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REVIEW ARTICLE

Impact of intravesical onabotulinumtoxinA (Botox) on sexual function in patients with overactive bladder syndrome: a systematic review and meta-analysis

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Abstract

Introduction and hypothesis The association between overactive bladder (OAB) syndrome and sexual dysfunction is well documented. Intra-detrusor onabotulinumtoxinA (Botox) has proven to be effective treatment for OAB syndrome. Our aim was to examine the impact of intravesical Botox injection on sexual function in patients with OAB, by systematically reviewing the literature.

Methods We reviewed the literature for studies that reported a change in sexual function after Botox treatment in patients suffering from OAB. This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement using pre-agreed keywords, from database inception to December 2020. Statistical analyses were performed using Review Manager (RevMan; v.5.4).

Results Initial results yielded 455 citations. Seven articles met our inclusion criteria. One article was double-reported, leaving 6 studies in the systematic review. Three observational before-and-after studies used the Female Sexual Function Index (FSFI) with sufficient information, and therefore were included in our meta-analysis. The pooled number of participants in all studies was 119 patients. In the meta-analysis, there was significant improvement in the following domains of the FSFI after Botox injection; desire (mean difference (MD) −0.51, $p=0.02$), arousal (MD −0.86, $p=0.02$), lubrication (MD −0.57, $p=0.03$), orgasm (MD −0.65, $p=0.0003$) and satisfaction (MD −0.46, $p=0.05$). Pain was the only domain that did not show improvement (MD −0.07, $p=0.79$). The total FSFI score was reported in 88 patients (two studies) showing significant improvement (MD −0.77, $p=0.006$).

Conclusions We report a systematic review of the effect of Botox treatment on sexual function in patients with OAB. Although studies are small, the results indicate a positive effect in patients with OAB.

Keywords OnabotulinumtoxinA · Overactive bladder · Urgency · Urge incontinence · Sexual function · Sexual dysfunction

Introduction

Overactive bladder (OAB) syndrome, defined by the International Continence Society (ICS) as "urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection (UTI) or other obvious pathology" [1]. It is one of the most prevalent problems in women and is estimated to affect around 11.8% of the population [2]. Although this prevalent condition is not life threatening, it remains a debilitating disease that has a vast impact on patients' quality of life and self-esteem [3, 4]. OAB has a profound unfavourable impact on quality of life including adverse consequences on the social, psychological, emotional and sexual aspects of a patient's life.

Data from this review previously constituted an oral presentation at the BSUG Research Urogynaecology Society meeting held in London on 9 November 2018 and as an iPoster at the RCOG World Congress held in London on 17–19 June 2019

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The association between OAB syndrome and sexual dysfunction is well documented in the literature, with several studies reporting significantly higher incidence of sexual dysfunction among women with OAB syndrome [5–7]. These studies reported reduced sexual function scores in OAB female patients compared with age-matched healthy controls [5]. Similarly, Patel et al. showed that, among 78 women with OAB, around 25% have reported some type of sexual dysfunction [6]. Furthermore, a study of 112 OAB female patients reported sexual dysfunction in 47% of OAB patients, of whom 47% suffered from sexual pain, 34% had reduced sexual desire, 25% reported arousal disorders, 25% had reduced lubrication, and 22% reported orgasmic deficiency [7].

The negative impact of OAB on sexual function is thought to be mediated through coital incontinence and body image [8]. Intra-detrusor onabotulinumtoxinA (Botox) injection is a minimally invasive procedure that has proven to be an effective treatment for OAB syndrome [9]. Nonetheless, the relationship between intra-detrusor Botox injection in female OAB patients and sexual health has only received attention lately. Therefore, the aim of the present study is to elucidate the impact of intra-vesical Botox injection on sexual function in female patients with OAB, by performing a systematic review of the literature and pooling relevant data when appropriate.

Materials and methods

As this is secondary research, ethical approval was deemed unnecessary. We conducted our review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [10].

Search strategy

We performed a literature search of the Cochrane central register of controlled trials, MEDLINE, Embase, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and the World Health Organisation-recognised, publicly registered trial databases, from database inception to December 2020. For our search, we used pre-agreed medical subject headings (MeSH terms) and free text search terms. The terms used in the search were: "Botox", "OnabotulinumtoxinA", "Onabotulinumtoxin A", "BOTA", "overactive bladder", "OAB", "urge incontinence", "urgency", "sexual function", "female sexual function", "sexual dysfunction" and "female sexual dysfunction". The search terms were used in single searches and in combination. No limitations were imposed on our search findings. All studies were published in peer-reviewed journals.

Two authors (SS/AK) performed the literature search independently and consensus was sought afterwards. Any conflict of opinions was resolved by a third deciding vote.

Study selection criteria

From our search results, we screened the titles of the studies, abstracts and papers, and we included the studies with the following criteria.

Population

Adult females suffering from overactive bladder syndrome (OAB) as defined by the International Continence Society (ICS). Patients were included despite the cause of OAB (i.e. neurogenic or idiopathic). A urodynamic diagnosis of detrusor overactivity was not mandatory.

Intervention

OnabotulinumtoxinA (Botox) injection into the bladder wall as treatment for OAB.

Comparator

We included studies that compared sexual function before and after OnabotulinumtoxinA (Botox) injection into the bladder in patients with OAB or studies that compared it with a control group.

Outcome

The outcome was sexual function as assessed by a validated patient-reported outcome tool.

We included all studies that met the inclusion criteria specified in the systematic review. Studies were excluded if no validated patient-reported outcome tool was used. Case reports, case series and conference abstracts were not included. Studies that only reported change in sexual function but did not report on sexual function scores before and after intervention were excluded. Studies with sufficient data were included in the meta-analysis. Authors were contacted by e-mail if there were insufficient study data and if no reply was received by the second contact, the study was excluded from the analysis.

Data extraction and risk of bias assessment

For all continuous outcomes, we extracted means, standard deviations, *p* values and sample sizes for the outcomes measure. Two independent reviewers (SS/AK) extracted the data and consensus was used to resolve any disagreement.

Where necessary, a third deciding vote was used (GJW/PB) if consensus was not reached.

In the cohort of non-randomised studies, risk of bias (ROB) was assessed using the "Risk of Bias in Non-randomised Studies of Interventions tool" (ROBINS-I) [11]. The ROBINS-I tool is composed of seven domains to assess bias due to confounding, selection of participants, classification of interventions, departures from intended interventions, missing data, measurement of outcomes and selection of the reported result. The risk of bias is then categorised as: low risk, moderate risk, serious risk, critical risk, or no information.

For the randomised controlled studies included in the meta-analysis, ROB was assessed using the "Revised Cochrane risk-of-bias tool for randomized trials" (RoB 2) [12]. The RoB 2 tool is composed of five domains to assess bias arising from the randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome, or bias in the selection of the reported result. The risk of bias is then categorised as low risk, some concerns or high risk.

Statistical analysis

Statistical analyses were performed using Review Manager (RevMan; version 5.4; The Nordic Cochrane Centre, Copenhagen, Denmark). We tested the heterogeneity of the results with quantity I^2 statistics. $I^2 \geq 50\%$ indicated a significant level of heterogeneity and random effects models were used to pool data from different studies.

Results

Study selection process

Figure 1 shows the PRISMA flow diagram for the identification, selection and inclusion/exclusion of studies in our review. Initial search results yielded 455 citations. A total of 321 records were screened after removal of duplicates. After screening of titles and abstracts, 7 papers required review of the full text for eligibility.

Of the 7 studies that met the eligibility criteria for inclusion, two of the studies were by Giannantoni et al. [13, 14], where we suspected that the same cohort of patients had been included in the analysis of both papers. Despite our attempts to contact the corresponding author, we were unable to obtain additional data. Therefore, to avoid duplication of results, we decided to exclude the paper by Giannantoni et al. published in 2017 [13] as it did not include the 3-monthly follow-up data, unlike the other paper, which did [14].

Systematic review

The characteristics of the six studies included in the systematic review are demonstrated in Table 1. Three studies were double-blinded randomised placebo-controlled trials that assessed the impact of Botox injections on the quality of life of patients with OAB in general rather than the patients' sexual function in particular [15–17]. Therefore, these studies used the King's Health Questionnaire (KHQ). The KHQ is a validated quality of life questionnaire that uses multiple domains to assess the impact of OAB on women's quality of life. One of these domains is "personal relationships", which is focused on the patient's sexual function. Therefore, these studies were included in the review but could not be included in the meta-analysis.

These three double-blinded randomised placebo-controlled trials had a pooled number of participants of 611 sexually active patients with OAB who received 100 units of Botox injection. All patients in the treatment and control arm completed the KHQ questionnaire pre-treatment and at the 3-month follow-up appointment. Two studies – with a pooled number of participants of 557 – reported significant improvement in the "personal relationships" domain compared with the control group [15, 16]. One smaller RCT by Fowler et al. did not report the data of the "personal relationships" domain but reported significant improvement of the overall score of the KHQ compared with the control group [17].

The other three studies included in the systemic review were observational before-and-after studies that assessed sexual function in OAB patients before and after Botox treatment using the Female Sexual Function Questionnaire (FSFI), and were included in our meta-analysis [14, 18, 19]. All three studies assessed the effect of 100 IU of Botox injection on sexual function 3 months post-treatment and reported improvement in the overall FSFI scores after Botox treatment.

Meta-analysis

Three studies were prospective observational studies that had improvement in sexual function among patients with OAB as their primary outcome; therefore, they used the FSFI [14, 18, 19]. The FSFI is a validated 19-item questionnaire that assesses various domains of sexual functioning [20]. All three studies were included in our meta-analysis [14, 18, 19].

The pooled number of participants in these three studies was 119 patients. All patients were sexually active with a confirmed OAB diagnosis. All patients received 100 units of Botox injections and completed the FSFI questionnaire pre-treatment and at the 3-month follow-up appointment.

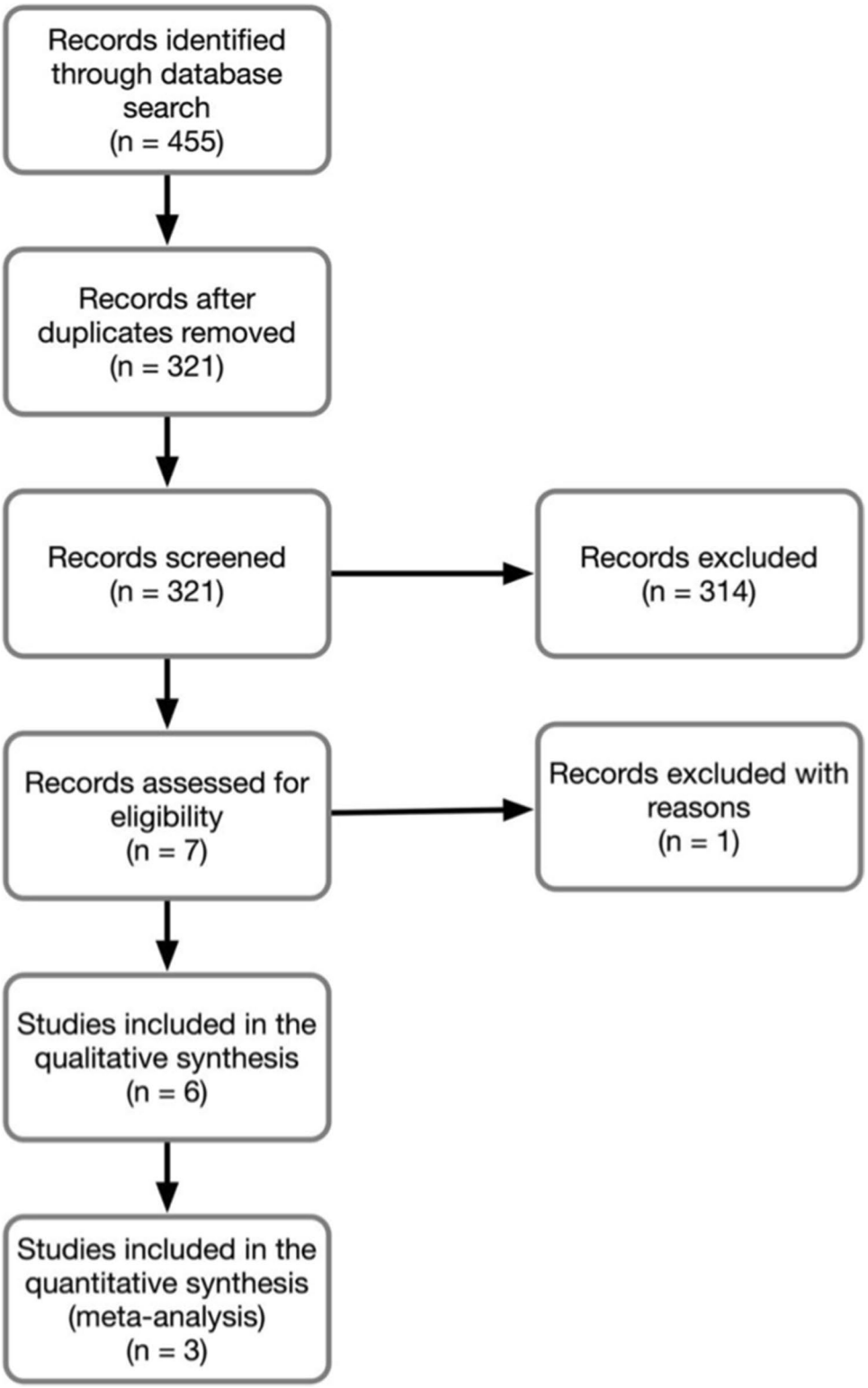

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of the study selection process for the systematic review and meta-analysis

Figures 2, 3, 4, 5, 6, 7 and 8 demonstrate the forest plots showing the meta-analysis of the results reported in all the domains of the FSFI after 100 units of Botox injection in patients with OAB. Significant improvement was reported in the following domains: desire (MD −0.51, 95% CI −0.93, −0.09, $p = 0.02$), arousal (MD −0.86, 95% CI −1.64, −0.08, $p = 0.02$), lubrication (MD −0.57, 95% CI −1.09, −0.05, $p = 0.03$) and orgasm (MD −0.65, 95% CI −1.00, −0.30, $p = 0.0003$). There was a trend towards improvement in the satisfaction domain (MD −0.46, 95% CI −0.92, 0.00,

Table 1 Summary of the studies included in the systemic review and meta-analysis

Study	Type of study	Number[b]	Control (number[b])	Assessment tool[d]	Impact on sexual function	*p* value
Balzarro et al. 2018 [18][a]	Prospective observational (before-and-after)	32	N/A	FSFI	Significant improvement	0.0008
Miotla et al. 2017 [19][a]	Prospective observational (before-and-after)	56	Healthy[c]controls	FSFI	Significant improvement	<0.001
Giannantoni et al. 2015 [14] [a]	Prospective observational (before-and-after)	31	N/A	FSFI	Significant improvement	<0.0001
Nitti et al. 2013 [15]	RCT	280	Placebo(277)	KHQ	Significant improvement	<0.001
Chapple et al. 2013 [16]	RCT	277	Placebo(271)	KHQ	Significant improvement	<0.001
Fowler et al. 2012 [17]	RCT	54	Placebo(44)	KHQ	Improvement in sexual function domains not reported separately[e]	

N/A not available

[a]Studied included in the meta-analysis

[b]Number of participants receiving Botox injection and completing follow-up on the reported domains

[c]Baseline line characteristics compared with healthy controls (no control arm in the study)

[d]Assessment tools used to assess sexual function outcome: *FSFI* female sexual function index, *KHQ* King's Health Questionnaire

[e]Study reported significant overall improvement on the KHQ (*p* value: <0.05), but did not report the improvement in individual domains

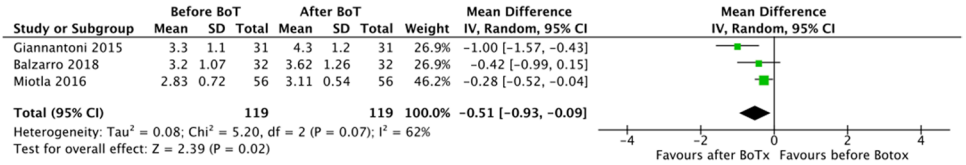

Fig. 2 Forest plot of the impact of Botox on the "desire" domain

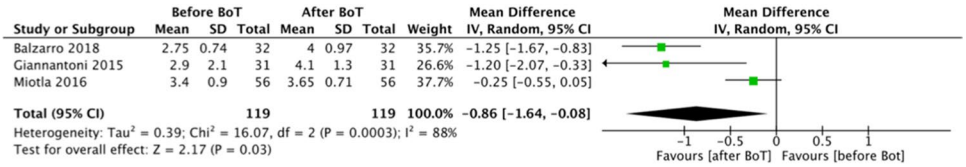

Fig. 3 Forest plot of the impact of Botox on the "arousal" domain

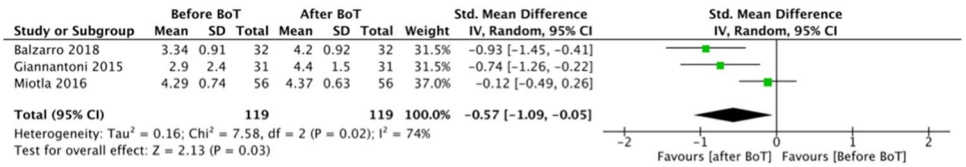

Fig. 4 Forest plot of the impact of Botox on the "lubrication" domain

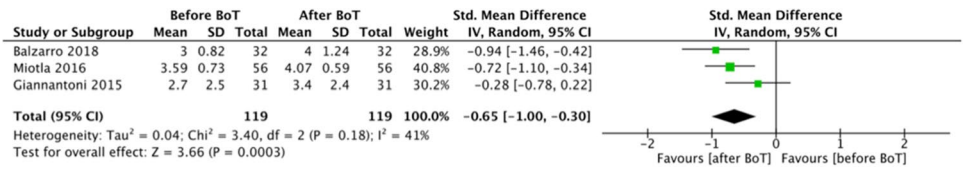

Fig. 5 Forest plot of the impact of Botox on the "orgasm" domain

$p = 0.05$). Pain was the only domain that did not show significant improvement (MD −0.07, CI [−0.57, 0.44], $p = 0.79$).

The total FSFI score was reported in only two studies with a total of 88 patients who showed significant overall improvement in sexual function after Botox injection (MD −0.77, 05% CI −1.31, −0.22, $p = 0.006$) [18, 19]. The third study by Giannantoni et al. reported "significant

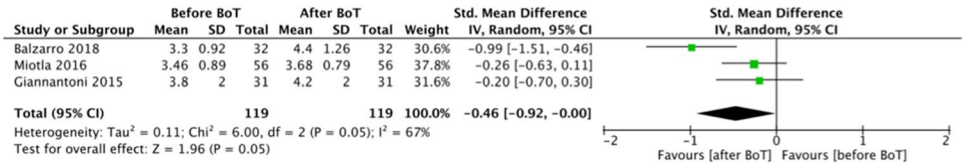

Fig. 6 Forest plot of the impact of Botox on the "satisfaction" domain

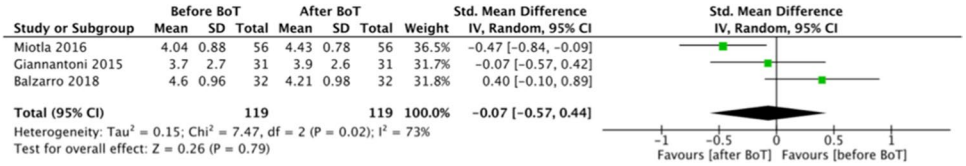

Fig. 7 Forest plot of the impact of Botox on the "pain" domain

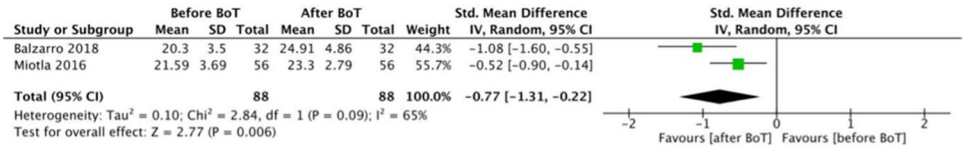

Fig. 8 Forest plot of the impact of Botox on the "overall FSFI score"

Table 2 Summary of the ROBINS-I risk of bias assessment of the studies included in the meta-analysis

Type of bias	Giannantoni et al. 2015 [14]	Balzarro et al. 2018 [18]	Miotla et al. 2017 [19]
Confounding factors	Serious	Serious	Moderate
Participants selection	Low	Low	Low
Interventions classification	Low	Low	Low
Unintended deviation from intervention	Low	Low	Low
Missing Data	Low	Low	Low
Outcome measure	Moderate	Moderate	Moderate
Reported results	Low	Low	Low
Overall risk of bias	Moderate	Moderate	Moderate

Table 3 Summary of the revised RoB 2 risk of bias assessment of the studies included in the systematic review

Type of bias	Nitti et al. 2013 [15]	Chapple et al. 2013 [16]	Fowler et al. 2012 [17]
Randomisation Process	Low	Low	Low
Deviations from intended interventions	Low	Low	Low
Missing outcome data	Low	Low	Some concerns
Measurement of the outcome	Some concerns	Some concerns	Some concerns
Selection of the reported result	Low	Low	Low
Overall risk of bias	Some concerns	Some concerns	Some concerns

improvement" in the overall FSFI score, but the data were not reported in the paper [14].

The overall risk of bias judgement for the non-randomised studies was considered to be "moderate risk of bias" on the ROBINS-I tool, as shown in Table 2. This means that "the studies provide sound evidence for a non-randomised study but cannot be considered comparable to a well-performed randomised trial" [11]. The overall risk of bias judgement for the randomised studies using the RoB 2 tool showed "some concerns" of risks of bias, as demonstrated in Table 3.

Discussion

Main findings

Overactive bladder syndrome is a highly prevalent disorder that largely affects the quality of life of sufferers. Female sexual dysfunction was previously reported to be significantly correlated with OAB. It is therefore crucial to understand the correlation between OAB treatments and female sexual function. Here, we present a systemic review of 6 studies and meta-analysis of 3 observational before-and-after studies to elucidate the effect of intravesical Botox treatment on female sexual function in OAB patients. Our results demonstrate significant improvement of sexual function as demonstrated by all six studies included in our review.

In our review, the RCT studies by Nitti et al. [15], Chapple et al. [16] and Fowler et al. [17] reported "significant improvement" of the patients' symptoms using the KHQ compared with the control arm.

The total number of participants pooled from the three studies included in the meta-analysis was 119. All three studies included in the meta-analysis reported significant improvement of sexual function after Botox injections. Interestingly, the domains reported to have improved in the FSFI following treatment were not the same in all three studies. The study by Balzarro et al. [18] reported significant improvement in most FSFI domains, except for the desire and pain domains, whereas the study by Miotla et al. [19] reported improvement in desire, arousal, lubrication, orgasm, satisfaction and pain. The third study, which was by Giannantoni et al. [14], observed significant improvement in desire, arousal, lubrication, orgasm and satisfaction, but not in the pain domain [14]. The Giannantoni et al. study did not report the data of the overall FSFI score [14]. We could not explain the variation in the domains reported to have improved in the different studies.

Strengths and limitations

This is the first meta-analysis exploring the impact of Botox bladder injection on sexual function in patients with OAB syndrome. All studies reported a positive effect of the treatment. The six studies included in our analysis included a total of 730 participants, where all participants received the same dosage and method of treatment (100 units of Botox injection into the bladder). All the studies were recent with the earliest reported in 2013. The three studies included in the meta-analysis used similar recruitment criteria and had the same follow-up period and condition-specific assessment tool (FSFI).

The main limitation to our review is the inability to pool the data from the three RCTs [15–17] in our review into a meta-analysis. These three studies used a more generalised quality of life questionnaire (KHQ), with only one domain addressing sexual function, which does not provide in-depth analysis of the change in sexual function in particular. The three studies that explored female sexual function specifically were all prospective observational studies, which increases the risk of performance bias. Another limitation is the small number of participants in the studies included in the meta-analysis (119 participants). We recognise the high level of heterogeneity ($I^2 \geq 50\%$), but we still believe that pooling the data is justified. We used a random model, as sexual function can be influenced by many other variables. Our literature search did not include unpublished results or search in the grey literature, as these were unlikely to include enough data for inclusion in our review. With the small number of studies included, we could formally assess for the risk of publication bias.

The study by Giannantoni et al. [14] examined the impact of Botox bladder injection on sexual function in patients suffering from OAB syndrome and already diagnosed with multiple sclerosis (MS). Although this includes a slightly different cohort of patients, we did not feel the need to exclude it as the study reported the change in sexual function score before and after Botox treatment, which would still be reflective on the impact of the treatment on sexual function. Total FSFI score was only reported in the two studies including patients with idiopathic OAB syndrome, which still showed a positive impact of Botox injections on sexual function. However, the authors appreciate the limited number of patients included in the meta-analysis of the FSFI, which is a limitation of this study.

Interpretation and previous studies

In the literature, a systematic review by Balzarro et al. [21] explored the impact of OAB treatment modalities on sexual function. However, it excluded patients with neurogenic bladder from the review. Our review included patients with neurogenic bladder [14]. The results of their review "suggested that OAB therapies improving OAB-wet significantly reduced female sexual dysfunction", which agrees with the results of our review. Another review by Levy and Lowenstein [22] acknowledged the under-reporting of an improvement of sexual dysfunction in women with OAB syndrome; however, the available literature suggests improvement of sexual dysfunction with OAB syndrome treatment modalities [21].

Many studies explored the impact of different treatment modalities of OAB syndrome on female sexual function. Zachariou et al. in a recent study involving 85 patients with

OAB syndrome, showed significant improvement in sexual function on the FSFI score after oral treatment with Mirabegron (beta3-adrenergic agonist) [23]. Many other studies showed improvement of sexual function after oral medical treatment with anti-cholinergic drugs [24–26].

Sacral neuromodulation is a recognised treatment modality of OAB syndrome where the sacral nerve is stimulated via an electrode attached to an implantable pulse generator [27]. Khunda et al. published a systematic review and meta-analysis examining the impact of sacral neuromodulation on sexual function in women with bowel or bladder dysfunction [28]. This review demonstrated significant improvement of sexual function (MD −0.39, 95% CI −0.58, −0.19, $p = 0.0001$).

Percutaneous posterior tibial nerve stimulation (PTNS) is another effective treatment modality for OAB syndrome in which the tibial nerve is stimulated by inserting a fine needle just above the ankle and passing a mild electric current into it [29]. Kershaw et al. reported a systematic review and meta-analysis of seven studies exploring the impact of PTNS on sexual function in women with pelvic floor dysfunction, including OAB syndrome [30]. This review showed significant improvement of sexual function after PTNS treatment (MD –0.41, 95% CI −0.79, −0.03, $p = 0.04$).

The above-mentioned studies raise the point that improvement in sexual function is probably attributed to the improvement of OAB symptoms regardless of the treatment modality. More research is needed to explore the comparison between the impact of the different treatment modalities on sexual dysfunction.

It is important to take the results of the above-mentioned studies with caution. A meta-analysis by Weinberger et al. showed that "67.7% of the treatment effect for female sexual dysfunction is accounted for by placebo" [31]. Although this study looked at patients with sexual dysfunction regardless of the presence or absence of urinary incontinence, the placebo effect of treatment should be considered while looking at these results.

Generally, the results of our review agree with those of further reviews exploring the impact of other different treatment modalities for OAB on sexual function. Although it is not an issue that is discussed routinely in clinical practice, it is probably information that should be used in the day-to-day counselling of this cohort of patients suffering from OAB. The negative impact of OAB on sexual function can be reversed by treatment of OAB.

Conclusions

We report a systematic review on the effect of Botox treatment on sexual function in patients with OAB syndrome. Although the studies are small, the results indicate a positive effect of Botox treatment on sexual function in this cohort of patients.

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Author contributions Sami Shawer: project development, data collection and analysis, manuscript writing; Aethele Khunda: project development, data collection, revision of the manuscript, overall supervision, and final approval;Gareth J. Waring: project development, revision of the manuscript and supervision; Paul Ballard: supervision of the project and final approval.

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Declarations

Conflicts of interest Sami Shawer: no conflicts of interest; Aethele Khunda: in the last 5 years, received educational grants from Medtronic, Olympus, Axonic and speaker fees from Astellas (I also received travel and accommodation expenses from conference organisers when invited as a speaker); Gareth J. Waring: no conflicts of interest; Paul Ballard: in the last 5 years, received an educational grant from Olympus.

References

1. Abrams P, Andersson KE, Birder L, et al. Fourth international consultation on incontinence recommendations of the international scientific committee: evaluation and treatment of urinary incontinence, pelvic organ prolapse, and fecal incontinence. Neurourol Urodyn. 2010;29(1):213–40. https://doi.org/10.1002/nau.20870.
2. Irwin DE, Milsom I, Hunskaar S, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: results of the EPIC study. Eur Urol. 2006;50(6):1306–14; discussion 1314–5. https://doi.org/10.1016/j.eururo.2006.09.019.
3. Abrams P, Kelleher CJ, Kerr LA, Rogers RG. Overactive bladder significantly affects quality of life. Am J Manag Care. 2000;6(11 Suppl):S580–90.
4. Perry S, McGrother CW, Turner K, Leicestershire MRC Incontinence Study Group. An investigation of the relationship between anxiety and depression and urge incontinence in women: development of a psychological model. Br J Health Psychol. 2006;11(Pt 3):463–82. https://doi.org/10.1348/135910705X60742.
5. Sen I, Onaran M, Tan MO, Acar C, Camtosun A, Sozen S, Bozkirli I. Evaluation of sexual function in women with overactive bladder syndrome. Urol Int. 2007;78(2):112–5. https://doi.org/10.1159/000098066.
6. Patel AS, O'Leary ML, Stein RJ, Leng WW, Chancellor MB, Patel SG, Borello-France D. The relationship between overactive bladder and sexual activity in women. Int Braz J Urol. 2006;32(1):77–87. https://doi.org/10.1590/s1677-55382006000100014.
7. Zahariou A, Karamouti M, Tyligada E, Papaioannou P. Sexual function in women with overactive bladder. Female Pelvic Med Reconstr Surg. 2010;16(1):31–6. https://doi.org/10.1097/SPV.0b013e3181bf51eb.
8. Jha S, Ammenbal M, Metwally M. Impact of incontinence surgery on sexual function: a systematic review and meta-analysis. J Sex

Med. 2012;9(1):34–43. https://doi.org/10.1111/j.1743-6109.2011.02366.x.
9. López Ramos H, Torres Castellanos L, Ponce Esparza I, Jaramillo A, Rodríguez A, Moreno Bencardino C. Management of overactive bladder with onabotulinumtoxinA: systematic review and meta-analysis. Urology. 2017;100:53–8. https://doi.org/10.1016/j.urology.2016.10.026.
10. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339:b2535. https://doi.org/10.1136/bmj.b2535.
11. Sterne JA, Hernan MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016;355:i4919. https://doi.org/10.1136/bmj.i4919.
12. Sterne JAC, Savovic J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. https://doi.org/10.1136/bmj.l4898.
13. Giannantoni A, Gubbiotti M, et al. Effects of Onabotulinum toxin a intradetrusor injections on urinary symptoms and sexual life in women affected by multiple sclerosis: a prospective controlled study. J Neurol Neurophysiol. 2017;8(3):1000427. https://doi.org/10.4172/2155-9562.1000427.
14. Giannantoni A, Proietti S, Giusti G, et al. OnabotulinumtoxinA intradetrusorial injections improve sexual function in female patients affected by multiple sclerosis: preliminary results. World J Urol. 2015;33(12):2095–101. https://doi.org/10.1007/s00345-015-1578-4.
15. Nitti VW, Dmochowski R, Herschorn S, et al. OnabotulinumtoxinA for the treatment of patients with overactive bladder and urinary incontinence: results of a phase 3, randomized, placebo controlled trial. J Urol. 2013;189(6):2186–93. https://doi.org/10.1016/j.juro.2012.12.022.
16. Chapple C, Sievert K-D, MacDiarmid S, et al. OnabotulinumtoxinA 100 U significantly improves all idiopathic overactive bladder symptoms and quality of life in patients with overactive bladder and urinary incontinence: a randomised, double-blind, placebo-controlled trial. Eur Urol. 2013;64(2):249–56. https://doi.org/10.1016/j.eururo.2013.04.001.
17. Fowler CJ, Auerbach S, Ginsberg D, et al. OnabotulinumtoxinA improves health-related quality of life in patients with urinary incontinence due to idiopathic overactive bladder: a 36-week, double-blind, placebo-controlled, randomized, dose-ranging trial. Eur Urol. 2012;62(1):148–57. https://doi.org/10.1016/j.eururo.2012.03.005.
18. Balzarro M, Rubilotta E, Braga A, et al. OnabotulinumtoxinA detrusor injection improves female sexual function in women with overactive bladder wet syndrome. Eur J Obstet Gynecol Reprod Biol. 2018;225:228–31. https://doi.org/10.1016/j.ejogrb.2018.05.002.
19. Miotla P, Cartwright R, Skorupska K, et al. Impact of intravesical onabotulinumtoxinA on sexual function in women with OAB. Neurourol Urodyn. 2017;36(6):1564–9. https://doi.org/10.1002/nau.23148.
20. Rosen R, Brown C, Heiman J, et al. The female sexual function index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther. 2000;26(2):191–208. https://doi.org/10.1080/009262300278597.
21. Balzarro M, Rubilotta E, Mancini V, et al. Impact of overactive bladder-wet syndrome on female sexual function: a systematic review and meta-analysis. Sex Med Rev. 2019;7(4):565–74. https://doi.org/10.1016/j.sxmr.2019.05.002.
22. Levy G, Lowenstein L. Overactive bladder syndrome treatments and their effect on female sexual function: a review. Sex Med. 2020;8(1):1–7. https://doi.org/10.1016/j.esxm.2019.08.013.
23. Zachariou A, Mamoulakis C, Filiponi M, et al. The effect of mirabegron, used for overactive bladder treatment, on female sexual function: a prospective controlled study. BMC Urol. 2018;18(1):61. https://doi.org/10.1186/s12894-018-0377-9.
24. Del Rosso A, Pace G, Di Pierro ED, Masciovecchio S, Galatioto GP, Vicentini C. Impact of overactive bladder on sexual function in women. Urologia. 2011;78(3):200–2. https://doi.org/10.5301/RU.2011.8547.
25. Cakir SS, Degirmentepe RB, Atalay HA, et al. The effect of overactive bladder treatment with anticholinergics on female sexual function in women: a prospective observational study. Int Urol Nephrol. 2019;51(1):27–32. https://doi.org/10.1007/s11255-018-2030-7.
26. Zachariou A, Filiponi M. The effect of extended release tolterodine used for overactive bladder treatment on female sexual function. Int Braz J Urol. 2017;43(4):713–20. https://doi.org/10.1590/S1677-5538.IBJU.2016.0303.
27. Autiero SW, Hallas N, Betts CD, Ockrim JL. The cost-effectiveness of sacral nerve stimulation (SNS) for the treatment of idiopathic medically refractory overactive bladder (wet) in the UK. BJU Int. 2015;116(6):945–54. https://doi.org/10.1111/bju.12972.
28. Khunda A, McCormick C, Ballard P. Sacral neuromodulation and sexual function: a systematic review and meta-analysis of the literature. Int Urogynecol J. 2019;30(3):339–52. https://doi.org/10.1007/s00192-018-3841-x.
29. Burton C, Sajja A, Latthe PM. Effectiveness of percutaneous posterior tibial nerve stimulation for overactive bladder: a systematic review and meta-analysis. Neurourol Urodyn. 2012;31(8):1206–16. https://doi.org/10.1002/nau.22251.
30. Kershaw V, Khunda A, McCormick C, Ballard P. The effect of percutaneous tibial nerve stimulation (PTNS) on sexual function: a systematic review and meta-analysis. Int Urogynecol J. 2019;30(10):1619–27. https://doi.org/10.1007/s00192-019-04027-3.
31. Weinberger JM, Houman J, Caron AT, et al. Female sexual dysfunction and the placebo effect: a meta-analysis. Obstet Gynecol. 2018;132(2):453–8. https://doi.org/10.1097/AOG.0000000000002733.