed the reply, or as a scale to assess efficacy. All questions were numbered and grouped by subject, and headings included for each question. Part 1 of the detailed questionnaire focused on the participant's specific prescription medications for LUTS/BPH (name, amount, prescriber, duration of prescription, efficacy, side effects etc). In part 2 of the questionnaire, patients were asked if they had ever taken phytomedicines for LUTS/BPH and how they perceived efficacy and experienced side effects. Due to the number of different available medications, patients were asked to fill in the name of the phytotherapeutic agent themselves. To minimize bias and reduce the influence of the physician's presence, the questions were phrased in a straightforward manner and simple written instructions accompanied every single question in the questionnaire. Following our analysis plan (Supplementary File 2), a clinical judgment discrimination process was crucial for determining all possible items and to identify the pertinent questions relevant to patient determinants. The initial version was evaluated, and questions deemed non-relevant or duplicated were rejected in the final version. Piloting was conducted in 20 patients. Following our previous experience,[17,19] the pilot revealed no issues with understanding the questions, and patients found it easy to proceed while waiting for their appointment. Participants were provided with a cover letter designed to encourage the respondent to participate in this study, including information on the organization conducting the survey and contact details of the responsible researcher. To reduce investigator bias, the patients were not given any oral instructions by healthcare personnel.

Data Analysis

Statistical and descriptive analysis was performed using SPSS V29.0 software (IBM SPSS Statistics, Armonk, NY). Results are given as percentages for categorial variables. Fisher's exact test and $\chi 2$ test were performed for categorial variables. All reported p-values were two-sided and considered statistically significant if $p < 0.05$. Graphing and one-way analysis of variance (ANOVA) with Tukey's test for comparison of all groups with each other was performed using GraphPad Prism 9.3.0 (GraphPad Software Inc., San Diego, CA, USA).

Results

In total, 690 appointments for patients at the urology consultation hours were available throughout the sampling period. Every single patient received a questionnaire upon their first presentation from January to December 2022, yielding 390 individual patients. We report a response rate of 77% (300/390) and analyzed 300 questionnaires. No questionnaire had to be discarded due to a low rate of answered questions, which was defined as a participant answering to less than half of the questions. To obtain an overview, we have listed a breakdown of our sample as study flow-chart in Figure 1.

Prescription Medications

With 72.7% (218/300), most of our study cohort had either taken or were currently on prescription medication for LUTS/BPH (Figure 2A). Patients reported being prescribed and taking various medications (n = 266). Of the prescribed LUTS

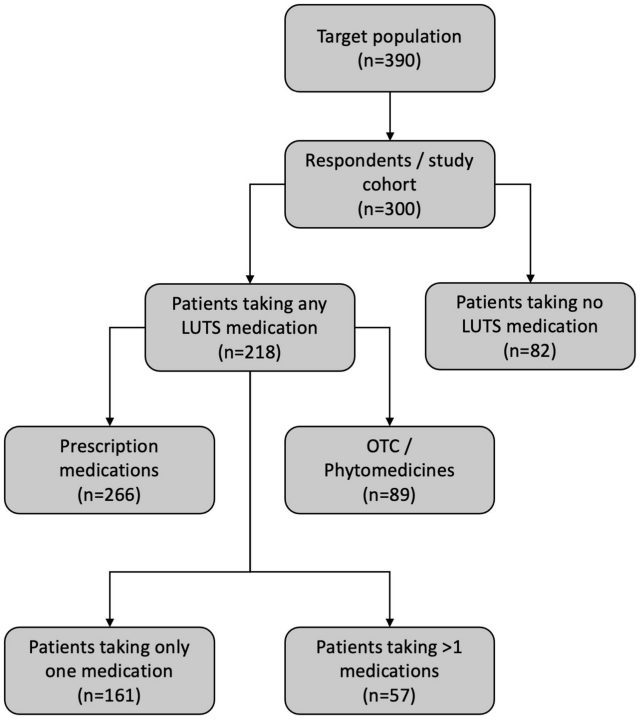

Figure 1 Study flow chart. Showing the detailed inclusion of patients into the study. According to the questionnaire patients answered if they had ever taken any medication for LUTS, and if they had ever taken phytomedicines for LUTS. Some patients took more than one medication simultaneously, or added another over time.
Abbreviations: LUTS, lower urinary tract symptoms; OTC, over the counter.

medication, 71.9% (191/266) had been α_1-blockers (tamsulosin, alfuzosin, terazosin, silodosin), 21.0% (56/266) 5-ARI (finasteride, dutasteride), 4.5% (12/266) phosphodiesterase 5 (PDE5) inhibitor tadalafil, 2.3% antimuscarinics (5/266), and 0.4% β_3-agonist mirabegron (1/266) (Figure 2B). In 91.7% medication was prescribed by urologist, while 8.3% were prescribed by the patients' general physician (GP). With most patients (73.7%) having taken only one medication, the mean of medications taken for LUTS/BPH was 1.35 (95 CI 1.28 to 1.42). However, 26.2% of patients were either primarily started on two or more medications or had added more medications over time. Thus, the total number of preparations reported exceeds the total number of patients taking LUTS medication.

Phytomedicines

Phytomedicines were taken by 40.8% (89/218) of patients who had either taken medication or were currently taking medication for LUTS/BPH (Figure 3A), making phytomedicines the second most common drug class taken by patients in our cohort, as identified by total medications listed in our patient cohort (Figure 3B). Most common preparations included extracts of saw palmetto fruit *Serenoa repens* (56.3%), phytosterols from pumpkin seed oils *Cucurbita pepo* (34.4%), rye-grass pollen *Secale cereale* (6.3%), and others. While the primary source of information for patients was advertisement through various media (47.8%), the attending physician, pharmacist, or complementary and alternative medicine (CAM) practitioners play the second most important role (37.7%), followed by family and friends (14.5%). Patients scored efficacy in the lower third. On a scale from 1 (limited efficacy) to 10 (high efficacy), patients scored phytomedicines at a mean of 3.0 (95% CI 2.4–3.7). However, 87% of patients attributed excellent tolerability, and only 9% experienced side effects, including constipation, dizziness, reduced ejaculation volume, and blocked nose. While 43% of patients recommended phytomedicines for other patients, 57% did not. Of those, 97% listed limited efficacy as the main reason, and 3% bothersome side effects. However, two-thirds of patients thought phytomedicines should be covered by statutory health insurance.

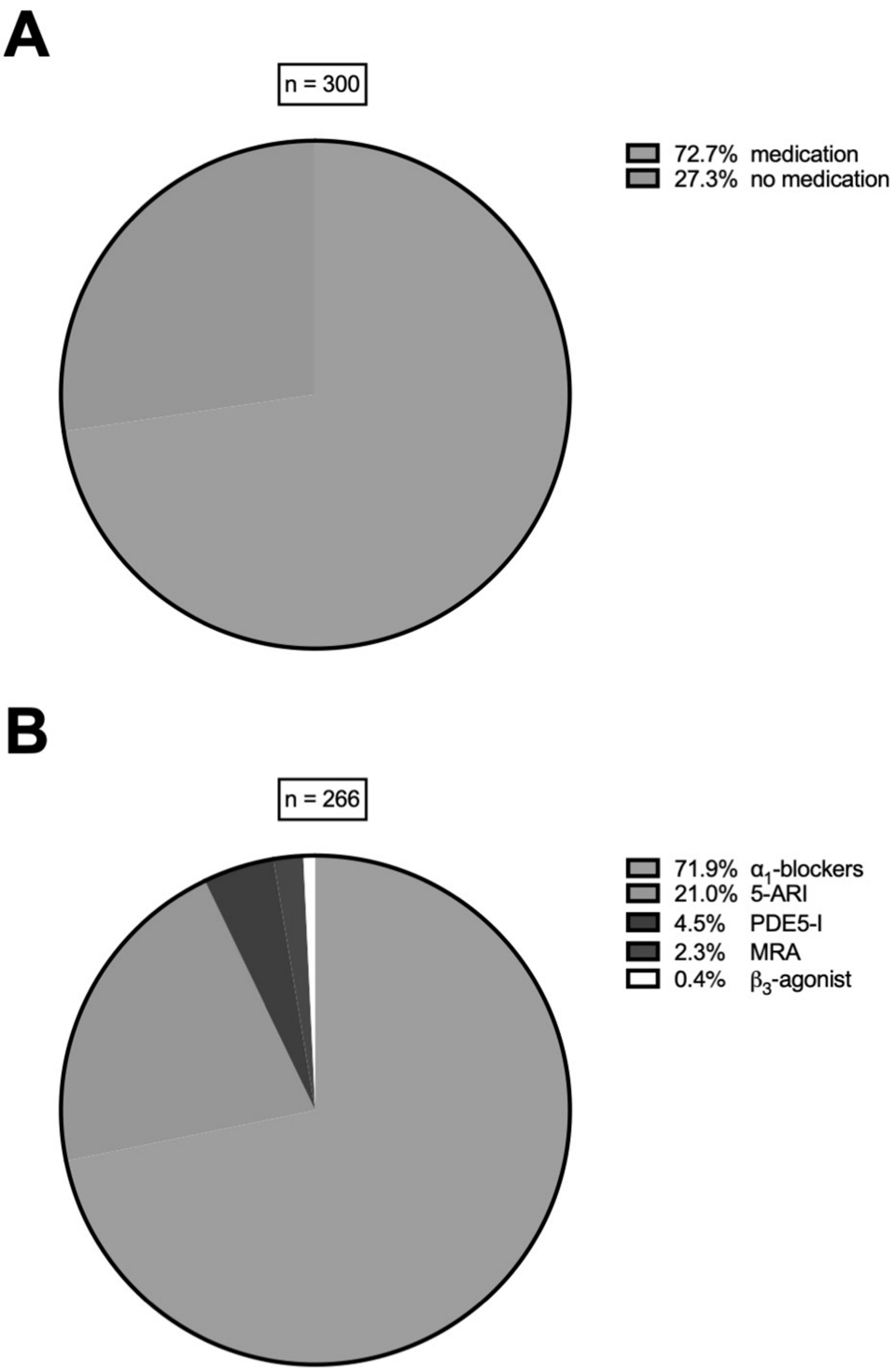

Figure 2 Percentage of patients taking any LUTS medication (**A**), prescription substance classes taken by patients (**B**). Substance classes include α_1-Adrenoceptor antagonists (tamsulosin, alfuzosin, terazosin, and silodosin), 5α-reductase inhibitors (finasteride, dutasteride), phosphodiesterase-5 inhibitor (tadalafil), muscarinic receptor antagonists (solifenacin, propiverine, trospium chloride), and β_3-agonist (mirabegron).

Abbreviations: α_1-blockers, α_1-adrenoceptor antagonists; 5-ARI, 5α-reductase inhibitors; PDE5-I, phosphodiesterase-5 inhibitors; MRA, muscarinic receptor antagonists; β_3-agonist, β_3-adrenoceptor agonist; LUTS, lower urinary tract symptoms.

Duration of Medication Use

Figure 4A gives an overview of the duration for which the different prescription medications were taken, divided for each specific substance. To cite specific pertinent results, 5-ARI finasteride and dutasteride were taken for a median duration

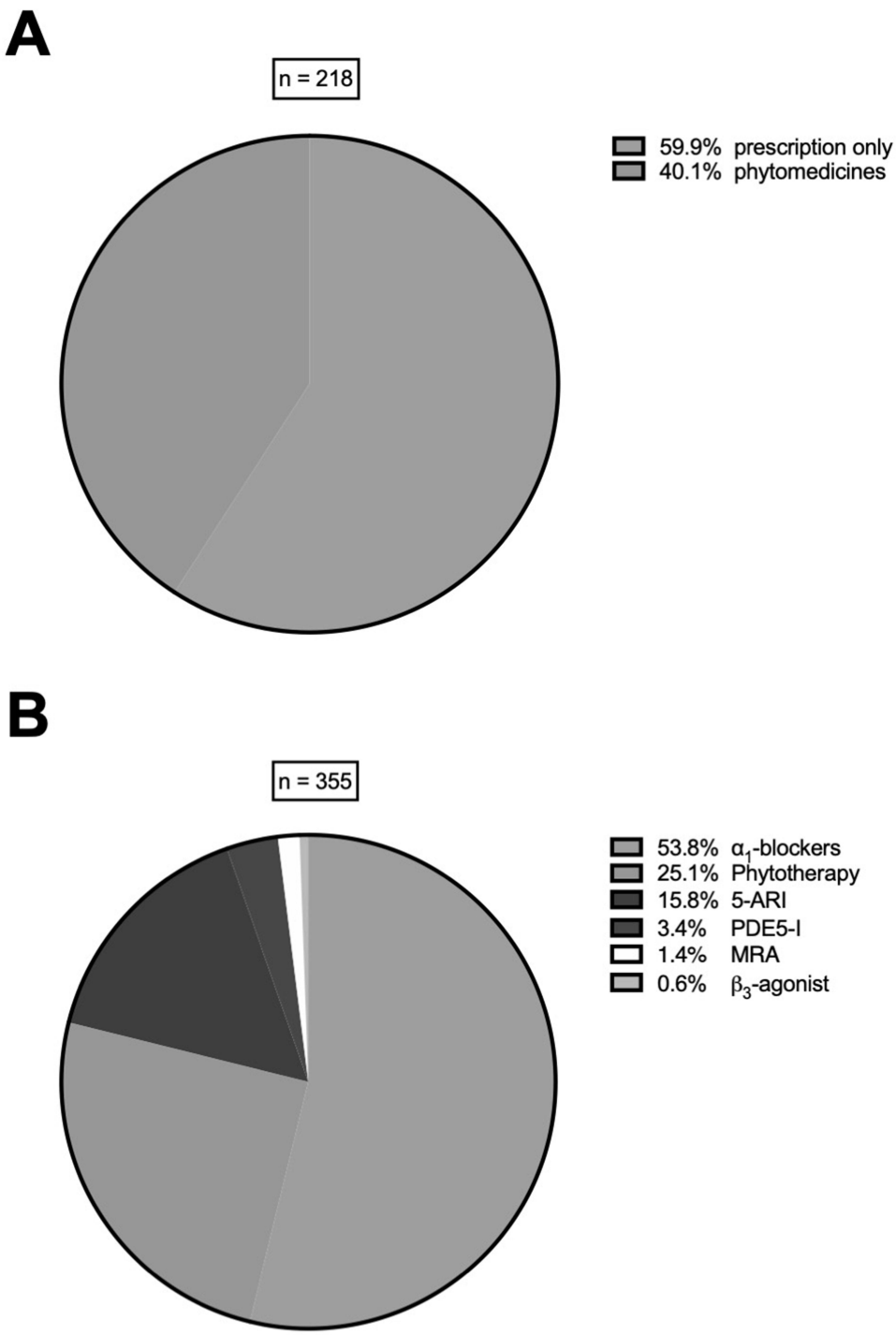

Figure 3 Percentage of patients taking any phytomedicines (**A**), substance classes taken by patients for LUTS, including phytomedicines (**B**). Substance classes include α_1-Adrenoceptor antagonists (tamsulosin, alfuzosin, terazosin, and silodosin), 5α-reductase inhibitors (finasteride, dutasteride), phosphodiesterase-5 inhibitor (tadalafil), muscarinic receptor antagonists (solifenacin, propiverine, trospium chloride), and β_3-agonist (mirabegron).
Abbreviations: α_1-blockers, α_1-adrenoceptor antagonists; 5-ARI, 5α-reductase inhibitors; PDE5-I, phosphodiesterase-5 inhibitors; MRA, muscarinic receptor antagonists; β_3-agonist, β_3-adrenoceptor agonist; LUTS, lower urinary tract symptoms.

of 1.3 years (IQR 0.8–4.8) and 1.0 years (IQR 0.5–2.8), respectively, while the α_1-blockers tamsulosin, alfuzosin, terazosin, and silodosin were taken for a median of 2.25 years (IQR 0.85–6.0), 2.5 years (IQR 0.29–6.0), 3.0 years (IQR 0.0–6.0), and 1.0 years (IQR 0.6–2.5), respectively, and the PDE5-inhibitor tadalafil was taken for a median duration of 2.0 years (IQR 1.0–5.0). Additionally, we compared the duration of use for the different substance classes. Patients took

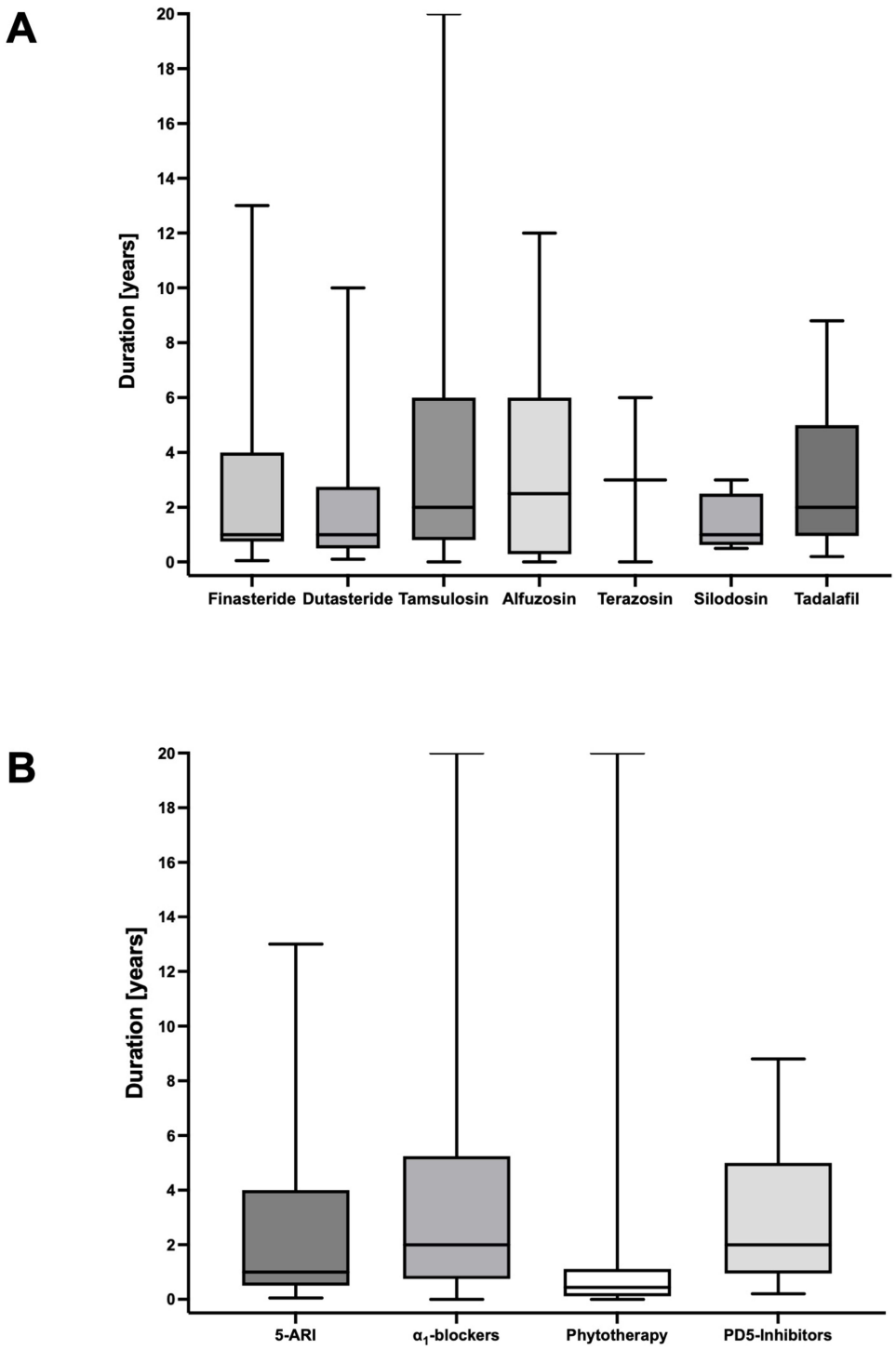

Figure 4 Overview of median duration for which the different prescription medications were taken (**A**), overview of median duration for which the different substance classes were taken, including phytomedicines (**B**). Data are shown as box plots with median and interquartile range (IQR) for α_1-Adrenoceptor antagonists (tamsulosin, alfuzosin, terazosin, and silodosin), 5α-reductase inhibitors (finasteride, dutasteride), phosphodiesterase-5 inhibitor (tadalafil), β_3-agonist (mirabegron), and phytomedicines (including extracts of saw palmetto fruit *Serenoa repens*, phytosterols from pumpkin seed oils *Cucurbita pepo*, rye-grass pollen *Secale cereale*, and others).
Abbreviations: α_1-blockers, α_1-adrenoceptor antagonists; 5-ARI, 5α-reductase inhibitors; PDE5-I, phosphodiesterase-5 inhibitors; β_3-agonist, β_3-adrenoceptor agonist.

5-ARI for a median duration of 1.0 years (IQR 0.5–4.0), α_1-blockers for 2.0 years (IQR 0.8–5.3), phytomedicines for 0.5 years (0.2–1.2), and PDE5-inhibitor for 1.0 years (1.0–5.0), which is shown in comparison to the other substance classes (Figure 4B). One-way ANOVA did not yield statistically significant differences in the duration of medication intake between the different substances or substance classes.

Efficacy and Safety

Of patients receiving medication, 61.6% were under active medication for LUTS/BPH at the time of survey, while 38.4% had stopped their medication. When asked by whom the medication was discontinued, only 29.6% had stopped taking medications themselves, while most patients (70.4%) had stopped according to their treating urologist or GP. The reasons were leaning towards side effects as being the main reason for stopping (60.4%) instead of the limited efficacy (39.6%). Main side effects included anejaculation and loss of libido, followed by orthostatic hypotension, blocked nose, diarrhea, and dry mouth, and constipation, among others (Table 1). Patients taking phytomedicines suffered from significantly less side effects than patients taking prescription medications (9.0% vs 37.2%, $p < 0.001$). However, 46.9% of patients suffered from more than one side effect during treatment.

Table 1 Side Effects During Treatment

Adverse Events (AEs)			
	Prescription Medication (n=218)	**Phytotherapy (n=89)**	***p* value**
Anejaculation n (%)	16 (7.3%)	1 (1.1%)	0.212
Loss of libido n (%)	16 (7.3%)	0 (0.0%)	**0.043**
Orthostatic hypotension n (%)	12 (5.5%)	1 (1.1%)	0.365
Blocked nose n (%)	8 (3.7%)	1 (1.1%)	0.635
Diarrhea n (%)	7 (3.2%)	0 (0.0%)	0.236
Xerostomia n (%)	6 (2.8%)	0 (0.0%)	0.291
Headache n (%)	3 (1.4%)	0 (0.0%)	0.457
Constipation n (%)	2 (0.9%)	2 (2.2%)	0.164
Other Median IQR	11 (5.1%)	3 (3.4%)	0.989
Total n (%)	81 (37.2%)	8 (9.0%)	**<0.001**

Notes: Shown are the number of patients who experienced adverse events (AEs) during treatment. Bold values mark statistically significant p values, where p<0.05.

Discussion

Influence of German Healthcare System

Patients in the German healthcare system provide an ideal study cohort, as Germany has one of the most restriction-free and consumer-oriented healthcare systems in the world, which is often recognized as the prototype of modern health system configurations. When health insurance coverage was expanded in 2009, it became compulsory for the whole population.[21] Compared to other healthcare systems, in which insurance networks may greatly influence patients' choice of medication or physician, according to a particular healthcare plan or healthcare provider, as is often the case in the US, the German healthcare system allows patients to seek nearly any type of care they wish, and whenever they want it.[22,23] With the Statutory Health Insurance Modernization Act back in 2004, one of the most extensive reforms of the German health care system was implemented.[21] In general, health care and medication costs are covered by the German health insurance system, and co-payment is limited to 10% or 10 EUR per prescription medication. Additionally, cost coverage for symptomatic medications for minor illnesses (eg, cold, cough, running nose, sore throat etc.) and phytomedicines was abolished. However, this is in stark contrast to recent EAU and German guidelines on the management of male LUTS, which represents the first ever recommendation of a plant extract by European urologic guidelines.[1,24]

While previous clinical trials suggested improvements in male LUTS by the phytotherapeutic HESr, which were superior to placebo and comparable to α_1-blockers,[15,16] underlying mechanisms have only recently been discovered.[18] With current findings on the mechanistic potential of HESr, there is now irrefutable evidence of actions to corroborate previous clinical data on the efficacy of phytomedicines for LUTS/BPH. Those findings point to concentration-dependent inhibition of smooth muscle contraction in the human prostate and detrusor tissues, and simultaneous inhibition of prostate stromal cell growth, mirroring the effects of α_1-blockers, antimuscarinics, and 5-ARI, respectively. These properties are critical for the treatment of male LUTS and represent important targets of standard-of-care medical therapy. For the first time in the current literature, this fully allows to explain the improvements of male LUTS by phytotherapeutics simultaneously from a clinical and basic scientific point of view.[15,16,18] Thus, questioning the reasoning of the Statutory Health Insurance Modernization Act in 2004, which dismissed phytomedicines as medications with limited clinical benefit and therefore excluded phytomedicines from coverage by the German statutory health insurance.

Regarding these data, and in an era after guidelines recommendation by two major urological associations for phytomedicines, our survey was conducted to assess the prevalence of phytotherapeutic agents for LUTS/BPH, and what patients presenting to our urology consultation hours thought in terms of efficacy and safety in a real-world setting.

Efficacy and Tolerability of Prescription LUTS Medications

Our tertiary referral center offers urology consultation hours every Wednesday for patients suffering from LUTS. We specifically targeted these patients and performed non-random sampling in this patient cohort. Thus, we were able to gain insight into patients' preference and adherence to pharmacotherapy for LUTS/BPH. With 72% of patients taking α_1-blockers as their prescription medication for LUTS/BPH, this is in line with international data.[25,26] However, discontinuation rates show limited treatment adherence to α_1-blockers after 12 months of about 30%,[6] which is well in line with data previously gathered at our department showing that 35% of patients presenting for BPH-related surgery were on active medication.[27] Our data corroborate that treatment discontinuation is mostly due to intolerable side effects or limited efficacy, which is also in line with international data.[6,25,26] While as expected, postural hypotension was among the most common side effects, loss of libido and reduced ejaculation volume together account for 38% of treatment-limiting side effects. Together, these data may explain patients' preference for OTC phytomedicines, even though they elicit significant costs as opposed to prescription medication, which is limited to minor co-payments.[21]

Efficacy and Tolerability of Phytomedicines for LUTS

Even though phytomedicines in combination with α_1-blockers have been reported as the most commonly prescribed combination treatment among French general practitioners, data on this subject are still limited.[28] While phytotherapy is an important and valuable treatment addition in various European countries, especially in France and Italy, the German health care system has only slowly started to realize the potential of phytotherapeutic agents, and they are not commonly

prescribed by doctors.[28,29] Our data point to that fact, as advertisement through various media is the most common source of information for OTC phytotherapeutics in our patient cohort. This is in line with findings by Joos and colleagues reporting that 80% of phytomedicines in Germany are sold OTC and only 20% as prescription medication.[30] In the past, urologists have been reluctant to prescribe phytomedicines for LUTS/BPH, because of the missing guideline recommendation. However, our data show that phytomedicines for LUTS/BPH are very popular as the second most common drug class used by our patient cohort. While one of the main reasons for discontinuation of LUTS medication is the combination of limited efficacy and bothersome side effects, our data point to favorable properties of phytomedicines in that regard. While patients mainly discontinued their prescription medication due to bothersome side effects, phytomedicines were taken for a similar duration as silodosin. Our cohort shows that silodosin was taken for the shortest duration of any α_1-blocker, even though patients report postural hypotension as similar to placebo, with anejaculation as the main bothersome side effect.[31] In line with the guideline recommendations by the German national and European guidelines, our data show patients perceived the efficacy of phytomedicines for LUTS/BPH as limited.[1,24] However, 43% of patients were satisfied with the efficacy of phytomedicines and recommended them to other patients. This may point to a favorable risk profile of phytomedicines, in which bothersome side effects are extremely rare. This is also corroborated by the fact that two-thirds of our patient cohort wished phytomedicines to be covered by health insurance, contrary to the Statutory Health Insurance Modernization Act of 2004.[21]

Patient Preference and Treatment Adherence

Medication adherence is key to sufficient treatment of LUTS/BPH. However, discontinuation rates of up to 90% for prescription medication due to treatment failure or therapy-limiting side effects are unacceptable. This highlights the limitations of current prescription medications for LUTS/BPH, which may ultimately explain our findings of patients' desire for OTC phytomedicines, even though their therapeutic efficacy may be limited.[6,8] Thus, patients should be counseled on the availability of phytotherapeutics, as they provide a superior safety profile with less bothersome side effects than prescription drug classes (α_1-blockers, PDE5 inhibitors, antimuscarinics, and 5-ARI).[32] While we could recently show the limited effect of standard-of-care LUTS medication on patients presenting for LUTS-related surgery,[27] patients may also be counseled as to the possibility of limited efficacy when using phytotherapeutic agents. However, and with their favorable safety profile, phytomedicines may be able to bridge an important gap in LUTS pharmacotherapy to provide sufficient treatment adherence and, ultimately, adequate improvement of symptoms.

Limitations

There are certain limitations to this study. Even though being a tertiary referral center with specialty consultation hours provides us with the advantage of streamlined patient selection, there may be a selection bias as our patient cohort may differ from outpatient consultations. Also, our findings reflect the situation in the German health care system. Attributed to national variations in medical systems and country-specific conditions, our findings may not be generalized without limitations. Nevertheless, and to the best of our knowledge, this is the only survey of patient preference and treatment adherence in LUTS/BPH evaluating the use of phytomedicines after recent guideline recommendations.

Conclusion

Our study provides important insight into patients' preference for and adherence to LUTS pharmacotherapy and the efficacy and safety of phytomedicines in patients suffering from LUTS/BPH. While medication adherence is key to sufficient treatment in LUTS, patients should be counseled on the availability of phytotherapeutics, as they provide a superior safety profile with less bothersome side effects than commonly prescribed drug classes. Taken together, phytomedicines may be able to bridge an important gap in LUTS pharmacotherapy to provide sufficient treatment adherence where prescription drug classes fail, and ultimately, adequate improvement of symptoms.

Statement of Ethics

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 helsinki declaration and its later amendments or

comparable ethical standards. For this type of study formal consent is not required and was waived by the institutional review board (University of Munich), as the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context. Additionally, the signature on the informed consent document would be the only record linking the subject to the research and the principal risk of harm to the subject would be a breach of confidentiality. All data were collected and analyzed anonymously.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

Thomas Kolben holds stock of Roche AG and a relative is employed at Roche AG. The authors report no other conflicts of interest in this work.

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