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ORIGINAL ARTICLE

Overactive bladder: results from patients treated by hyaluronic acid-chondroitin sulphate therapy

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ABSTRACT

BACKGROUND: Overactive bladder (OAB) is a chronic condition. This study was prompted by the need to fill the gap between medical treatment and advanced therapies allowing improvement in Quality of Life. The aim of the current study was to evaluate the association between treatment type (Ialuril®; IBSA Farmaceutici, Lodi, Italy; in combination with antimuscarinic or alone after drop-out of antimuscarinic, relative to antimuscarinic alone treatment) and functional outcomes (number of micturitions, pelvic pain, urinary incontinence, nocturia, urgency).

METHODS: Of all patients newly diagnosed (January 2016 – January 2022) with OAB syndrome, we retrospectively identified 150 patients. They harbored three groups of 50 patients each: group 1 (antimuscarinic drug), group 2 (antimuscarinic drug + hyaluronic acid-chondroitin sulphate [HA-CS]), group 3 (antimuscarinic dropout patients). Univariable linear and logistic regression models were fitted for number and rates of incontinence, urgency, pelvic pain, nocturia, respectively.

RESULTS: A significant mean reduction of 1.5 micturition (P=0.02) was recorded in group 2 compared to group 1. Conversely, no statistically significant mean difference was recorded in group 3 compared to group 1. Regarding pelvic pain, both group 2 and group 3 were associated with lower rate of pelvic pain (P<0.001). Regarding urgency, a statistically significant protective OR was recorded for group 2 (OR=0.39; P=0.04), compared to group 1.

CONCLUSIONS: The combination therapy was associated with symptom improvement in antimuscarinic naïve OAB patients. Conversely in antimuscarinic dropped-out patients only pelvic pain improved with the HS-CA. No statistically significant differences were recorded for other functional outcomes, such as incontinence and nocturia.

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KEY WORDS: Urinary bladder, overactive; Chondroitin; Hyaluronic acid.

Overactive bladder (OAB) is a chronic condition defined as a storage symptom syndrome represented by urgency, usually accompanied by nocturia and increased daytime urinary frequency in absence of urinary tract infection or other obvious pathology. It could also be accompanied by urgency urinary incontinence (UUI).[1] Even if this diagnosis is not exclusively related to elderly patients, it usually involves over 40 years old patients with a prevalence of 16.5%.[2, 3] This data may be underestimated considering that many patients do not ask for a medical consult because of embarrassment or ignorance.[4]

The most common symptom is urgency which

is essential in the diagnosis of OAB. It is associated with nocturia, decreased sleep quality, and increased urinary frequency with an overall reduction of Quality of Life.[5, 6] This syndrome results in noteworthy effects on the performance of daily activities and in Quality of Life (QoL), both in men and women. Urinary tract infections, urinary stress incontinence or metabolic disorders must be excluded to consider OAB diagnosis. Accurate personal history, physical examination and laboratory tests are mandatory, in order to exclude urinary disorders such as recurring urinary infections, bladder neoplasms, bladder stones or risk factors that may underlie incontinence, such as diabetes mellitus, previous strokes, spine injury or neurological pathologies such as Parkinson, multiple sclerosis, or dementia. A post-void residual volume should be evaluated in patients with obstructive symptoms.[7] Moreover, it is useful to investigate previous pelvic surgery or radiation, obstetric history, as well as psychiatric pathologies. Nonetheless, extensive pharmacological anamnesis should be conducted, in order to assess the possible drug effect of OAB's symptom presentation, such as diuretics, benzodiazepine.[8]

Many factors occur in the pathophysiology of OAB Syndrome determining a detrusor overactivity and four theories have been proposed.[9] First, one theory supports the idea that the neurogenic origin of the symptoms is due to a reduction in the neural inhibition pathway and an increase of the afferent impulses triggering the voiding reflex. Second, another one underlines that the alteration of the phasic activity should be generated by muscarinic stimulation. Third, the myogenic theory involves the detrusor muscle that seems to become more responsive to the cholinergic stimulation with a subsequent increased spontaneous activity. Fourth, the last theory supports the idea that during the filling, spontaneous bladder contractions increase the afferent signal with a powered awareness of bladder filling.

The damage of the urothelial glycosaminoglycan (GAG) barrier layer is one of the principal causes of interstitial cystitis/bladder pain syndrome (PBS/IC) and recurrent urinary tract infections. The loss of this natural barrier determines the penetration in the bladder wall of urinary constituents causing C-Fiber activation, mast cell and histamine release. These factors are the base of neurogenic inflammation with smooth muscle contraction and bladder hypersensitivity with urgency and frequency. Indeed, Sodium Hyaluronic Acid-Chondroitin Sulphate (HA-CS) (Ialuril®; IBSA Farmaceutici, Lodi, Italy) is usually used in patients affected by painful bladder syndrome/interstitial cystitis or recurrent urinary tract infections (rUTIs) in order to restore the loss of glycosaminoglycan layer and the integrity of the bladder epithelium. The intravesical treatment with HA-CS restores the urothelium and stabilizes the coating layer reducing both the release of proinflammatory cytokines and its permeability.[10] Considering that neurogenic inflammation is a determining cause of OAB, it may benefit from GAG replacement therapy with HA-CS.[11] Indeed, it has been shown that urine of patients affected by OAB have a lower concentration of GAGs against the control patients' group which may explain the efficacy of HA-CS replacement giving the chance to restore or improve the integrity of the urothelial GAG layer that is translated in a better QOL ad a reduced urinary frequency.[12]

Treatment of OAB

Treatment modality choice for OAB syndrome must ponder risks and benefits and consider how much the symptoms are bearable and interfere with patient's normal life. Patient should be aware that achieving reasonable symptom control can be a long process that requires adjustments or changes in treatment lines and symptoms are not always eliminated.[13] The European Association of Urology and the Japanese Urological Society recommend non-pharmacological and pharmacological treatments for OAB. The first-line therapy to consider is behavioral treatment for its effectiveness and absence of side effects.[14] Lifestyle changes, such as avoiding bladder irritants (for example chili, coffee and X), weight loss, and stop smoking in association with bladder training, timed voiding, pelvic floor exercises or pelvic floor stimulation, promote better symptom control with a sensible improvement in QoL.[15]

Pharmacological Treatment is considered the second-line therapy. Two different classes of

drugs are available: antimuscarinic agents and beta-adrenergic agents.[7] Treatment choice depends on contraindications, side effects reported, and patient tolerance. Even if a complete resolution of symptoms is uncommon, there would be a significant benefit for many patients. Patient compliance is poor precisely because of the side effects and this often leads to abandonment of the therapy.[16] Side effects of antimuscarinic drugs include dry mouth, bowel movements, dry eyes, urinary retention, impaired cognitive functions, increased risk of falls. Their main contraindications are high post-voiding residue, the decline in cognitive functions, narrow-angle glaucoma, and alterations in the kinetics of gastric emptying.[17] As for the beta 3 adrenergic agonists, their effectiveness is also limited by side effects such as constipation and dry mouth. They are usually used in case of contraindications to use or intolerance to antimuscarinics[18] with similar efficacy and greater patient compliance.[19] In addition to behavioral changes and pharmacological treatment, there are advanced therapies such as tibial nerve stimulation, sacral neuromodulation or intradetrusorial injection of botulinum toxin for the treatment of OAB. These treatments are recommended in case of contraindications or failure of drug therapy and their use must be strictly related to an assessment of the risk/benefit profile by the patient.[7]

Our study was prompted by the need to fill the gap between medical treatment and advanced therapies that allow the patient to improve their quality of life through an improvement in symptoms and above all that could guarantee better patient compliance with the treatment. Given the effectiveness of Ialuril® (IBSA Farmaceutici) against the damage of the GAG layer, the current study evaluated the association between treatment type (Ialuril®, IBSA Farmaceutici; in combination with antimuscarinic or alone after drop-out of antimuscarinic, relative to antimuscarinic alone treatment) and functional outcomes (number of micturitions, pelvic pain, urinary incontinence, nocturia, urgency).

Materials and methods

The study has been approved by the institutional research ethics committee of the San Carlo Hospital (Potenza, Italy) in accordance with the principles set forth in the Helsinki Declaration with registered number 20230036438. All patients have given their informed consent.

Study population

From January 2016 to January 2022, of all patients in the urology department of hospital San Carlo, Potenza, Italy, with OAB syndrome diagnosis, we retrospectively identified 150 consecutive patients aged from 18 to 70 years, with normal renal function, absence of hydronephrosis, and absent post-void residual. All patients had a history of high micturition (more than 6 per day) and urgency. Patients with urinary tract infections, a history of acute urinary retention, bladder cancer or pelvic were excluded (Table I).

They comprised three distinct groups: the first received standard therapy with antimuscarinic medication at therapeutic dosage; the second received antimuscarinic medication at therapeutic dosage along with weekly instillations of Ialuril® (IBSA Farmaceutici) prefill for eight weeks, followed by daily administration of Ialuril® (IBSA Farmaceutici) soft gel for one month; the third group consisted of patients who discontinued an-

TABLE I.—*Baseline descriptive characteristics of 150 patients diagnosed with overactive bladder between January 2016 and January 2022, according to different treatment group: 1) group 1 – antimuscarinic drug; 2) group 2 – combination therapy, hyaluronic acid plus antimuscarinic drug; and 3) antimuscarinic dropout cohort treated with hyaluronic acid.*

Characteristics	Overall, N.=150[a]	Group 1, N.=50 (33%)[a]	Group 2, N.=50 (33%)[a]	Group 3, N.=50 (33%)[a]	P value[b]
Micturition events	10.6 (3.4)	10.2 (3.4)	10.8 (3.4)	10.8 (3.4)	
Pelvic pain	99 (66%)	32 (64%)	33 (66%)	34 (68%)	0.9
Incontinence	41 (27%)	12 (24%)	16 (32%)	13 (26%)	0.6
Nocturia	126 (84%)	41 (82%)	41 (82%)	44 (88%)	0.6
Urgency	141 (94%)	48 (96%)	46 (92%)	47 (94%)	0.9

[a]Mean (SD), N. (%); [b]Pearson's χ^2 test; Fisher's Exact Test.

timuscarinic therapy due to its adverse effects and instead underwent a weekly protocol of Ialuril® (IBSA Farmaceutici) prefill for eight weeks, followed by daily administration of Ialuril® (IBSA Farmaceutici) soft gel for one month.

Variables of interest

For each patient, the following variables of interest were recorded at time four time points (time zero, three months, six months, and 12 months): number of micturition, pelvic pain (yes *vs.* no), incontinence (yes *vs.* no), nocturia more than 2 episodes per night (yes *vs.* no), urgency (yes *vs.* no).

Statistical analysis

Three analytical steps were completed. First, we tabulated baseline patients' characteristics. Descriptive statistics included frequencies and proportions for categorical variables. Means and standard deviations (SD) were reported for continuously coded variables. The Kruskal-Wallis and the χ^2 tests were used to compare medians and proportions, respectively. Second, mean number of micturition and rates of pelvic pain, incontinence, nocturia and urgency, were plotted. Third, a univariable linear regression model was fitted to address the reduction of symptom presentation in the three different groups of treatment (Table II). Moreover, univariable logistic regression models were fitted to examine the association between the different treatment modality (group 1 *vs.* group 2 *vs.* group 3) and symptoms' rate (pelvic pain, incontinence, nocturia, urgency) (Table III).

TABLE II.—*Univariable linear regression predicting micturition event, according to different groups.*

Parameters	Micturition		
Characteristics	Beta	95% CI	P value
Group 1	—	—	Ref
Group 2	-1.500	-2.790, 0.210	0.024*
Group 3	1.00	-0.290. 2.990	0.131

CI: Confidence Interval.
*Statistically significant.

Results

Baseline characteristics

Of all 150 patients, the mean number of micturition was 10.6. The rates of pelvic pain, incontinence, nocturia and urgency were 66%, 27%, 84% and 94%, respectively.

In group 1, the mean number of micturition was 10.2. The rates of pelvic pain, incontinence, nocturia and urgency were 64%, 24%, 82% and 96%, respectively. In group 2, the mean number of micturition was 10.8. The rates of pelvic pain, incontinence, nocturia and urgency were 66%, 32%, 82% and 92%, respectively. In group 3, the mean number of micturition was 10.8. The rates of pelvic pain, incontinence, nocturia and urgency were 68%, 26%, 88% and 94%, respectively.

No statistically significant differences were recorded in symptom distribution, according to the three different groups (all P values >0.05).

Patients' characteristics at 12 months

Of all 150 patients, the mean number of micturition was 7.43. The rates of pelvic pain, incontinence, nocturia and urgency were 27%, 13%, 29% and 39%, respectively.

In group 1, the mean number of micturition was 7.2. The rates of pelvic pain, incontinence, nocturia and urgency were 56%, 14%, 24% and 36%, respectively. In group 2, the mean number of micturition was 6.3. The rates of pelvic pain, incontinence, nocturia and urgency were 8%, 8%, 24% and 18%, respectively. In group 3, the

TABLE III.—*Univariable logistic regression predicting symptom presence (pelvic pain, incontinence, nocturia, urgency), according to different groups.*

Characteristic	Pelvic pain			Incontinence			Nocturia			Urgency		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Group 1	—	—	Ref	—	—	Ref	—	—	Ref	—	—	Ref
Group 2	0.068	0.018, 0.199	<0.001*	0.534	0.132, 1.897	0.343	1.000	0.396, 2.522	0.900	0.390	0.149, 0.963	0.046*
Group 3	0.150	0.055, 0.369	<0.001*	1.170	0.387, 3.613	0.780	1.941	0.826, 4.702	0.133	3.160	1.415, 7.286	0.006*

OR: Odds Ratio; CI: Confidence Interval.
*Statistically significant.

mean number of micturition was 8.8. The rates of pelvic pain, incontinence, nocturia and urgency were 16%, 16%, 38% and 64%, respectively.

The rate of pelvic pain was statistically significant lower in group 2 (8%), followed by group 3 (16%) and group 1 (56%), in that order (P<0.001). Similarly, the rate of urgency was statistically significant lower in group 2 (18%), followed by group 1 (36%) and group 3 (64%), in that order (P<0.001). No statistically significant differences were recorded in incontinence rate and nocturia according to the three different groups (all p-values >0.05).

Linear and logistic regression models

In univariable linear regression model addressing the association between different treatment modality (group 1 *vs.* group 2 *vs.* group 3) and number of micturition, a statistically significant mean decrease of 1.5 events was recorded in group 2, relative to group 1 (P=0.02). Conversely, no statistically significant decrease or increase was recorded in group 3 relative to group 1 (Table II).

In univariable logistic regression model addressing the association between the different treatment modality and pelvic pain, group 2 (Odds Ratio [OR]=0.07; 95% Confidence interval [CI]: 0.02-0.2; P<0.001) and group 3 (OR=0.15; 95% CI: 0.06-0.37; P<0.001) exhibited protective Odds Ratio. In univariable logistic regression model addressing the association between the different treatment modality and incontinence, group 2 and group 3 failed to exhibit protective odds ratio, relative to group 1. In univariable logistic regression model addressing the association between the different treatment modality and nocturia, group 2 and group 3 failed to exhibit protective OR, relative to group 1. In univariable logistic regression model addressing the association between the different treatment modality and urgency, group 2 (OR=0.39; 95% CI: 0.15-0.96; P=0.04) was associated with lower urgency. Conversely, group 3 (OR=3.16; 95% CI: 1.42-7.29; P=0.006) was associated with higher urgency (Table III, Figure 1).

Discussion

Overactive bladder syndrome represents a QoL-affecting disease. It occurs mainly in older than 40 years patients, with a prevalence of 16.5% worldwide.[4] With ageing populations, the health burden of this condition that is more common in older people, is likely to increase.[20] However, although it causes a significant negative socio-economic impact and determines a severe deterioration of QoL of sufferers,[21] the prevalence of the disease may be underestimated considering that many patients do not ask for a medical consult because of embarrassment or ignorance.[4] To date, different treatment modalities are available, starting with behavioral changes, followed or associated with drug treatments (antimuscarinics and beta 3 adrenergic agonists), and finally to more invasive treatment, such as intradetrusorial botulinum injection.

The current study was prompted by the need to fill the gap between medical treatment and advanced therapies that allow the patient to improve their quality of life through an improvement in symptoms and above all that could guarantee better patient compliance with the treatment. One possible pathway mechanism causative of OAB is supposed to be represented by neurogenic inflammation, due to augmented pain impulses to the neuronal fibers, for GAG layer deficiency.[11] Therefore, treatments that can restore GAG layer (such as HS-CA) may be of benefit for OAB syndrome patients. The current study aimed to test the association between HS-CA treatment plus antimuscarinics agent *versus* antimuscarinic alone focusing on functional outcomes (number of micturitions, pelvic pain, incontinence, nocturia, urgency) in patients diagnosed with OAB syndrome. Moreover, we tested the association between HS-CA and functional outcomes (number of micturitions, pelvic pain, incontinence, nocturia, urgency) in patients who dropped out from antimuscarinic treatment.

A statistically significant mean reduction of 1.5 micturition (P=0.02) was recorded in group 2 (antimuscarinic plus HS-CA) compared to group 1 (antimuscarinic alone). Conversely, no statistically significant difference was recorded in group 3 compared to group 1. These observations highlighted the role of HS-CA in combination with antimuscarinic treatment to improve this functional outcome in the naïve population. Conversely, the improvement in treatment with

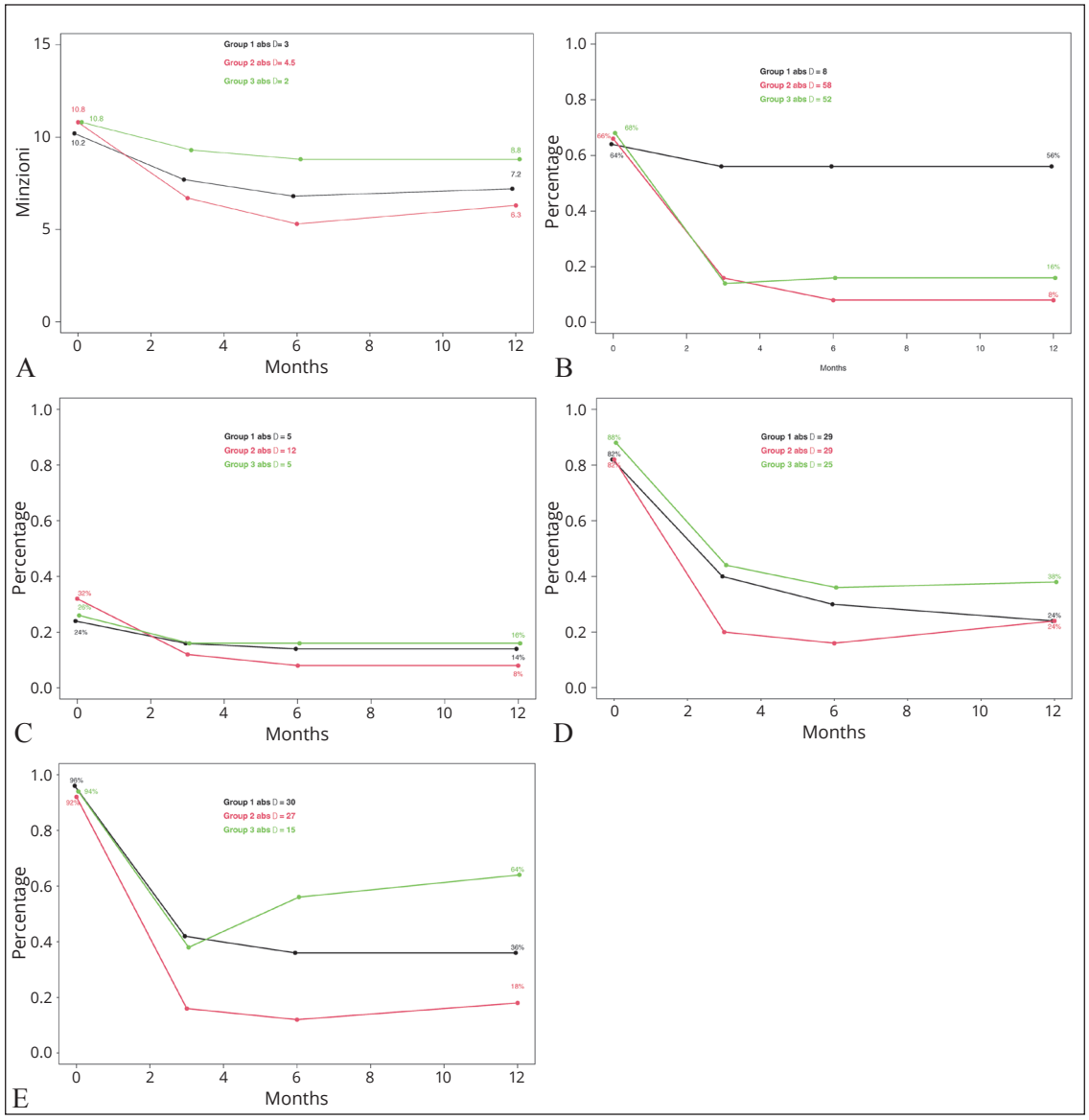

Figure 1.—Graphical description of: A) mean number of micturition; B) rate of pelvic pain; C) rate of incontinence; D) rate of nocturia; and E) rate of urgency, from baseline (time 0) to 12 months.

HS-CA was not associated with improvement in the number of micturitions in patients who dropped out of antimuscarinic treatment. However, the current observations cannot be directly compared with previous publications, since no publication addressing this topic are available. Therefore, this finding should ideally be validated by future investigations.

Regarding pelvic pain, the treatment combination of HS-CA plus antimuscarinic drug (group 2) was associated to a statistically significant lower rate of pelvic pain. Specifically, in univariable logistic regression, group 2 exhibited a very protective OR of 0.07 (P<0.001). Moreover, a statistically significant protective OR was recorded also for group 3, compared to group 1 (OR=0.15; P<0.001). These results are consistent with previous publications addressing the role of HS-CA in the management of pelvic pain in patients with IC/PBS.[10] Indeed, the common mechanism path-

way of these two different entities may suggest the efficacy of HS-CA treatment.[22, 23] It is noteworthy that HS-CA resulted in pelvic pain benefits in both naïve and dropped-out antimuscarinic patients. Regarding urgency, a statistically significant protective OR was recorded for group 2 compared to group 1 (OR=0.39; P=0.04). Similar results were reported by Peng *et al.* focusing the effect of HS-CA in IC/PBS.[24] Data regarding the dropped-out cohort (group 3) confirmed the need to intensively treat patients with OAB syndrome. In this cohort, HS-CA was not able to significantly reduce the urgency rate. Indeed, an OR of 3.16 was recorded in this group compared to group 1. These results must be interpreted with caution since the observations were far and distant in between. For this reason, no definitive recommendation can be made for the dropped-out patients. These results should ideally be investigated in future studies.

Limitations of the study

Despite its novelty, the current study is not devoid of limitations. First, its retrospective non-randomized nature limited the strength of our conclusion. Future studies, ideally, randomized-controlled trials should be performed to investigate the role of HS-CA in the treatment of OAB syndrome patients. Second, the current study relied on a total cohort of 150 patients. This sample size allowed to finalize some conclusive results for the naïve patients. However, for the dropout cohort no definitive suggestions can be made, and may be of interest to investigate this cohort in a deep fashion. Third, the retrospective nature of the current work does not allow us to have more granular data regarding baseline patient characteristics. Last but not least, we acknowledge that the use of validated questionnaires to better define the syndrome would have added value to the current paper. However, symptoms were recorded as present/absent without being characterized using validated questionnaires. Further studies should acknowledge and address this gap.

Conclusions

The combination therapy with HS-CA plus antimuscarinic drug is associated to symptom improvement (number of micturitions, pelvic pain and urgency) in antimuscarinic naïve patients. Conversely in antimuscarinic dropped-out patients only pelvic pain improved with the HS-CA therapy. Finally, no statistically significant differences were recorded for other functional outcomes, such as incontinence and nocturia. Future randomized studies should validate the role of HS-CA in OAB syndrome patients.

References

1. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, *et al.*; Standardisation Sub-Committee of the International Continence Society. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology 2003;61:37–49.

2. Milsom I, Abrams P, Cardozo L, Roberts RG, Thüroff J, Wein AJ. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. BJU Int 2001;87:760–6.

3. Morra S, Collà Ruvolo C, Napolitano L, La Rocca R, Celentano G, Califano G, *et al.* YouTubeTM as a source of information on bladder pain syndrome: A contemporary analysis. Neurourol Urodyn 2022;41:237–45.

4. Stewart WF, Van Rooyen JB, Cundiff GW, Abrams P, Herzog AR, Corey R, *et al.* Prevalence and burden of overactive bladder in the United States. World J Urol 2003;20:327–36.

5. Van Dijk MM, Wijkstra H, Debruyne FM, De La Rosette JJ, Michel MC. The role of nocturia in the quality of life of men with lower urinary tract symptoms. BJU Int 2010;105:1141–6.

6. Di Bello F, Napolitano L, Abate M, Collà Ruvolo C, Morra S, Califano G, *et al.* "Nocturia and obstructive sleep apnea syndrome: A systematic review". Sleep Med Rev 2023;69:101787.

7. Lightner DJ, Gomelsky A, Souter L, Vasavada SP. Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults: AUA/SUFU Guideline Amendment 2019. J Urol 2019;202:558–63.

8. Steele AC, Kohli N, Mallipeddi P, Karram M. Pharmacologic causes of female incontinence. Int Urogynecol J 1999;10:106–10.

9. Leron E, Weintraub AY, Mastrolia SA, Schwarzman P. Overactive Bladder Syndrome: evaluation and Management. Curr Urol 2018;11:117–25.

10. Costantini E, Lazzeri M, Pistolesi D, Del Zingaro M, Frumenzio E, Boni A, *et al.* Morphological changes of bladder mucosa in patients who underwent instillation with combined sodium hyaluronic acid-chondroitin sulphate (Ialuril®). Urol Int 2013;91:81–8.

11. Bassi PF, Costantini E, Foley S, Palea S. Glycosaminoglycan Therapy for Bladder Diseases: Emerging New Treatments. Eur Urol 2011;10:451–9.

12. Siracusano S, Cucchi A, Ciciliato S, Lampropoulou N, Vittur F. Urinary levels of glycosaminoglycans in patients with idiopathic detrusor overactivity. Int Urogynecol J 2009;20:1477–80.

13. Raju R, Linder BJ. Evaluation and Treatment of Overactive Bladder in Women. Mayo Clin Proc 2020;95:370–7.

14. Burgio KL, Locher JL, Goode PS, Hardin JM, McDowell BJ, Dombrowski M, *et al.* Behavioral vs drug treatment for urge urinary incontinence in older women: a randomized controlled trial. JAMA 1998;280:1995–2000.

15. Subak LL, Wing R, West DS, Franklin F, Vittinghoff E, Creasman JM, *et al.*; PRIDE Investigators. Weight loss to treat urinary incontinence in overweight and obese women. N Engl J Med 2009;360:481–90.

16. Reynolds WS, McPheeters M, Blume J, Surawicz T, Worley K, Wang L, *et al.* Comparative Effectiveness of Anticholinergic Therapy for Overactive Bladder in Women: A Systematic Review and Meta-analysis. Obstet Gynecol 2015;125:1423–32.

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18. Kelleher C, Hakimi Z, Zur R, Siddiqui E, Maman K, Aballéa S, *et al.* Efficacy and Tolerability of Mirabegron Compared with Antimuscarinic Monotherapy or Combination Therapies for Overactive Bladder: A Systematic Review and Network Meta-analysis. Eur Urol 2018;74:324–33.

19. Linder BJ, Gebhart JB, Elliott DS, Van Houten HK, Sangaralingham LR, Habermann EB. National Patterns of Filled Prescriptions and Third-Line Treatment Utilization for Privately Insured Women With Overactive Bladder. Female Pelvic Med Reconstr Surg 2021;27:e261–6.

20. Izett M, Zacchè M, Giarenis I, Robinson D, Cardozo L. Drug therapy for overactive bladder. Minerva Ginecol 2015;67:557–74.

21. Palleschi G, Tubaro A, Miano L. Valutazione clinica e modulazione degli effetti della terapia antimuscarinica [Overactive bladder: modulating the effects of antimuscarinic therapy]. Minerva Urol Nefrol 2005;57:237–45. [Italian].

22. Hung MJ, Tsai CP, Lin YH, Huang WC, Chen GD, Shen PS. Hyaluronic acid improves pain symptoms more than bladder storage symptoms in women with interstitial cystitis. Taiwan J Obstet Gynecol 2019;58:417–22.

23. Ghaith AF, Radwan MH, Rashed Taha M, Elbendary MA, Al Damhogy ME, Hagras AM. Evaluation of pain and quality of life after hyaluronic acid instillation in addition to botulinum toxin-A injection in women with refractory Interstitial Cystitis/Painful Bladder Syndrome: A pilot study. Arch Ital Urol Androl 2022;94:447–50.

24. Peng YC, Yueh-Hsia Chiu S, Feng M, Liang CC. The effect of intravesical hyaluronic acid therapy on urodynamic and clinical outcomes among women with interstitial cystitis/bladder pain syndrome. Taiwan J Obstet Gynecol 2020;59:922–6.

Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions

Roberto Falabella and Giuseppe Carrieri have given substantial contributions to study conception, Simone Morra and Vincenzo F. Caputo to study design, and software development, Sabrina La Falce, Giuseppe Di Fino and Saveriano Lioi to study validation, Luigi Milella, Franco C. Ponti and Vincenzo F. Caputo to data analysis, Franco C. Ponti to data investigation, Simone Morra and Vincenzo F. Caputo to manuscript writing, Vito Mancini to manuscript writing, revision and editing, Roberto Falabella and Giuseppe Carrieri to study supervision, Roberto Falabella and Aldo Di Fazio to project administration. All authors read and approved the final version of the manuscript.

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