The Effect of Anticholinergics for Prevention of Storage Symptoms After Prostate Photovaporization

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Purpose: To evaluate the efficacy of oral anticholinergics as a preventive strategy of storage symptoms and urinary incontinence associated with the early postoperative period after Greenlight laser photovaporization of the prostate (PVP). To analyze potential variables related to the onset of these symptoms.

Materials and methods: Retrospective study of 105 patients who underwent PVP using a 180-W Greenlight laser (XPS). Patients were divided into two groups, depending on whether they were or weren´t prescribed anticholinergics when discharged (oral solifenacin 5 mg for 1 month after surgery). Differences between both groups were analyzed according to IPSS, ICIQ-SF and OABq-SF scores at 1 and 6 months. The potentially predictive variables of the symptomatology after undergoing PVP that we analyzed included age, prostate volume, PSA, IPSS, ICIQ-SF, OABq-SF, Qmax, previous use of a permanent urinary catheter, energy used, and laser application time.

Results: 58 patients in the group with anticholinergics and 47 in the group without anticholinergics were compared. No significant differences were observed between both groups in IPSS (p = .521), ICIQ-SF (p = .720) or OABq-SF (p = .851) at 1 and 6 months after surgery. Regardless of the use of anticholinergics, there was a significant score improvement between the first and second checkup in all the questionnaires: there was a significant decrease in the mean IPSS (p < .001) and the mean score of the eighth IPSS question on patient's quality of life (p = .026), ICIQ- SF (p = .010) and OAB-q related to symptoms (p = .001) as well as a significant increase in the mean OAB-q score regarding quality of life (p = .005). None of the variables analyzed showed a significant relation to the storage-symptom rate, rate of incontinence, or ICIQ-SF and OABq-SF scores.

Conclusion: The use of solifenacin 5 mg after Greenlight laser PVP is not an effective preventive treatment for storage and incontinence symptoms associated with this procedure, which seem to self-limit over time.

Keywords: anticholinergics; greenlight laser; oral anticholinergigs; prostate; storage symptoms

INTRODUCTION

180-W GreenLight (XPS) photoselective vaporization of the prostate is considered to be a safe and efficacious treatment option for lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH)[1, 2], being particularly useful for anticoagulated patients, or in patients with other comorbidities [3]. Nevertheless, compared with TURP, photovaporization of the prostate (PVP) using a greenlight laser (GL) has been associated with a higher rate of dysuria, storage symptoms, and urinary incontinence during the early months after surgery[4,5]. These irritative symptoms, which are frequent after GL PVP, have not been studied enough and have not been completely understood[6,7]. To date, no study has determined which treatment or strategy should be used to prevent the onset of these symptoms. Oral anticholinergics are a possible therapeutic option for this symptomatology, as it has been previously demonstrated for other urological procedures[8,9]; however no study on this matter has been carried out[10].

The main objective of our research was to evaluate the efficacy of oral anticholinergics as a preventive strategy of storage symptoms and urinary incontinence associated with the early postoperative period of GL PVP. As secondary objective, variables possibly related to the onset of these irritative symptoms were analyzed.

MATERIALS AND METHODS

The study is a retrospective and descriptive study with a cohort of 105 patients diagnosed with LUTS due to BPH that underwent GL PVP at our department from October 2012 to March 2016. Patients and variables measured were consecutively included in a prospective database.

Before surgery, the following measurements were collected: prostate volume by transrectal ultrasound, PSA, flowmetry (Qmax), International Prostate Symptom Score (IPSS), and scores of International Consultation on Incontinence Questionnaire-short form (ICIQ-SF) and OverActive Bladder questionnaire-short form (OABq-SF). During the procedure, the energy used and the exposure time were recorded. In the first and second checkups after surgery (at the first postoperative month

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Table 1. Preoperative characteristics of patients.

	MEAN ± SD	MEDIAN	P25-P75
Age (years)	68.75 ± 9.46	70	60-76.5
Prostate volume (cc)	64.29 ± 27.52	62	45.6-80
PSA (ng/mL)	3.33 ± 2.32	2.68	1.6-4.7
Qmax (ml/seg)	8.74 ± 3.02	9	6.9-10.7
IPSS	22.17 ± 5.55	22	19.75- 2.25
QoL IPSS	4.48 ± 1.05	4	4-5
ICIQ-SF	4.11 ± 6.35	0	0-9
OABQ- SF-sym	37 ± 22.33	31.36	22.47-60.82
OABQ- SF-QoL	70.85 ±- 15.41	70	61.55-83.87
		n(%)	
Permanent urinary catheter		33(31.4%)	
Treatment prior to surgery		Alpha-blockers 24(22.9%)	
		Combined treatment (dutasteride + tamsulosin) 80(76.2%)	
Current anticoagulant use up to surgery		17(16.2%)	
Anesthetic risk (ASA)	ASA I 9(8.7%)	ASA III 37(35.6%)	
	ASA II 53(51%)	ASA IV 5(4.8%)	

and between the sixth and ninth months) flowmetric data and scores of the three previous questionnaires were recorded. Also, it was qualitatively recorded whether patients showed storage symptoms or urinary incontinence. Thus, the presence of dysuria, urgency, or pollakiuria, regardless of their amount, reported by the patient was considered storage symptoms. Also, leakage, regardless of its amount, reported by the patient was considered urinary incontinence. At the second checkup, patient satisfaction with the procedure was assessed in a questionnaire.

Treatment prescribed to patients when discharged was retrospectively reviewed, dividing them into two groups according to whether they were prescribed oral anticholinergics (AC group), or not (nAC group). Some physicians prescribed them routinely to all patients to avoid irritative symptoms, and others didn´t, which allowed us to separate the patients into two groups, without there being any type of randomization. In all cases, the anticholinergic prescribed during the first postoperative month was solifenacin 5 mg, and the alternative was not receiving any treatment at all. The association of this event with urinary symptoms after surgery was statistically analyzed, checking whether there were differences among the mean scores of IPSS, ICIQ-SF, and OABq-SF questionnaires in postoperative checkups.

As potentially predictive pre- and intraoperative variables of storage symptoms and/or urinary incontinence after undergoing PVP, we analyzed age, prostate volume, PSA, IPSS, ICIQ-SF, OABq-SF, Qmax, previous use of a permanent urinary catheter, energy used, and laser application time.

Continuous variables were expressed as mean and standard deviation, median and 25-75 percentiles in non-parametric cases. Categorical variables were expressed through absolute and relative frequencies. The hypothesis of normality was confirmed using the Shapiro-Wilks test. Differences between treatment groups were compared using the bivariate analysis: Student's t-test for independent samples, and the Mann-Whitney U test in cases of non-normality. To analyze the potential change of outcome variables at the different measured times, we used Student's t-test for related samples or repeated measures ANOVA, and Kruskal-Wallis and Friedman tests for non-parametric cases. A p-value under .05 was considered significant. Data were analyzed using IBM SPSS Statistics 19 software.

RESULTS

The study included 105 patients. Patient characteristics are listed in **Table 1**. None of them used to take anticholinergics before surgery.

Mean Qmax and IPSS significantly improved in the series as a whole due to the procedure. There were no significant changes in ICIQ-SF and OABq-SF scores before and after surgery. The percentage of patients with storage symptoms and incontinence in the first checkup was 46.8% and 50%, respectively. The percentage of patients with storage symptoms and incontinence interestingly decreased from the first to the second checkup, although this decrease was only statistically significant for storage symptoms (**Table 2**).

Intraoperative complications were reported in only 6 patients (5.7%), which consisted of 5 cases of intraoperative bleeding and 2 perforations of the prostatic capsule. 32 patients (30.5%) reported postoperative complications: 12 patients had hematuria (11.4%), 1 (1%) required a red blood cell transfusion, 13 (13.3%) suffered from UTI, 8 (7.6%) had acute urinary retention, 6 (5.7%) developed a posterior urethral stricture,

Table 2. Changes in functional variables between the preoperative period and the postoperative checkups.

	PREOPERATIVE	1 MO	6-9 MO	*P*
Mean Qmax ± SD (ml/s)	8.4 ± 1.45	13.24 ± 2.36	15.27 ± 1.87	.048
Mean IPSS ± SD	22.89 ± 0.91	12.03 ± 0.98	9.78 ± 1.13	< .001
Mean IPSS QoL ± SD	4.45 ± 0.22	2.41 ± 0.34	2.09 ± 0.37	< .001
Mean ICIQ-SF ± SD	4.41 ± 1.61	8.23 ± 1.70	5.76 ± 1.66	.191
Mean OABq-SF-sym ± SD	37.43 ± 5.56	31.73 ± 5.92	22.92 ± 5.86	.132
Mean OABq-SF-QoL ± SD	71.94 ± 15.15	76.82 ± 20.91	83.07 ± 19.38	.125
Incontinence (% of total)	(a)	50%	40.3%	.109
Storage symptoms (% of total)	(a)	46.8%	25.8%	.007

(a) Non-collected variables during the preoperative period.

Table 3. Comparison of variables to determine the homogeneity of the groups.

	nAC (n=47, 44.8%)	AC (n=58, 55.2%)	*P*
Preoperative IPSS (mean ± SD)	22.87 ± 4.85	21.65 ± 6.04	0.428
Preoperative Qmax ml/s (mean ± SD)	8.52 ± 2.66	8.91 ± 3.28	0.661
Preoperative PSA ng/ml (mean ± SD)	3.51 ± 2.54	3.20 ± 2.15	0.527
Preoperative prostate volume cc (mean ± SD)	62.57 ± 25.75	65.6 ± 28.96	0.577
Preoperative ICIQ-SF (mean ± SD)	6.20 ± 7.68	1.78 ± 3.56	0.144
Preoperative OABq-SF-sym (mean ± SD)	44.42 ± 21.84	29.61 ± 21.43	0.232
Preoperative OABq-SF-QoL (mean ± SD)	67.70 ± 16.17	74.01 ± 14.85	0.452
Previous combined treatment (dutasteride + tamsulosin)	35(76.1%)	45(77.6%)	1
ASA II	23(50%)	30(51.7%)	0.139
Energy applied Joules (mean ± SD)	270935.48 ± 104564.79	315066 ± 123010.97	0.100
Application time min (mean ± SD)	26.20 ± 8.95	32.12 ± 12.65	0.240
Urinary catheter days (mean ± SD)	1.87 ± 0.92	1.79 ± 0.99	0.675
Hospital stay days (mean ± SD)	2.28 ± 0.19	2.31 ± 0.19	0.901
Intraoperative bleeding	2(4.3%)	3(5.2%)	1
Postoperative hematuria	4(8.5%)	8(13.8%)	0.398
Postoperative UTI	6(12.8%)	8(13.8%)	0.878
Postoperative AUR	4(8.5%)	4(6.9%)	1
Postoperative urethral stricture	3(6.4%)	3(5.2%)	1
Postoperative cell sclerosis	4(4.3%)	4(6.9%)	0.689

and another 6 (5.7%) developed bladder neck stricture. 30 patients (28.6%) had to be attended in the ER after being discharged from the hospital due to complications resulting from surgery. According to the Clavien-Dindo classification, 11 (34.4%) out of the 32 complications were grade I; 12 (37.5%), grade II; 4 (12.5%), grade IIIA; and 5 (15.6%), grade IIIB.

Regarding patient satisfaction with the procedure, most patients were very satisfied or satisfied (17.7% and 51.9%, respectively), 21.5% stated that they were not so satisfied, and 8.9% stated they were dissatisfied. 71.8% of the patients would recommend the surgery to someone.

To study homogeneity between both groups (AC vs nAC), some preoperative (Qmax, PSA, prostate volume, prior treatment, anesthetic risk, IPSS, ICIQ-SF, OABq-SF), intraoperative (energy used and laser application time) and postoperative (days of urinary catheter, hospital stay, complications) variables were compared. There were no statistically significant differences between both groups in any of these variables (**Table 3**). After the surgery, there were no statistically significant differences between both groups in mean IPSS, ICIQ-SF and OABq-SF in the checkups that follow (**Table 4**). Regardless of anticholinergic treatment, there was a significant improvement in both groups between the first and second checkups in the mean scores of all the mentioned questionnaires. As shown in the results of the questionnaires listed in **Table 4**, there was a significant decrease in the mean IPSS ($p < .001$) and the mean score of the eighth IPSS question on patient's quality of life ($p = .026$), ICIQ- SF ($p = .010$) and OAB-q related to symptoms ($p = .001$) as well as a significant increase in the mean OAB-q score regarding quality of life ($p = .005$). However, the percentage of patients that reported incontinence between the first and second checkup did not significantly change in AC group ($p = .180$) or nAC group ($p = 1$). Likewise, the number of patients who reported storage symptoms did not change significantly ($p = .057$ and $p = .125$, respectively).

There were no significant differences between both groups regarding the grade of satisfaction (55% vs 54.3% of patients were satisfied in the AC and nAC groups, respectively, $p = .909$), or in patient´s recommendation of the procedure (70.5% vs 73.5%, respectively, $p = .805$).

None of the variables studied (age, prostate volume, PSA, IPSS, ICIQ-SF, OABq-SF, maximum flow rate, the use of a permanent urinary catheter, energy used, and laser application time) showed a statistically significant relation to storage symptom and incontinence rates and mean postoperative scores of ICIQ-SF and OABq-SF.

DISCUSSION

TURP is still the gold standard technique for BPH treatment[1]. However, during recent years, new laser technologies are changing the surgical approach to this disease[11]. Among them, GL PVP has demonstrated a better perioperative profile than TURP, with a shorter hospital stay and a shorter postoperative period of uri-

Table 4. Questionnaire comparison between groups at the two postoperative checkups.

		1 month	6-9 months	*p*
IPSS	nAC	11.89 ± 6.05	8.81 ± 6.81	.521
	AC	12.65 ± 6.27	10.46 ± 8.27	
IPSS QoL	nAC	2.39 ± 1.42	1.94 ± 1.70	.520
	AC	2.43 ± 1.91	1.64 ± 1.95	
ICIQ-SF	nAC	8.94 ± 5.98	6.19 ± 6.46	.720
	AC	7,29 ± 7,63	3.71 ± 5.90	
OABQ-SF-sym	nAC	34.63 ± 23.47	21.98 ± 24.43	.851
	AC	30.93 ± 23.27	16.87 ± 20.57	
OABQ-SF-QoL	nAC	75.59 ± 22.14	84.52 ± 19.21	.894
	AC	77.03 ± 21.14	86.81 ± 19.02	

Variables expressed in mean ± SD.

nary catheterization[5].

The most important study comparing bipolar TURP with GL PVP is the GOLIATH Study, which showed that, after a two-year follow-up, GL PVP is a valid and long-lasting option for BPH treatment, with similar results to TUR in terms of efficacy and safety[12]. However, GL PVP was associated with a higher rate of storage symptoms and urinary incontinence in the early months after surgery[5]. To date, no study has determined which treatment or strategy should be used to prevent the onset of such symptomatology[10].

Since anticholinergics are a widely-used treatment for storage symptoms and for symptoms derived from an overactive bladder[1], our working group considered that they could be an adequate treatment for irritative and storage symptoms after GL PVP.

During the study of our series, we observed that the percentage of patients with storage symptoms and incontinence decreased from the first to the second checkup. Based on this, we thought it would be interesting to analyze the potential role of anticholinergics in the prevention of irritative symptomatology during the early months after surgery.

The functional results of our series of patients are equivalent to those of the GOLIATH Study, although the improvement in the flowmetry and the IPSS at 6 months after surgery is moderately smaller (Qmax 15.25ml/s vs 23.3ml/s, IPSS 9.78 vs 6.8, IPSS QoL 2.09 vs 1.5, respectively)[5]. The number of patients with incontinence at 6 months (40.3%) was slightly higher than in other trials. Only 11% of GOLIATH patients reported incontinence at 6 months. These differences are probably due to the different baseline characteristics of our patients as well as the different criterion applied to define incontinence. Thus, the mean prostate volume of our patients was 64.2cc while that of GOLIATH patients was much lower (48.6cc)[5]. The percentage of patients with irritative symptoms at 6 months was 25.8%, similar to the percentage of the GOLIATH Study and of other studies [13,14].

Only 6 patients (5.7%) suffered from intraoperative complications, fundamentally intraoperative bleeding, similar to other studies[14]. Regarding postoperative complications, patients principally reported UTI (13.3%), hematuria (11.4%), acute urinary retention (7.6%), posterior urethral stricture (5.7%), and bladder neck stricture (5.7%), and 71.9% were grades I or II on Clavien-Dinco. UTI and hematuria rates at 6 months are below those in the GOLIATH Study, although in our series, the percentage of patients taking oral anticoagulants was 4 times higher[5]. Mean hospital stay and mean postoperative time using a urinary catheter were similar [5], thus confirming the excellent perioperative profile of this technique.

It has not been established if there is an effective treatment for temporary storage symptoms after prostate surgery, and no predictors have been found either[10]. In our series of patients, none of the preoperative variables influenced either the proportion of patients with postoperative storage symptoms and/or incontinence, or the ICIQ-SF and OABq-SF scores during follow-up.

Both groups characteristically improved in IPSS, ICIQ-SF, and OABq-SF scores between the first and second checkups, regardless of whether they took anticholinergics. This finding is in line with other studies which show that this irritative syndrome is temporary and significantly improves before the end of the first postoperative year[13,14,15].

The main limitation of our research is that it is a retrospective study, which divided the patients into two different groups (AC and nAC) according to clinical criteria. This fact could lead to prescribing anticholinergics more often to the more symptomatic patients. However, the main pre-, intra- and postoperative objectifiable variables proved to be homogeneously distributed between both groups, allowing for their objective comparison. On the other hand, IPSS is a questionnaire that has not been validated to quantify storage symptoms after endoscopic prostate surgery, since it requires symptoms to be stable for at least 3 weeks[10]. Therefore, new validated questionnaires capable of quantifying such symptomatology would be necessary to disseminate and compare results between studies. In addition, the definitions of incontinence and storage and dysuria symptoms are different in every study reviewed, which could explain the existing differences in the percentages of patients who have them.

Moreover, there is no accurate urodynamic diagnosis of each patient prior to surgery. Since detrusor overactivity in patients with obstruction to bladder emptying due to BPH may reach 45%[16], this may be a potential bias in determining the percentage of incontinence and emptying symptoms that are actually secondary to GL PVP. In our study, we tried to avoid this bias by excluding those patients who had taken oral anticholinergics at some time before surgery.

Finally, in our series, only solifenacin 5mg was used as a prophylactic treatment, avoiding the use of higher doses to reduce the risk of postoperative urinary retention. However, new studies with higher doses or with other anticholinergics may be considered to test its efficacy as a preventive treatment for this irritative syndrome.

A stronger confirmation of our results would require prospective studies with a correct randomization of patients, probably comparing different therapeutic strategies.

CONCLUSIONS

This is the first study to determine that the use of low-dose oral anticholinergic drugs after PVP with a 180-W Greenlight laser (XPS) is not an effective preventive strategy for storage symptoms and incontinence associated with this procedure, which seem to self-limit over time.

Neither prostate volume, nor total energy used, nor laser application time were predictors of the risk of suffering this postoperative irritative syndrome.

CONFLICT ON INTEREST

The authors declare no conflict of interest.

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