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Research Article

Effect of Saw Palmetto Extract on Erectile Dysfunction and Libido in Patients with Lower Urinary Tract Symptoms Because of Benign Prostatic Obstruction

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Abstract

Background: Herbal medicinal products containing extracts of saw palmetto berries (*Serenoa repens*) are used for treatment of Lower Urinary Tract Symptoms (LUTS) because of Benign Prostatic Obstruction (BPO). Improvement of sexual dysfunctions was also shown.

Methods: Here we performed a multicentric open label clinical study on 84 men to confirm its effects on LUTS/BPO on Slovenian population and this is only the second study investigating the effect on sexual dysfunctions.

Results: In 6 months of treatment the International prostate symptom score (IPSS) improved from 12.7 to 9.2 ($p = 7.0\times10^{-12}$) and the quality of life score improved from 2.4 to 1.7 ($p = 9.2\times10^{-4}$). Prostate-Specific Antigen (PSA) levels did not change. The proportion of patients with unsatisfactory libido reduced from 26.5 % to 13.2 % (p=0.036) during the therapy and a non-significant trend of reduction of erectile dysfunction was observed.

Conclusion: Our results are in agreement with the previous research on the efficacy of saw palmetto, but regarding the libido and erectile dysfunction, further controlled studies are needed.

Keywords: Berries; Erectile Dysfunction; Libido; Saw Palmetto (*Serenoa Repens*); Slovenian Population

List of Abbreviations

BPE : Benign Prostatic Enlargement;

BPH : Benign Prostatic Hyperplasia;

BPO : Benign Prostatic Obstruction;

ED : Erectile Dysfunction;

IPSS : International Prostate Symptom Score;

LUTS : Lower Urinary Tract Symptoms;

PSA : Prostate-Specific Antigen;

QoL : Quality of Life

Background

Extracts of saw palmetto berries (*Serenoa repens*) are used for treatment of mild to moderate LUTS/BPO, Erectile Dysfunctions, to improve testicular atrophy and sperm production, and as a genitourinary and sexual stimulant [1]. The plant is endemic to Florida and neighbouring regions in the south east of United States.

The prostate is positioned below the urinary bladder of man and surrounds the urethra [2]. In man after the age of 40,

the prostatic tissue enlarges (Benign Prostatic Enlargement - BPE) because of Benign Prostatic Hyperplasia (BPH) which often causes Benign Prostatic Obstruction (BPO) [3]. It constricts the urethra and causes urgent and frequent urination, nocturia, incomplete bladder emptying and weak urine stream. This occurs in 30% of men in their 60s and 50% of men older than 80 [4].

In addition to obstructive and irritative symptoms, BPO also affects sexual functions [5]. Patients with LUTS/BPO are at 3.7-fold higher risk of developing erectile dysfunction, compared with patients without LUTS/BPO and the severity of the LUTS correlates with frequency and severity of erectile and ejaculatory dysfunctions [6]. The main medical treatments for LUTS/BPO are alpha blockers and 5-alpha-reductase-inhibitors. Both treatment options are effective on the LUTS/BPO; but they have further negative impact on sexual functions [7-8]. Sexual dysfunctions are the most often reported adverse events of 5-alpha-reductase-inhibitors [9].

More than 32 controlled clinical trials investigated efficacy of saw palmetto preparations for LUTS/BPO treatment [10-11]. In most cases, the tested products contained 320 mg lipophilic berry extract per day [12]. Compared with placebo, the studies demonstrate good efficacy of long-term saw palmetto use to treat LUTS/BPO symptoms; the results are similar to finasteride [13] and tamsulosin [14], but saw palmetto has a much better safety profile than these substances particularly in regards to sexual dysfunctions [10]. As modes of action, *in vitro* and *in vivo* inhibition of both isoforms of the 5-alphareductase [15-16] and anti-inflammatory activities [17-18] have been reported, as well as inhibition of autonomous receptors in the lower urinary tract [19]. It is very desirable to find a treatment that not only improves the symptoms of BPO but also has no negative or possibly even a beneficial impact on sexual dysfunctions [20]. A pilot clinical trial showed that a saw palmetto extract improved sexual dysfunctions in patients with mild to moderate BPO [21]. Here we performed a multicentric clinical study to confirm the results. There are more than 32 studies investigating the effects of saw palmetto on LUTS/BPO, but this is only the second study investigating its effect on sexual dysfunctions.

Methods

The study was approved by the Medical Ethics Committee of the Republic of Slovenia (No. 16-234/3). 84 men with LUTS / BPO aged between 45 and 84 years of age (average 62.3 ± 9.2 years), were enrolled in this prospective, open, multicentric clinical trial. They were in good general health and they signed an informed consent to voluntary participate in the trial. The patients were enrolled by 19 physicians at the primary level.

The study did not include patients who have had surgery on the urinary bladder, prostate or pelvis, irradiation for pelvis, proven neurogenic bladder, stenosis of the bladder neck or urethra, stones in the bladder or urethra, recurrent urinary tract infections, cancer of the bladder and prostate, severe hepatic or renal insufficiency, diabetes mellitus, clinically significant cardiovascular or cerebrovascular disease, nervous system diseases, known intolerance to Saw Palmetto, therapy with inhibitors of 5-alpha reductase, blockers of alpha adrenergic receptors or phosphodiesterase 5-inhibitors. The study also did not include patients who have not been able to understand the research.

Upon entering the study all patients were clinical examined, digital rectal examination of the prostate was performed, they filled in the questionnaires for International Prostate Symptom Score (IPSS) and Quality of Life (QoL), gave the blood for total PSA analyses. Patients were also asked about a possible Erectile Dysfunction (ED) and libido. All patients then began treatment with the medicinal product Prostasan (Bioforce, Swizerland), 1 capsule per day containing 320 mg of the soft extract of saw palmetto berries (*Serenoa repens*) (W. Bartram) Small (synonym *Sabal serrulata)* (Michx.Schult.). The product was purchased on Slovenian market. Drug to extract ratio was*;* DER 9-12:1, extraction solvent 96% V/V ethanol. 1capsule per day was taken during or after a meal for 6 months. The data was collected at first (baseline) examination (at the start of treatment) and at second and third examination after 3 and 6 months of treatment. Patients came to second and third examination after 3 and 6 months of treatment. The same parameters were monitored as at the beginning of treatment. In addition, we collected the opinion of patients and their doctors about the efficacy and safety of the treatment, and recorded possible side effects. For statistical analysis, t-test and chi-square test were used.

Results

The study included 84 patients with LUTS/BPO, treated by 19 participating physicians (Figure 1).

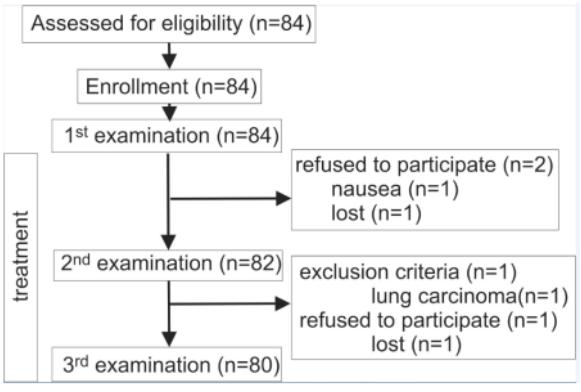

Figure 1: Flowchart of the clinical trial.

The average age was 62.3 ± 9.2 years.

Treatment was prematurely terminated by 7 patients: one stopped treatment due to undesirable events (nausea), 3 patients were excluded due to exclusion criteria (lung cancer, stenosis of the bladder and alpha blocker therapy), and 3 patients left the study for unknown reason.

After 3 and 6 months of treatment the improvement of IPSS and the quality of life was statistically significant (Table 1 and Table 2). The values of total PSA levels after 3 and 6 months of treatment did not change significantly. The "difference in average" (Table 1) and the "average difference" (Table 2) are not exactly the same, since only the patients completing the therapy (3 months or 6 months respectively) are taken into account in Table 2, and all available data is considered in Table 1.

		IPSS	QoL	Total PSA
Baseline	average	12.67	2.39	1.575
	SD	5.06	1.22	1.164
	min	4	0	0.090
	max	27	6	6.600
After 3 month therapy	average	10.27	2.04	1.468
	SD	5.02	1.15	0.892
	min	2	0	0.120
	max	30	6	4.300
After 6 month therapy	average	9.19	1.75	1.673
	SD	5.44	1.16	1.493
	min	1	0	0.180
	max	28	6	7.270
Difference in average between baseline and 3 month of therapy		-2.41	-0.35	-0.107
Difference in average between baseline and 6 month of therapy		-3.49	-0.65	0.098

Table 1: IPSS, QoL and total PSA at baseline and after 3 and 6 months of therapy. Negative values represent lowering (improvement) of signs and symptoms. SD = standard deviation.

		IPSS	QoL	Total PSA
After 3-month therapy	average difference	-2.60	-0.34	-0.118
	SD	3.23	0.98	0.365
	Min	-16	-3	-1.370
	Max	6	3	0.600
	p (t-test)	5.1×10^{-10}	5.1×10^{-3}	0.062
After 6 month therapy	average difference	-3.64	-0.58	-0.018
	SD	3.81	1.37	0.972
	Min	-12	-4	-1.250
	Max	8	5	5.150
	p (t-test)	7.0×10^{-12}	9.2×10^{-4}	0.91

Table 2: The difference in IPSS, QoL and total PSA from baseline to 3 and 6 months.

In 6 months of therapy, the proportion of patients with unsatisfactory libido significantly reduced (Table 3) from 26.5% to 13.2% (p=0.036). The trend of improvement was seen already in 3 months when 18.1% of patients had unsatisfactory libido. There was only a non-significant (p = 0.102) trend of reduction of erectile dysfunction from 36.9%, to 25.7% and to 28.9% at baseline, and after 3 and 6 months of therapy, respectively. Erectile dysfunction was strongly connected to IPSS (p = 0.004), and weakly with the quality of life (p = 0.08). Libido was not connected to any of those parameters (p > 0.25).

		Erectile dysfunction		Libido	
		present	absent	unsatisfactory	satisfactory
Baseline	number of patients	31	53	22	61
	%	36.9	63.1	26.5	73.5
After 3 month of therapy	number of patients	26	75	15	68
	%	25.7	74.3	18.1	81.9
	p (chi-square test)	0.102		0.191	
After 6 month of therapy	number of patients	22	54	10	66
	%	28.9	71.1	13.2	86.8
	p (chi-square test)	0.285		0.036	

Table 3: Erectile dysfunction and satisfaction by the libido at baseline and after therapy.

The vast majority of patients were satisfied with the therapy (Table 4) and they assessed the efficacy as good or moderate (Table 5). The physicians' assessments of effectiveness were very similar (Table 5). They strongly correlated to patient's assessments both at 3 months (Spearman Correlation = 0.776, p= 1.1×10^{-17}) and at 6 months (Spearman Correlation = 0.735, p= 4.1×10^{-15}). Both patients and physicians assessed the safety of the therapy as good in average in more than 95% of cases (Table 4).

		After 3 month of therapy		After 6 month of therapy	
		Number of patients	%	Number of patients	%
Satisfaction	yes	74	90.3	70	91.0
	no	8	9.7	7	9.0
Patient assessment of safety	bad	2	2.4	1	1.3
	moderate	1	1.2	4	5.3
	good	79	96.3	71	93.4
Physicians' assessment of safety	bad	1	1.2	0	0.0
	moderate	1	1.2	4	5.1
	good	79	97.5	74	94.9

Table 4: Satisfaction, patient's assessment of effectiveness and safety and physician's assessment of effectiveness and safety.

ssessment after 3 months		Physicians' assessment of effectiveness				
		good	modarate	bad	Total	
Patient assessment of effectiveness	good	39	2	1	42	51.%
	moderate	4	26	1	31	37.8%
	bad	1	4	4	9	11.0%
	Total	44	32	6	82	100.0%
		53.7%	39.0%	7.3%	100.0%	

Assessment after 6 months		Physicians' assessment of effectiveness				
		good	modarate	bad	Total	
Patient assessment of effectiveness	good	46	6	0	52	68.4%
	moderate	4	13	1	18	23.7%
	bad	0	3	3	6	7.9%
	Total	50	22	4	76	100 %
		65.8%	28.9%	5.3%	100%	

Table 5: Correlation of patient's and physician's assessment of effectiveness after 3 and 6 months.

After the 3 month of therapy the patients were asked how quickly the effect of the therapy appeared. In average it appeared after 4.5 weeks (median: 3 weeks, modus: 4 weeks). The 6 patients reported that the effect did not appear yet after 3 months.

Two undesirable effects were reported after 3 months of therapy (moderate nausea and light polyuria). No undesirable effect was reported after 6 months of therapy.

Discussion

The interest for the treatment with natural medicines worldwide is constantly increasing. It is estimated that 30-50% of urological patients in the United States use herbal preparations [22].

In this prospective, open, multicentric clinical trial we confirmed in population of Slovenian man, that the herbal medicinal product containing 320 mg of the extract of saw palmetto berries is efficient in reducing LUTS/BPO. The patients were enrolled by family doctors, making study design closer to the real life situation in comparison to most other studies on palmetto which were conducted by urologists. Another advantage of this study is that the therapy lasted for 6 months, compared to 2 or 3 months in most previous studies; which proves the long term safety of palmetto. As in previous reports we found significant improvement of IPSS and Quality of life, but not in the concentration of total PSA [13,14,23,24]. Furthermore we confirmed that the product is well tolerated and safe with only mild and infrequent undesirable effects. Libido was significantly improved, and for erectile dysfunction we observed a trend of improvement. This support previous study were also erectile function and ejaculatory function significantly improved [21]. On the other hand, non-herbal LUTS/BPO therapies (e.g. 5-alpha-reductase inhibitors) are known to cause Erectile Dysfunction and decreased libido. The weakness of this study is, that the erectile dysfunction was assessed only as present/not present, and there was no control group therefore we cannot exclude the influence of placebo effect.

Conclusions

In this study we confirmed that the saw palmetto extract improves the BPH symptoms: International Prostate Symptom Score (IPSS) and the quality of life. We also showed the improvement of libido during the therapy. For the effect on erectile dysfunction and libido further studies are needed before the final conclusions will be made.

Declarations

Ethics approval and consent to participate

The study was approved by the Medical Ethics Committee of the Republic of Slovenia (No. 16-234/3). The participants signed an informed consent to voluntary participate in the trial.

Consent for Publication

All authors approved the publication of this manuscript

Availability of Data and Materials

The original data is available upon request.

Competing Interests

None of the authors have any competing interests in the manuscript.

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The research was founded by the institutions where the authors are affiliated

Authors' Contributions

Both authors equally contributed to the design of the study. BT organised the enrolment of the patients and physician's examinations. SK made statistical analysis. Both authors wrote the article.

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