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OVERACTIVE BLADDER (U LEE AND S ADELSTEIN, SECTION EDITORS)

Is Vaginal Laser Effective for Overactive Bladder? Results of a Systematic Review

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Abstract

Purpose of Review The aim of this review is to determine the efficacy of laser treatment in overactive bladder (OAB) syndrome in women.

Recent Findings In international literature, there are few studies focusing on OAB symptoms. The proposed treatments included thulium laser, fractional CO2 laser and Erbium:YAG laser.

Summary Although the analysed studies are not RCTs, the results show the efficacy of laser treatment in OAB symptoms, also compared to conventional medical and surgical treatments. However, these tests must be implemented with RCTs and with large patient samples.

Keywords Overactive bladder · Laser treatment · Vaginal laser · Genitourinary syndrome of menopause · Incontinence · Female

Introduction

Overactive bladder (OAB) is a symptom-based condition, defined as urinary urgency, usually accompanied by increased daytime frequency and/or nocturia, with urinary incontinence (OAB-wet) or without (OAB-dry), in the absence of urinary tract infection or other detectable disease [1]. The prevalence of OAB in adult women ranges from 8 to 42% and is particularly common in elderly people, often representing a "piece" of the genitourinary syndrome of menopause (GSM) [1]. However, the heterogeneity and underreporting of symptoms by patients make the prevalence and incidence of overactive bladder difficult to establish [2, 3]. It may cause significant disability, reduced quality of life (QoL), along with social relationship and sexual function deterioration, making it certainly a problem of social importance [4, 5].

There are different proposed approaches for treating OAB in females, mainly based on conservative or medical therapies. The conservative treatments, including lifestyle changes, pelvic floor muscle and/or bladder training, biofeedback and electro-magnetic stimulation of the pelvic floor, have had frequently poor and/or temporary results [6].

The clinical efficacy of antimuscarinic drugs has been clearly shown and are often used as first-line pharmacotherapy

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in the management of OAB. However, the choice of the drug should be individualized, considering the patient's comorbidities, concomitant medications and the pharmacologic profiles of different drugs, also considering that patients often discontinue this therapy for many reasons, including intolerable side effects [6, 7, 8•]. Some investigators have suggested that an operative cure of stress urinary incontinence (SUI) could have beneficial effects for OAB, although more than half of the patients with preoperative OAB who underwent transobturator or retropubic mid-urethral sling could not resolve the OAB-related symptoms [9–11].

Recently, some studies have reported on the application of laser technology to improve OAB symptoms, by stimulating neo-collagenesis and reactivating the extracellular matrix synthesis, which change the composition of pelvic floor structures, above all the vaginal canal and the lower urinary tract [12, 13••, 14]. Based on recent published experiences, this "regeneration" effect, involving the entire length of the urethra, seems to positively affect OAB symptoms [15••].

In this review, current evidence-based data, including recent high-quality articles in the field of the application of vaginal laser will be discussed.

Methods

Data Sources

A comprehensive literature search was performed, using PubMed/MEDLINE, Embase, Google Scholar and Cochrane Databases to identify relevant articles on use of laser in the treatment of overactive bladder, published from 2014 to 2019 (last search date 16 March2019). For the search, we used the string "(overactive AND bladder) AND (laser) NOT (prostate)".

Literature search and data extraction from the papers were performed by two independent authors (M.M. and G.C.). We selected only studies published as full-length papers in English. We reviewed the reference lists of the retrieved papers to identify and include any other relevant publications on the topic. No effort was made to identify papers published in other languages or unpublished studies. All reports related to experimental studies conducted on in vitro or animal models were excluded from the analysis. Proceedings of scientific meetings and abstracts were not considered.

Study Selection

All published studies focused on the application of laser to treat or improve symptoms associated with OAB in female patients were considered for inclusion in the study. Following the *International Urogynecological Association (IUGA)/International Continence Society (ICS)* criteria [1], we considered only literature experiences on female urinary urgency, accompanied or not by increased daytime frequency and/or nocturia, with or without urinary incontinence. In the case of papers on "genitourinary syndrome of menopause" (GSM), we included only those articles reporting data regarding the effect of laser on urological signs and symptoms, typical of OAB syndrome (urgency, frequency, nocturia, urgency incontinence). Papers reporting data exclusively on the use of laser for stress urinary incontinence (SUI), external genital symptoms or, in any case, not associated to OAB symptom treatment, were subsequently excluded. Review articles, with no specific original data and results, were not considered.

Relevant aspects of every article were recorded and commented, with particular attention to the different types of laser used in this field, the specific achieved outcomes and eventual complications that occurred. Review was therefore undertaken following the PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*) guidelines [16].

Quantitative and Qualitative Analysis

The quality of study and risk of bias were assessed according to the *"Cochrane Handbook for Systematic Reviews of Interventions" (Version 5.1.0)* [17]. This is a tool that addresses seven specific domains: namely sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and 'other issues', achieved by assigning a judgement of 'Low risk' of bias, 'High risk' of bias, or 'Unclear risk' of bias.

Results

Of the 92 articles identified using the above search strategy, title/abstract evaluation resulted in the exclusion of 73 articles that were not directly relevant or not in English. Detailed assessment of the remaining studies resulted in exclusion of a further 11 papers; therefore, 8 publications were included for the analysis (Fig. 1). To better present the achieved results, we decided to divide them into 2 specific descriptive sections based on the type of laser used: *Fractional CO_2 vaginal laser* and *Erbium:YAG vaginal laser*. Main aspects of the selected papers are explained in Table 1.

Fractional CO_2 Vaginal Laser

Intravaginal CO_2 laser has recently been proposed for the treatment of GSM, with promising data regarding beneficial effects on vaginal health and flora, sexual function and urinary incontinence [21–24]. In particular, this CO_2 laser system, equipped with a Vulvovaginal Laser Reshaping (V_2LR)

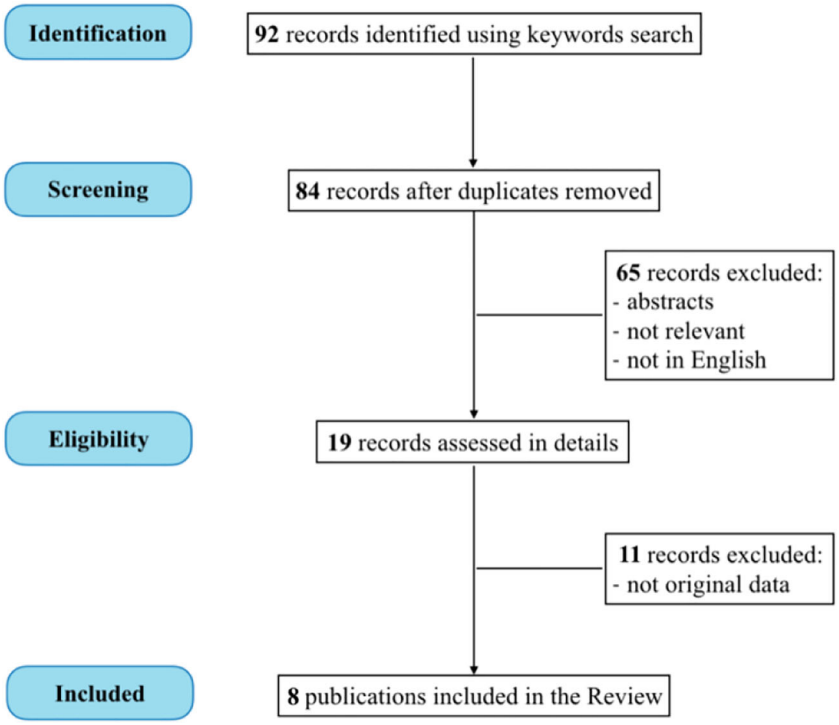

Fig. 1 PRISMA flow-diagram of studies identified in this systematic review

scanning system and appropriate probes for the vaginal area, seems to induce topical remodelling of connective tissue as well as the production of collagen and elastic fibers. A laser beam is emitted fractionally, and the CO_2 laser is focused in small spots (called *DOTs*) that are separated by healthy tissue: the beam penetrates the tissue and releases heat only when the set depth is reached [25].

Selecting the *D-Pulse* mode, the depth (*SmartStak* parameter, from 1 to 3) and the quantity of heat to be transferred to the tissue, the system allows careful control of vaporization depth and thermal action. The *D-pulse* mode consists of two parts: a constant, high-energy peak power, for rapid superficial removal of the atrophic epithelium with low water content and a lower peak power, with longer emission times that allows the energy heat to penetrate deeper into the epithelium [25]. The pulses are distributed over the vaginal wall and are spaced (*DOT spacing*) to cover the entire treatment area, using a specific probe to deliver the pulses with an energy emission at 360°. This *D-pulse* mode combined with *DOTs* treats a low percentage of the vaginal wall with high specificity achieving regeneration and protection collagen and elastic fibers of the surrounding tissues [13••, 25, 26••].

In 2016, Perino et al. published an interesting pilot study on 30 menopausal women who had complained of one or more symptoms related to VVA and who experienced symptoms of OAB [13••]. They defined OAB syndrome as all the cases in which woman complained for ≥3 months of frequency of micturition, an average ≥ 8 times per 24 h and at least 3 episodes of urgency (grade 3 or 4), with or without incontinence, during a 3-day micturition diary period at baseline. Each patient underwent a complete cycle of 3 treatment sessions, spaced over a period of at least 30 days with the fractional CO_2 vaginal laser system *(SmartXide2 V2LR, Monalisa Touch, DEKA, Florence, Italy)*. No local therapy was recommended after the laser sessions and patients were advised to avoid coital activity at least for a week following each laser application. At baseline (T0) and 30 days after the last laser application (T1), eligible patients adduced a micturition diary, which was to be completed during the 3 days preceding the visit. The authors considered any disorder, discomfort or injury, both local and general, arising in relation to the application of the vaginal fractional CO_2 laser as an adverse event. The authors observed a statistically significant improvement (expressed as median/IQR) in micturition diary (10/2.5 vs. 6/2; $p < 0.0001$), in number of urge episodes (3/1 vs. 0/1; $p < 0.0001$) and in OAB-q (18.5/4.25 vs. 8/2.25; $p < 0.0001$). Nine of the 30 patients suffered from incontinence episodes and had an improvement at T1 (3/1 vs. 1/1.5 episodes in 24 h; $p = 0.006$). No adverse events due to fractional CO_2 laser treatment occurred. In no case was it necessary to stop the procedure because of patient pain or intolerance.

In the same year, Pitsouni et al. reported the results of a prospective observational study on the effect of fractional CO_2 laser therapy on vaginal pathophysiology and GSM symptoms, enrolling 53 menopausal symptomatic women [23]. Patients were asked to complete a questionnaire reporting their symptoms (dyspareunia, genital dryness, burning,

Table 1 Characteristics and outcomes of the studies included in this review

References	Study design (n. patients)	Types of laser	Timing of treatment	Site of application	Objective	Follow-up	Main results
[14]	Prospective intervention (175)	Erbium:YAG	2–3 session (2nd session after 4–6 weeks, 3rd after 6 months)	vagina	To evaluate the role of laser in the treatment of MUI in peri- and post-menopausal women	2–6-12 months	1. At 12 months FU, ISI decreased in all women ($p < 0.001$) 2. At 12 months FU, 34% of women with MUI exhibit no UI
[13••]	Prospective observational (30)	Fractional CO_2 laser	3 sessions (every 30 days)	vagina	To evaluate the role of laser treatment in the relief of OAB symptoms in post-menopausal women	3 months	1. Improvement in the micturition diary, urge episodes and OAB-q ($p < 0.0001$)
Pitsouni [22]	Prospective observational (53)	Fractional CO_2 laser	3 sessions (every 30 days)	vagina	To assess the effect of laser on GSM symptoms	3 months	1. Dysuria, frequency, nocturia, urgency, urge incontinence, stress incontinence and scores on the ICIQ-FLUTS, ICIQ-UI SF, UDI-6 and KHQ decreased significantly ($p < 0,001$)
[12]	Prospective intervention (30)	Erbium:YAG	2 sessions (every 30 days)	vagina	To investigate the effect of laser on OAB syndrome in pre- and post-menopausal women	1–3-12 months	1. At 3 months FU, mean 1-h pad test decreased from 13.2 g (±17.7) g to 6.1 g (±11.6) ($p = 0.039$) 2. At 3 months FU, OABSS was significantly improved ($p = 0.027$) 3. The symptom scores were not sustained at 12 months FU
Gaspar [26]	Prospective intervention (29)	Erbium:YAG	2 sessions (every 3 weeks apart)	intraurethral	To assess the safety and efficacy of laser on GSM symptoms	3–6 months	1. ICIQ-SF improved 64% at 3 months and 40% at 6 months 2. 1-h pad test: decreased by 59% at 3 months and by 42% at 6 months 3. Dysuria dropped to 13% and 31% at 3 and 6 months FU 4. Urgency dropped to 23% and 47% at 3 and 6 months FU 5. Frequency dropped to 22% and 43% at 3 and 6 months FU
[18]	Prospective intervention (150)	Erbium:YAG	3 sessions (alternate months)	vagina	To compare the effects of TVT, TOT sling and laser therapy in the treatment of MUI	12 months	1. 1-h pad test improved in all 3 groups ($p < 0.001$) after treatment 2. OABSS: only patients of laser therapy group showed significant improvement ($p < 0.001$) after treatment
[18, 19••]	Prospective intervention (150)	Erbium:YAG	3 sessions (every 30 days)	vagina	To compare the effects of anticholinergics and β3-adrenoceptor agonists with laser, in the treatment of OAB in post-menopausal women	12 months	1. OABSS significantly improved compared with the pre-treatment scores in all groups: frequent urination ($p < 0.001$), nocturia ($p < 0.001$), urinary urgency ($p < 0.001$) and urgency urinary incontinence ($p < 0.001$).
[20]	Prospective (60)	Fractional CO_2 laser	3 sessions (every 30 days)	vagina	To assess the efficacy of laser in the treatment of GSM	1–4 months	1. Urinary urgency, frequency and nocturia improvement, evaluated by the VAS score (100%)

itching, dysuria, urinary frequency, urgency), followed by a 10-cm Visual Analogue Scale (VAS) of the severity of each symptom. Participants of the study protocol received intravaginal therapy once a month for 3 months, with CO_2 laser system *(SmartXide2 V2LR, Monalisa Touch, DEKA, Florence, Italy)*. The efficacy of the CO_2 laser on lower urinary tract symptoms (LUTS) was measured using the International Consultation on Incontinence Questionnaires (ICIQ) modules, at baseline and 4-weeks after the last laser therapy (12-week follow-up): ICIQ-Female Urinary Tract Symptoms (ICIQ-FLUTS Filling Domain) and ICIQ-Urinary Incontinence Short Form (ICIQ-UI SF); patients also completed the Urogenital Distress Inventory (UDI-6), and the King's Health Questionnaire (KHQ). Satisfaction of the treatment was assessed with the Patients Global Impression of Improvement (PGI-I) at 12-weeks' follow-up.

LUTS were improved significantly as reflected by the significant reduction of the scores of ICIQ-FLUTS, UDI-6, ICIQ-UI SF and KHQ. At baseline, 40% (21/53), 34% (18/53), 23% (12/53) and 4% (2/53) of the participants had urinary frequency of 1–6, 7–8, 9–10 and ≥ 13 times a day, respectively. At the 12-weeks' follow-up, 47% (25/53), 47% (25/53), 4% (2/53) and 1% (1/53) passed urine during the day 1–6, 7–8, 9–10, and 11–12 times, respectively. The improvement of KHQ questionnaire was >5 points in all participants ($p < 0.001$).

Another fractional CO_2 laser-based study was published in 2019 by Tovar-Huamani et al. [20]. Authors enrolled 60 women in amenorrhea for at least a year, with symptoms of VVA. The patients received 3 sessions of CO_2 laser in a fractional manner at an interval of 30 days. All the procedures were performed after topical analgesia. After treatment, no additional estrogenic medication was prescribed, nor analgesic, only sexual and exercise restriction for 1 week. The primary outcome of the study was VAS change in 10 categories of symptoms commonly associated with VVA; secondary outcomes included several aspects, such as OAB symptoms and, in particular, urinary urgency was assessed using the USMEX Spanish Overactive Bladder Questionnaire-Short Form (Spanish OAB qSF), a specific instrument to evaluate symptoms and QoL in patients with OAB. Measurements were taken at baseline, 1 month after treatment and 4 months after the last session.

There were improvements in vaginal symptoms, such as vaginal dryness and dyspareunia, after the first month of treatment above 60% according to the VAS, reaching almost 100% at the end of the treatment cycle ($p < 0.001$). Hyperactive hypoestrogenic bladder symptom improvements were shown, evaluated by the VAS, basically focused on urinary urgency, frequency and nocturia, reaching 100% finished treatment ($p < 0.001$).

Erbium:YAG Laser

The Erbium:YAG (Er:YAG) laser was initially introduced in gynaecological treatments for treating vaginal tissue. It has a wavelength of 2940 nm and a non-ablative deep thermal effect on the vaginal epithelium, using a pulse-controlled pattern: using a SMOOTH™ mode, the laser has low fluence (defined as optical energy per unit area) and long-shaped erbium pulses that allow a controlled deep thermal effect, without ablation [26••]. The low fluence pulses sequences of the Er:YAG laser are absorbed by the tissue surface and cause transient heat increase of the mucosa, inducing restructuring of the lamina propria, microvascularization and new vessel formation, improving VVA symptoms [28, 29]. Recently, several studies have tried to demonstrate the effectiveness of Er:YAG laser also in urinary symptoms due to menopause or to urinary incontinence (UI).

The first study was published by Ogrinc et al in 2015 [14]. In their prospective, single centre, non-randomized study, 175 women with clinically confirmed UI were enrolled and divided into 2 groups according to type of incontinence: stress UI (SUI) and mixed UI (MUI), respectively. Each woman filled out the standard ICIQ-SF to evaluate the severity of incontinence, expressed in terms of incontinence severity index (ISI): consequently, patients were categorized into four grades of UI, which were mild, moderate, severe, and very severe. Then, patients received 2 or 3 sessions of laser treatment. Follow-up was performed at 2, 6, and 12 months after complete treatment. At one-year-follow-up, ISI significantly decreased in all women ($p < 0.001$). Age did not affect the outcome of UI treatment. On the other hand, the effectiveness of the treatment varied according to the type of incontinence: in patients with SUI, UI significantly improved in 77% of the cases (88 patients) while the patients diagnosed with MUI only improved in 34% of the cases (20 patients). Patients reported no significant side effects after the therapy. In general, they were all satisfied with the procedure and experienced no or only mild discomfort and/or pain during the procedures.

In 2017, a study by Lin et al. enrolling 30 women with OAB symptoms and UI was published, treated with Er:YAG laser [12]. All included patients received evaluations including Overactive Bladder Symptom Score (OABSS) questionnaire for assessment of OAB, at baseline, at 3 months and at 12 months' post-laser follow-up. Treatment consisted of two sessions, 4 weeks apart using the Er:YAG laser. Outpatient follow-ups were performed at 1 week, 1 month and 3 months after first treatment. OABSS symptom scores were significantly improved at 3 months' follow-up ($p = 0.027$), especially in the symptom of urinary frequency (Q1 $p = 0.001$). However, the symptom scores were not sustained at 12 months follow-up ($p = 0.576$). During laser therapy, most patients described mild but tolerable pain and burning sensation. The average VAS pain score during laser treatment was 4.2 ± 2.0.

After laser therapy, only 4 patients (13.3%) found increased vaginal discharge or vaginal spotting and these side effects persisted for several days. No major adverse effects were noticed.

A prospective pilot study of Gaspar et al. on the use of Er:YAG in 29 postmenopausal women with a diagnosis of GSM and urodynamic diagnosis of overactive detrusor was published in 2018 [28]. All patients were treated with 2 Er:YAG laser treatment sessions, 3 weeks apart. Follow-up evaluations were scheduled 3 and 6 months after the second laser treatment. The primary clinical outcome measures were subjective assessment of the severity of urinary symptoms of GSM using the VAS scale. The severity of patient's incontinence was assessed using ICIQ-UI SF and the 1-h pad test, which was done without retrograde filling; improvement rates higher than 50% of the baseline value were considered a clinically meaningful improvement. The average baseline VAS values for dysuria, urgency, and frequency were 66, 58, and 49, respectively. At the 3-month follow-up, VAS values were 8.3, 13, and 11, respectively and at 6 months these values were 20, 28, and 21, respectively. There is a statistically significant difference ($p < 0.0005$) between values at 3 months as well as at 6-month follow-up appointments compared to baseline values. After 3 months, dysuria improved in all of the patients, urgency improved in 93% of patients and frequency improved in 97% of patients. Average improvement rates in dysuria, frequency, and urgency at the 3-month follow-up were 87%, 79%, and 77%, respectively. At the 6-month follow-up average values were 64%, 44%, and 52%, respectively. The ICIQ-UI scores and 1-h pad test revealed a clinically meaningful improvement in 79% and 90% of patients at 3-month follow-up, respectively. After 6 months, clinically meaningful improvement was observed in 45% and 38% of patients. Observed side effects were mild and transient and mostly resolved without intervention in less than 24 h.

In 2018, in the first of two studies, Okui et al. enrolled 150 patients with SUI aged 20–65 years dividing them into 3 treatment arms: 50 patients who underwent the TVT procedure (TVT group), 50 who underwent the TOT procedure (TOT group), and 50 who underwent the Er:YAG laser therapy (laser therapy group) [18]. Laser irradiation was performed 3 times every alternate month. Before and 12 months after treatment, subjects underwent a 1-h pad test, International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF) and overactive bladder symptom score (OABSS). Although the mean values of the 1-h pad test significantly improved in all three groups ($p < 0.001$) after treatment, as well as the ICIQ-SF score ($p < 0.001$), the OABSS, as indicator of OAB function for MUI patients, showed great variation among the population: only patients in the laser therapy group showed significant improvement ($p < 0.001$) after treatment. In the laser therapy group, no adverse effects were observed. The following year a second study was published by Okui et al. on a female population aged 60–69 years who presented with symptoms of OAB [19••]. The diagnosis was determined according to the Japanese guidelines requiring ≥2 points for question Q3 indicating urinary urgency (how often do you have a sudden desire to urinate, which is difficult to defer?) of the OAB symptom score (OABSS); in addition, the Vaginal Health Index Scale (VHIS) was used. The subjects were divided into 3 arms: vaginal Er:YAG laser (VEL) ($n = 50$), anticholinergic (n = 50) and β3-adrenoceptor agonist (β3) (n = 50). In the anticholinergic and β3 groups, 4 mg fesoterodine and 25 mg mirabegron were administered once daily after breakfast, respectively. In the VEL group, laser energy was applied once per month for 3 months. Follow-up observation was performed for 1 year, with day 0 being the day of first administration of treatment. The OABSS questionnaire was completed during the initial examination and at 1 year following treatment initiation. Overall, OABSS after treatment significantly improved compared with the pre-treatment scores in all groups ($p < 0.001$). In the VEL, anticholinergic, and β3 groups, the scores improved from 8.16 ± 2.86 to 3.76 ± 3.30, 7.96 ± 2.49 to 4.16 ± 2.59, and 8.30 ± 2.88 to 5.25 ± 3.08, respectively. Regarding VHIS following treatment, a significant improvement was observed only in the VEL group ($p < 0.001$). Considering safety, in the VEL group, there was no occurrence of adverse events.

Risk of Bias

Overall, the selection bias was at high risk (in 6 studies) or uncertain (in the remaining 2 studies), since in no case was there a negative control group. In addition, the performance and detection biases were evaluated at high (in 5 studies), uncertain (in 2 studies) and low risk (in 1 study), as in most studies it was not specified whether the staff and patients were blinded. Instead the attrition bias and the reporting bias were overall low risk, except in one case only (high risk) (Fig. 2B).

Discussion

Gynaecologists and plastic surgeons pioneered the application of lasers in medicine and surgery almost 5 decades ago, initially exclusively used for the ablation of cervical and vaginal diseased tissue in the gynaecological field. In successive years, technological developments triggered several publications, assessing the efficacy of laser used intermittently (known as fractional or pulsed use) on the vaginal wall in reversing natural aging processes [30]. Studies have shown that a fractional laser system can irradiate deeper layers of the vagina stimulating the reactivation of the extracellular matrix and collagen synthesis proliferation, which leads to the recovery of vaginal tissue trophism with minimal trauma to superficial areas [25, 31, 32•]. Consequently, all the symptoms

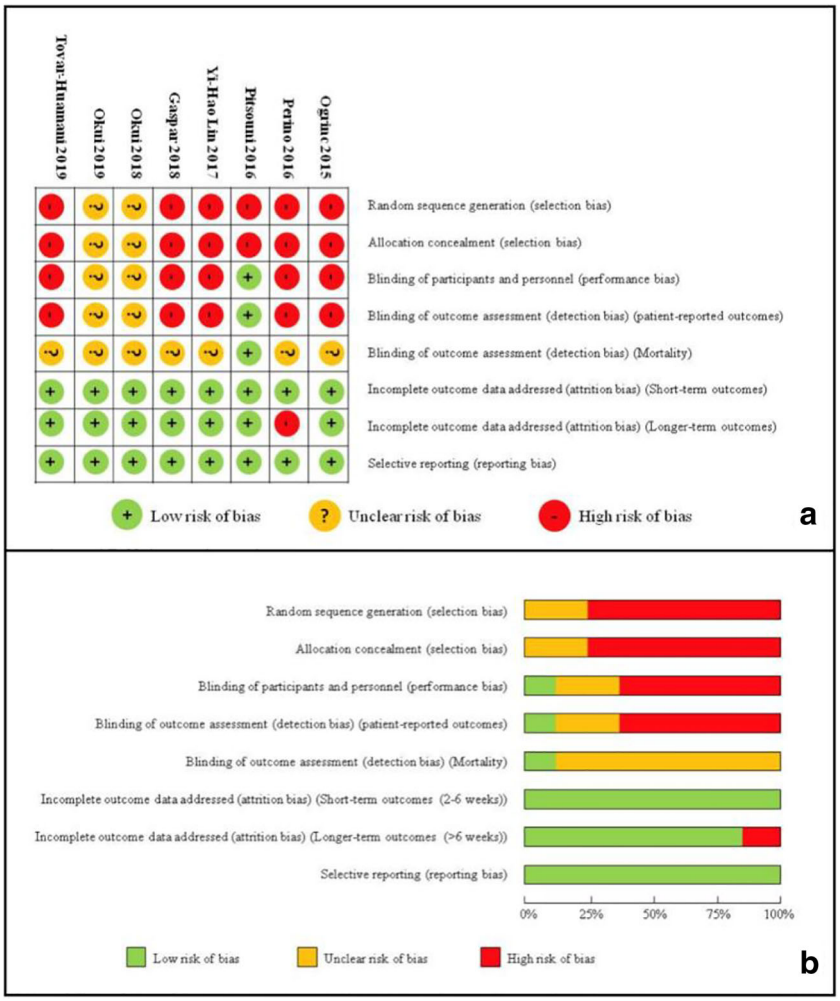

Fig. 2 A-B Assessment of risk of bias. (A) Summary of risk of bias for each trial. +, low risk of bias; −, high risk of bias;?, unclear risk of bias. (B) Risk of bias graph including each risk of bias item presented as a percentage across all included studies

of vulvovaginal atrophy or, according to the most recent classification, GSM, secondary to a clinical state of hypoestrogenism in peri- and post-menopausal women, are significantly improved [31, 32•, 33, 34]. GSM include vulvovaginal symptoms such as vaginal dryness, vaginal burning, vaginal itching, dyspareunia, and urologic symptoms, like OAB, incontinence, haematuria, and recurrent urinary tract infections [34].

With these premises, it is evident that most published data on the use of vaginal laser are based, to date, on populations of symptomatic menopausal female, even if symptoms of GSM can also affect women who have undergone premature menopause while being treated for medical conditions such as breast cancer or endometriosis. In fact, the possible role of laser in the treatment for OAB arises from the experience of a concomitant relevant improvement in urinary symptoms in patients who had first been submitted to laser therapy for GSM disorders.

The early approach to the OAB problem involves conservative measures such as dietary controls, fluid modification and pelvic floor muscle rehabilitation, but the results are frequently poor; antimuscarinic agents are used as first-line pharmacotherapy with well-documented effectiveness in clinical literature. However, patients often discontinue this therapy for many reasons including intolerable side effects or/and lack of sufficient symptom relief [35, 36]. Regarding recent therapeutic options, such as mirabegron and intravesical botulinum toxin, controlled trial data on benefits and safety are still lacking [13••, 37–39]. Indeed, urinary symptoms related to GSM are usually managed indirectly with the use of vaginal hormonal therapy, which have a loco-regional effect, resulting in improved trophism of the vaginal mucosa as well as urethral mucosa: it is known that the thickness of the urethral mucosa and the vascularization of the submucosa confer its sealing properties and then, improving urethral trophism, it improves the continence [40]. Although the mechanism of continence has not yet been fully clarified, the phenomenon on OAB symptoms related to GSM seems to start from the anatomical characteristics of the urogenital tissue, considering that urogenital organs are highly sensitive to the influence of oestrogen (oestrogen receptors have been found in the urethra and bladder trigone, as well as in the round ligaments and

levator ani muscles) and, as occurs in vaginal tissue, the progressive decline of oestrogen during the menopause produces atrophy of the urethral and bladder mucosa, with relative symptoms [41, 42]. Based on these considerations, it is possible to presume that the "regeneration" effect of the vaginal laser application, also involving the lower urinary tract, produces the reported improvements of urogenital aging symptoms, first of all OAB disorders.

Our review on this topic showed that only two types of lasers have been most thoroughly investigated for the treatment of OAB and/or urinary symptoms of GSM: fractional CO2 vaginal laser and vaginal erbium laser (non-ablative, solid-state erbium in yttrium aluminium-garnet crystal - Er:YAG laser). Only 8 papers were included and analysed, and in particular 3 articles reported on the use of CO2 vaginal laser and the remaining 5 on the use of Er:YAG laser (vaginal application in all cases, with the exception of one paper based on "intraurethral" use).

Our results confirmed that, to date, there are minimal published data on the use of lasers specifically for the improvement of OAB symptoms, despite improvements in vulvovaginal atrophy symptoms having been widely assessed [13••, 24, 26••, 31]. In particular, no well-controlled study or RCTs were present and all the interventions were performed on small sample sizes. Thus, long-term evaluations are needed, mainly to understand the mechanisms of laser effects on urogenital tissues and define the potentialities of this approach. In this sense, it would be interesting to study the long-term outcomes also on patients submitted to previous vaginal surgery and "cancer survivor" patients.

Published studies did not cite any experiences of serious adverse events related to vaginal laser use. However, as reiterated by the FDA (US Food and Drug Administration), there are few reports of adverse events in literature and hence no full reassurances can be taken from them. Additional data from more rigorous clinical trials is clearly needed to further assess safety. The published study included in this review suggested that vaginal lasers can be defined an emerging option for OAB symptoms related to GSM, with encouraging preliminary results on the topic. In fact, the majority of data were based on menopausal women suffering of a variety of symptoms associated with physical changes of the vulva, vagina, and lower urinary tract, related with oestrogen deficiency. At the present time, there are insufficient data to support the promotion of this approach for the treatment of exclusively OAB syndrome, with or without incontinence.

Conclusions

The use of vaginal laser for GSM is an encouraging addition to gynaecologic strategies to treat a condition that is an important health-care problem, affecting a large percentage of the female population. It could also be a possibility for women with GSM who have contraindications to hormonal therapy, such as breast cancer. Further larger, long-term and well-controlled studies are required to explore the use of vaginal laser in comparison with different therapeutic options, in order to offer a procedure as an alternative or in association with proven therapies, as a new safe and effective option to treat GSM symptoms and/or OAB in female population. The hope is better management of these patients by offering a "tailored-made" solution, with critical counselling comprehensively regarding their options.

Compliance with Ethical Standards

Conflict of Interest Gloria Calagna, Marianna Maranto, Ognibene Emanuela, Salvatore Polito, Pasquale De Franciscis, Roberta Granese and Gaspare Cucinella declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

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