REVIEW PAPER

FUNCTIONAL UROLOGY

Role of gabapentin in the management of neurogenic overactive bladders: A systematic review

Roshan Chanchlani[1], Ketan Mehra[2], Pramod K. Sharma[1], Sudarsan Agarwal[3], Amit Gupta[1], Reyaz Ahmad[1], Rakesh Mishra[4], Amit Agarwal[4], Suresh Kumar Thanneeru[1]

[1]*Department of Pediatric Surgery, All India Institute of Medical Sciences, Bhopal, India*
[2]*Department of Urology, All India Institute of Medical Sciences, Bhopal, India*
[3]*Department of Neurosurgery, SVRRGGH Tirupati, India*
[4]*Department of Neurosurgery, All India Institute of Medical Sciences, Bhopal, India*

Citation: Chanchlani R, Mehra K, Sharma PK, et al. Role of gabapentin in the management of neurogenic overactive bladders: A systematic review. Cent European J Urol. 2025; 78: 61-69.

Article history
Submitted: May 30, 2024
Accepted: Sep. 24, 2024
Published online: Mar. 21, 2025

Corresponding author
Suresh Kumar Thanneeru
Department of Pediatric Surgery,
All India Institute of Medical Sciences,
2nd-floor Hospital Building,
Academic block,
AIIMS, Bhopal,
Madhya Pradesh, India
tanirsuresh@yahoo.in

Introduction Neurogenic lower urinary tract dysfunction is typically managed through a step-up approach, beginning with anticholinergic medications, progressing to Botulinum toxin injections, and surgical interventions. Gabapentin offers a less invasive option, either as an adjunct to anticholinergics or as a standalone therapy. This systematic review examines gabapentin's efficacy and safety in treating neurogenic overactive bladders (NOAB) in both paediatric and adult populations.
To determine gabapentin's effect on reducing bladder pressure, increasing bladder capacity, and alleviating incontinence symptoms in NOAB patients.

Material and methods A systematic search was conducted on PubMed, Scopus, ScienceDirect, and Cochrane to identify studies on gabapentin for NOAB. Articles were sorted according to PRISMA guidelines, and the risk of bias was assessed using the JBI clinical appraisal tool. Data from the selected articles were synthesized qualitatively.

Results Of the 116 identified articles, 6 were selected. Two focused on paediatric patients with neural tube defects, while four studies involved adults with conditions like spinal trauma, Parkinson's disease, and multiple sclerosis. Urodynamic parameters improved in four studies, whether gabapentin was used alone or as an adjunct. All 6 studies reported significant improvements and minimal side effects.

Conclusions While limitations in dosages and study durations hinder a definitive endorsement of gabapentin, the overall positive response across studies suggests its potential efficacy in managing NOAB. Further high-quality randomized controlled trials comparing gabapentin with other treatments and exploring factors related to non-responsiveness are warranted for conclusive insights.

Key Words: gabapentin ‹› anticholinergics ‹› neurogenic overactive bladder

INTRODUCTION

Neurogenic bladder overactivity is prevalent among both pediatric and adult patients with Neurogenic lower urinary tract dysfunction. Management typically progresses from oral medication, with or without clean intermittent catheterization (CIC), to interventions such as Botulinum toxin injections and, in some cases, surgical procedures [1]. Anticholinergics represent a common pharmacological approach, yet their efficacy is variable, with many patients experiencing significant side effects that impact tolerability [2]. In response, alternative treatments have been explored, including gabapentin, which operates via a distinct mechanism from anticholinergics. Although gabapentin has been investigated in limited studies as either an adjunct or standalone therapy for this indication, the overall evidence remains fragmented. This systematic review aims to synthesize and evaluate existing findings to elucidate

the current understanding of gabapentin's efficacy and safety profile in the treatment of neurogenic overactive bladder (NOAB).

PICO Question

In patients with neurogenic overactive bladder (P), does the use of gabapentin (I) reduce bladder pressure, increase bladder capacity, and alleviate symptoms of incontinence (O)?

MATERIAL AND METHODS

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for conducting the present review [3].

Search strategy

A systematic literature search was conducted on PubMed, SCOPUS, the Cochrane Library, and ScienceDirect databases using the search terms outlined in Table 1. Additionally, the reference lists of included studies were reviewed for potentially relevant articles. Four investigators (SKT, AA, SA, and RC) independently screened abstracts, with selected articles undergoing full-text evaluation. Conflicts were resolved through consensus, resulting in a final list of studies.

Inclusion criteria

Studies assessing the efficacy of gabapentin, either alone or in combination with other drugs, for managing patients with NOAB were considered. This includes randomized controlled trials, non-randomized studies, prospective and retrospective observational studies, and case series published in English.

Exclusion criteria

Studies not using gabapentin or studies using gabapentin but not for NOAB, postmortem studies, case reports, letters to the editor, abstracts from congresses, conferences, symposiums, reports published in meeting booklets, and literature not in English were excluded.

Data extraction

Four investigators (SKT, AA, SA, and RC) independently assessed studies and extracted data using a pre-designed proforma based on the inclusion criteria. The study selection process is illustrated in Figure 1 using the PRISMA flowchart. Details

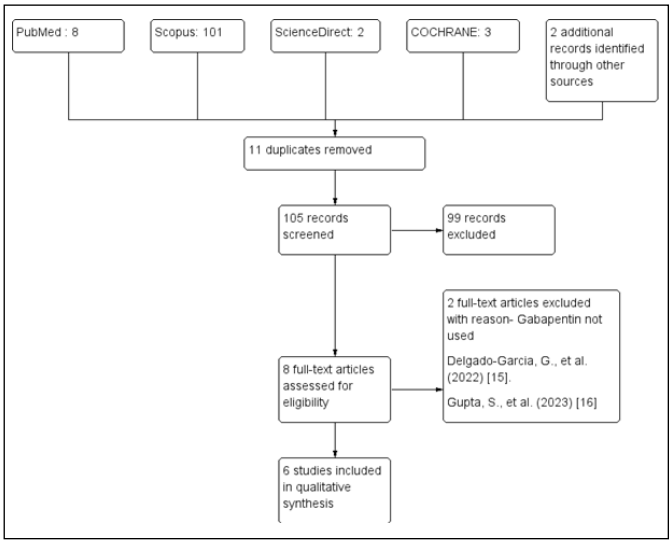

Figure 1. *PRISMA Flow Chart.*

extracted included Study ID, Journal, Country of Publication, Study Design, Number of Participants, Patient Characteristics, Objectives, Results, Key Conclusions, and Outcomes. Specific information collected encompassed urodynamic parameters such as bladder capacity and volume, as well as data related to bladder diary entries, including incontinence episodes, total voided volume, and other symptomatology scores.

Missing data

Authors were contacted for missing data, and any discrepancies were resolved through consensus.

Risk of bias and quality assessment

We utilized the revised JBI (Joanna Briggs Institute in Royal Adelaide Hospital in Melbourne) critical appraisal tool to assess the risk of bias in accordance with the methodologies of the included studies [4], encompassing randomized controlled trials [5], Qausi experimental studies [6], cohort studies, case series [7], and observational analytical studies.

RESULTS

Study selection

Our search strategy yielded 114 studies, with 11 identified as duplicates. After excluding 99 records based on title search, 6 full-text articles were selected for review. Additionally, 2 articles were added based on citations from the selected articles, while 2 were excluded with reasons. In total, 6 arti-

cles were included for qualitative synthesis. Details of the study selection process are illustrated in Figure 1 using the PRISMA chart.

Study characteristics

Of the 6 articles included in our review, two focused on pediatric patients, while the remaining four studied adults. Combined, these articles involved a total of 243 patients. Both pediatric studies were conducted in India, while the adult studies spanned Turkey, Italy, the USA, and the Philippines. In the pediatric studies, neural tube defects were the primary pathology, while spinal cord injury was the focus of one adult study, and various spinal and supraspinal pathologies were examined in the other three. Three studies utilized gabapentin as an adjunct therapy, while three employed it as a standalone treatment. Outcomes assessed included maximum bladder capacity and detrusor pressure through urodynamic studies in four of the included studies, while symptom improvement was evaluated in all six studies. The detailed study characteristics are mentioned in Table 2.

The dosage of gabapentin used across all the studies

For paediatric patients, Ansari et al. [8] utilized gabapentin at 10-20 mg/kg/day in three divided doses for a mean duration of 14.5 ±7.5 months, while Dash et al. [2] administered gabapentin at a dosage of 20 mg/kg/day for 6 months to 1 year.
In studies involving adult patients, Cakici et al. [9] initiated gabapentin with incremental doses ranging from 100 mg/day to 3600 mg/day. Carbone et al. [10] administered gabapentin at a dosage of 300 mg once daily, which was increased to 900 mg/day over 1 month. Kim et al. [11] prescribed gabapentin at 100 to 300 mg at bedtime, gradually titrating up to 3,000 mg based on symptoms, with follow-up ranging from 12 weeks to 12 months. Chua et al. [12] utilized gabapentin at a dosage of 100 mg OD, up to a maximum of 900 mg OD.

Table 1. *Details of search strategy*

Database	Search details
COCHRANE	3 trials matching gabapentin neurogenic bladder in Title Abstract Keyword
PubMed	(“gabapentin” [MeSH Terms] OR “gabapentin” [All Fields] OR “gabapentine” [All Fields] OR “gabapentin s” [All Fields]) AND (“urinary bladder, neurogenic” [MeSH Terms] OR (“urinary” [All Fields] AND “bladder” [All Fields] AND “neurogenic” [All Fields]) OR “neurogenic urinary bladder” [All Fields] OR (“neurogenic” [All Fields] AND “bladder” [All Fields]) OR “neurogenic bladder” [All Fields])) AND (1000/1/1:2024/4/24[pdat])
ScienceDirect	Title, abstract, keywords: gabapentin neurogenic bladder
SCOPUS	TITLE-ABS-KEY (gabapentin AND neurogenic AND bladder)

Results with respect to urodynamic study indicators

Four studies reported outcomes regarding urodynamic parameters, namely Ansari, M. S., et al. (2013) [8], Cakici, O. U., et al. (2021) [9], Carbone, A., et al. (2006) [10], Dash, V., et al. (2016) [2]. Across these four studies, there was a significant trend of improvement in urodynamic parameters following gabapentin usage. There were significant reductions in maximal detrusor pressure from the baseline reported across all the studies. Similarly, the bladder capacity was reported to have significantly enhanced. Detailed results are presented in Table 3.

Results with respect to symptomatic improvement

Six studies reported outcomes related to patient-reported outcome measures, including Ansari, et al. [8], Cakici et al. [9], Carbone et al. [10], Dash et al. [2], Kim et al. [11], Chua et al. [12]. All these studies demonstrated a significant improvement in symptomatic outcomes following gabapentin usage. The symptomatic outcomes were mainly a reduction in incontinence episodes, improvement in patient/parent perception of bladder contraction (PPBC), voiding volumes, decrease in frequency, and nocturia. Detailed results are presented in Table 3.

Risk of bias and quality assessment

Of the six articles included in our review, two were randomized controlled trials (RCTs), one was a quasi-non-randomized trial, one was a retrospective cohort study, one was a cross-sectional analytical study, and one was a case series. We utilized the JBI tool to assess the risk of bias and the quality of the methodology. Detailed assessments are provided in Table 4.
Chua et al. [12], conducted an RCT with a lower risk of bias. Dash et al. [2], conducted an RCT with a moderate risk of bias. Ansari et al. (2013) [8], conducted a Quasi-Non-Randomized study with a moderate risk of bias. Cakici et al. [9], conducted a retrospective cohort study with moderate risk of bias. Kim et al. [11], conducted an analytical cross-sectional study with moderate risk of bias. Carbone et al. [10], conducted a case series with a lower risk of bias. Additional details are provided in Table 3.

Table 2. *Characteristics of included studies*

Study authors (year)	Country	Type of study	Participants	Sample size	Mean age (years)	Inclusion criteria	Exclusion criteria	Dosage and follow-up	Outcomes/Results	Adverse effects	Conclusion
Ansari et al. 2013 [8]	India	Quasi Randomised trial	Paediatric spina bifida (84.61%) Tethered cord (11.54%) Sacral agenesis (3.85%)	NB – 26, NNB – 5	8.5 ±5.3	Children with LUTS with urodynamically proven Detrusor overactivity ± low compliance; not responding to anticholinergics for 6 months	UTI and bladder stones	GP 10–20 mg/kg/ day in three divided doses. The mean duration of treatment was 14.5±7.5 months	**UDS:** Max bladder capacity: p <0.02; Max Detrusor contraction: p <0.05 **PPBC scale:** p <0.05 **Symptoms:** Voided volume: p <0.03 Urge incontinence/ day: p <0.05 PVR >10%: NS	46.7% did not respond to GP. Concentration problems, mood swings, hyperactivity, somnolence, anxiety. 1 patient had drowsiness, dizziness, and headache – stopped GP	GP has given moderate results in OAB refractory to conventional anticholinergics with fewer adverse effects
Cakici et al. 2021 [9]	Turkey	Retrospective cohort study	Adults with spinal cord injury above the sacral level	27	32.03 ± 6.7	Spinal cord injury patients with UDS showing OAB despite anticholinergic and mirabegron	Not clear	GP incremental doses starting with 100 mg/day to 3,600 mg per day	**Symptoms:** Visual Analogue Scale: p <0.001 Daily incontinence episodes: p< 0.001 **UDS:** Max detrusor pressure: p <0.01 Max bladder volume: p <0.01	Response is seen in only 11 (40.17%), unresponsive in 16 (but they have an improvement in pain). No side effects were mentioned	GP can be considered for 3rd or further option before Botulinum toxin injection for OAB-NB who are not responding
Carbone et al. 2006 [10]	Italy	Case series	Multiple infarctions, Parkinson's, multiple sclerosis, post-infectious myelitis, frontal syndrome	16	61.69 ±10.72	Patients with detrusor overactivity due to neurogenic origin	Not clear	GP 300 mg once daily and increased to 900 mg/day; 1 month follow-up	**Symptoms:** IPSS score: p <0.023; **UDS:** Medium amplitude of involuntary detrusor contractions: NS Bladder capacity: p = 0.05 P Det/Qmax: p = 0.05	2 patients (12.5%) minor adverse reactions- dizziness and somnolence	GP can be a novel treatment for the treatment of overactive bladder
Chua et al. 2018 [12]	Philippines	RCT	Adults with overactive bladder symptoms	GP – 31 Solifenacin – 31 Placebo – 32	GP – 55.2 Solifenacin – 57.2 Placebo –53.9	Ambulatory patients with OAB symptoms for > 3 months based on OAB-Q scores	Contraindi-cation for drugs GP and solifenacin; UTI, stones, mixed incontinence, outlet obstruction	GP 100 mg OD to max of 900 mg OD; solifenacin 5 mg OD to 10 mg OD for 3 months	**Symptoms:** Mean change in urge incontinence episodes/ day; nocturia; mean volume per void were significant in GP and solifenacin groups **The health-related quality of life domain assessment is significant, and sleeping is significantly improved with GP**	5 patients (16%) in placebo, 5 (16%) in GP, and 11 (35%) in solifenacin group have adverse effects but not significant	Study was able to evaluate the efficacy of GP by showing the improvement in OAB symptoms

Table 2. *Continued*

Study authors (year)	Country	Type of study	Participants	Sample size	Mean age (years)	Inclusion criteria	Exclusion criteria	Dosage and follow-up	Outcomes/Results	Adverse effects	Conclusion
Dash et al. 2016 [2]	India	RCT	Children operated for lumbo-sacral menin-gomyelocele	Oxybutynin group – 14 GP – 17 Both drugs group – 13	6.1	At least 3 years old, not on anticholinergics, and had detrusor instability	VUR, bladder areflexia, already on medication, post-surgery for neurogenic bladder	GP 20 mg/kg/ day; oxybutynin 5 mg twice a day, follow up for 6 months and 1 year, drugs were stopped 3 weeks before UDS	**Symptoms:** DVSS improvement (1 year): p 0.076 Mean incontinence grade: p 0.774; **UDS:** Mean compliance: p = 0.322; Peak detrusor pressure: p = 0.04 Bladder capacity: p = 0.008	2 patients (30%) had severe headaches and were taken off the study	GP is a good alternative to oxybutynin for overactive bladders, both as mono and add-on therapy
Kim et al. 2004 [11]	USA	Analytical cross-sectional study	OAB/Nocturia due to Multiple sclerosis, mixed urge, and stress incontinence, transurethral resection of the prostate, 3 microwave of prostate	31	51	Patients with OAB and nocturia not responding to anticholinergic therapy (at least for 8 weeks)	Not clear? Bladder outlet obstruction, dyssynergia	GP – 100 mg to 300 mg at bedtime and slowly titrated to 3,000 mg based on symptomatology. Followed up for 12 weeks to 12 months	14 of the 31 patients responded Symptoms: Frequency at 12 weeks-improved with p = 0.01 Nocturia – improved with p = 0.03	6 patients had adverse effects of drowsiness and lethargy	GP well tolerated and can be considered in selective patients with failed anticholinergic therapy

GP – gabapentin; IPSS – International Prostate Symptom Score; LUTS – lower urinary tract symptoms; NB – neurogenic bladder; NNB – non-neurogenic-neurogenic bladder; PPBS scale – Patient/Parent perception of bladder condition; PVR – post-void residue; UDS – urodynamic studies; UTI – urinary tract infection

Table 3. *Results of the included studies*

Author	Urodynamic parameters		Symptomatic parameters	
	Detrusor pressure	Bladder capacity	Continence	Others
Ansari et al. 2013 [8]	Decreased pressures from 75 ±35 to 25 ±15 cm H_2O (p < 0.02)	Increased bladder capacity from 210 ±94 to 360 ±110 ml (p < 0.02).	Improved continence in 53% of patients, with an increase in voiding volume from 170 ±90 to 320 ±110 ml (p < 0.03)	Reported significant improve-ment in PPBC scale (p < 0.05)
Cakici et al. 2021 [9]	Decreased pressures from 38.81 ±15.17 to 21.72 ±8.62 cm of H_2O (p = 0.01)	Improved bladder volume from 239.63 ±58.19 to 262.81 ±48.01 ml (p = 0.01)	Improvement in daily incontinence episodes in the responsive group (p < 0.001), from 6.54 episodes before treatment to 2.27 episodes after treatment	NA
Carbone et al. 2006 [10]	Decreased medium amplitude of involuntary detrusor contraction pressures from 49 ±16 cm H_2O to 42.4 ±17 cm of H_2O (p = not significant)	Increased bladder capacity from 342 ±99 ml to 430 ±98 ml (p = 0.05)	Observed a decrease in incontinence episodes per day from 3 (2) to 1 (0.3)	Significant improvement in the IPSS (p < 0.023). 14.8 before tre-atment to 8.8 after treatment
Chua et al. 2018 [12]	NA	NA	Significant changes in mean urge incontinence episodes/ day: 0.68 (0.14) with a p-value of <0.001	Nocturia: 1.39 (0.15) with a p-value of <0.001 The volume of void urine im-proved from a baseline of 44.39 (1.72) ml with a p-value of <0.001
Dash et al. 2016 [2]	Maximum detrusor pressure from 69.40 ±16.36 to 44.73 ±17.40 cm of H_2O (p = 0.04)	Improvement in bladder capacity from 10.24% to 16.72% (p = 0.008)	Mean incontinence grade (p = 0.774).	Improvement in DVSS (p = 0.076)
Kim et al. 2004 [11]	NA	NA	Improvement in frequency (p = 0.01)	Improvement in nocturia (p = 0.03)

DVSS – Dysfunctional Voiding Symptom Score; IPSS – International Prostate Symptom Score; NA – not applicable; PPBC – Patient/Parent perception of bladder condition

Table 4. *JBI critical appraisal tool for RCTs*

Study ID	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13
Chua et al. 2018 [12]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Dash et al. 2016 [2]	Yes	Unclear	Yes	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
JBI critical appraisal tool for analytical cross-sectional studies													
Kim et al. 2004 [11]	Unclear	Yes	Yes	No	Unclear	Unclear	Yes	Yes					
JBI critical appraisal tool for qasi experimental studies													
Ansari et al. 2013 [8]	Yes	No	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes				
JBI critical appraisal tool for cohort studies													
Cakici et al. 2021 [9]	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes		
JBI critical appraisal tool for case series													
Carbone et al. 2006 [10]	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes			

JBI – Joanna Briggs Institute in Royal Adelaide Hospital in Melbourne

DISCUSSION

NOAB can affect individuals across the lifespan, from children with neural tube defects to the elderly. The pathophysiology of NOAB involves neurogenic origins, including reduced inhibitory neural impulses and increased afferent impulses from the bladder, a sensitive detrusor muscle exhibiting increased spontaneous activity, and an autonomous bladder with muscarinic stimulation. This can affect the upper tracts with increased pressures generated in the bladder, leading to renal damage. Moreover, NOAB significantly impacts daily activities such as work, travel, physical exercise, sleep, and sexual function. Early recognition and management of NOAB and reduction of the pressures generated in the bladder can help prevent renal damage due to back pressure changes and improve the quality of life in these patients [1].

Anticholinergics are commonly employed as first-line management for NOAB, exerting their effect by relaxing bladder smooth muscle via action on muscarinic receptors. However, these medications are associated with side effects such as dry mouth, fever, constipation, blurred vision, and somnolence. Studies have shown that only 50% of patients remain compliant with anticholinergic medication due to these adverse effects [1]. Consequently, newer anticholinergics have been introduced to mitigate these side effects. Patients who are refractory to pharmacotherapy may undergo botulinum injection and, if unsuccessful, may require surgical intervention.

Gabapentin, a gamma-aminobutyric acid analogue, is FDA-approved for epilepsy and neuropathic pain but has been utilized off-label for various conditions, including bipolar disorder, complex regional pain syndrome, attention deficit disorder, restless leg syndrome, sleep disorders, and alcohol withdrawal [13]. Although gabapentin shares structural similarities with GABA, it does not act directly on GABA receptors. The exact mechanism of action of gabapentin on neurogenic lower urinary tract symptoms (LUTS) is not known. Gabapentin and pregabalin, which is the S-enantiomer of 3-isobutyl GABA, are known as gabapentinoids. The excitation of afferent C fiber activity might be a possible cause of lower urinary tract symptoms in neurogenic bladder dysfunction. These gabapentinoids act on the $\alpha 2\delta$ subunits of voltage-gated calcium channels. By binding to these subunits, they inhibit calcium currents, thereby decreasing calcium influx. This results in a decreased release of neurotransmitters such as glutamate, noradrenaline, and substance P in the presynaptic area. The reduction in these signals can help the bladder relax and improve symptoms like urinary frequency [13, 14]. Gabapentin was first employed in urology for the treatment of interstitial cystitis [8]. However, its use and safety profile in children, particularly those under five years old, are not well-established despite its established use in epilepsy [16]. Given its distinct mechanism of action compared to anticholinergics, gabapentin may have an additive effect in managing NOAB. This review aims to assess the efficacy of gabapentin and elucidate its safety profile, particularly in children

Of the included studies, two are from the pediatric population. Ansari et al. [8] conducted a quasi-experimental study involving pediatric patients with neural tube defects and a mean age of 8.5 ±5.3 years. they focused on patients who did not respond to anticholinergics, using gabapentin in combination with anticholinergics for a minimum follow-up period of 6 months. Dash et al. [2] conducted a randomized controlled trial (RCT) on children with a mean age of 6.1 years diagnosed with lumbosacral myelomeningocele (MMC). These children had undergone surgery before the age of three and exhib-

ited detrusor instability. This study included three groups: anticholinergic therapy alone, gabapentin alone, and a combination of both. Unlike Ansari et al. [8], they included patients irrespective of their response to anticholinergics.

Both studies reported significant improvements in maximum detrusor pressure and bladder capacity with gabapentin. Dash et al. highlighted that combination therapy showed the most significant improvement compared to monotherapies, and gabapentin was better tolerated than oxybutynin. Ansari et al. [8] reported 46% non-responders to gabapentin, while Dash et al. did not report any non-responders to gabapentin.

Ansari et al. [8] used the patient/parent perception of bladder condition (PPBC) scale ($p < 0.05$), bladder dairy for continence, and voided volume, which was improved significantly. However, Dash et al. [2] used the Dysfunctional Voiding Symptom Score (DVSS) ($p = 0.076$) and mean incontinence grade ($p = 0.774$), which showed improvement but were not statistically significant.

Both studies showed substantial improvement in urodynamic parameters and Patient-Reported Outcome Measures (PROM) with gabapentin. However, the differences in the statistical significance of PROM improvements and non-responders to gabapentin may be attributed to sample size, which was small from both the studies and patient inclusion criteria where Ansari et al. [8] specifically included patients who were non-responders to anticholinergics, potentially indicating a more refractory patient population. In contrast, Dash et al. included all patients with detrusor instability, providing a broader patient base.

The remaining four studies are from the adult population. Cakici et al. [9], conducted a retrospective cohort study involving adults with spinal cord injuries above the sacral level who had refractory overactive detrusor that did not respond to anticholinergics and mirabegron and had neuropathic pain. The mean age of participants in their study was 32.03 ±6.7 years. Carbone et al. [10], presented a case series involving 16 patients with supraspinal pathologies such as multiple infarctions, Parkinson's disease, and multiple sclerosis. The mean age of their patients was 61.69 ±10.72 years. Kim et al. [11], conducted an analytical cross-sectional study on adult patients with various causes of overactive bladder (OAB), including multiple sclerosis, mixed urge and stress incontinence, and post-prostate resection, among others. The mean age of the patients was 51. They specifically included patients who had not responded to anticholinergic therapy and gabapentin was used as an add on therapy. Chua et al. [12], conducted a randomized controlled trial (RCT) in adults presenting with OAB symptoms, with a mean age of 55 years. They compared gabapentin with solifenacin and placebo.

With respect to the urodynamic profiles, two studies by Cakici et al. [9] and Carbone et al. [10] published their results. Both showed improvement in urodynamic parameters like maximum detrusor pressure, medium amplitude of involuntary detrusor contraction, and maximum bladder volume. However, Cakici et al. [9] reported that only 40% of the patients were responsive to gabapentin add-on therapy. The difference might be due to the use of gabapentin in patients already non-responsive to anticholinergics and mirabegron. Carbone et al. [10] did not report on maximum detrusor pressure per se but reported on the medium amplitude of involuntary detrusor contractions, which was decreased but not significant. This might be due to the very small number of included patients and the methodology being a case series. However, they reported that Pdet/Qmax in the pressure flow study showed a significant improvement with $p = 0.05$.

All four studies reported the results of the PROMs. Cakici et al. [9] reported a significant decrease in daily incontinence episodes in the responsive group from 6.54 (2.7) episodes before gabapentin to 2.27 (1.54) episodes after the treatment with a $p < 0.001$. Even though the incontinence episodes decreased in the unresponsive group also, the values were not significant. Carbone et al. [10] reported significant improvement in IPSS score, from 14.8 before treatment to 8.8 after treatment, with a p-value of 0.023. Chua et al. [12] reported improvement in urge incontinence episodes per day, nocturia, and volume per void with a p-value of <0.001. However, the results were not significant in comparison with solifenacin except for nocturia. Kim et al. [11] reported response in 14 out of 31 patients included. As mentioned before, gabapentin was used in refractory cases as an add-on therapy. Frequency has been improved in responders from 14.1 ±2.2 episodes before therapy to 10.0 ±2.1 episodes after therapy with a p-value of 0.01. Nocturia improved in responders from 4.0 ±1.3 to 1.0 ±0.3 with a p-value of 0.03.

Ansari et al. [8] reported serious adverse effects like drowsiness, dizziness, and headache in only one patient (3.3%), which required stoppage of gabapentin. 80% of the patients experienced mild adverse effects like concentration problems, mood swings, and hyperactivity. Dash et al. [2] reported severe headaches in two of their patients with gabapentin that required discontinuation of therapy, and 70% of the patients did not report any adverse reactions.

They also mentioned that only 43% of the patients were able to tolerate oxybutynin without any adverse effects, making a better comparison profile between gabapentin and oxybutynin. Cakici et al. [9] highlighted the abusive potential of gabapentin; however, they did not report any such side effects in their study population. Carbone et al. [10] reported no severe adverse reactions or discontinuation of gabapentin in their study. However, minor adverse reactions like dizziness and somnolence were reported in 12.5% of the patients. Chua et al. [12] reported minor adverse reactions with gabapentin, which were similar to the placebo group (16%). However, the solifenacin group reported side effects in 35% of patients even though they were not statistically significant. All the side effects of gabapentin were reported to improve spontaneously. Kim et al. [11] reported no discontinuation of therapy, and all the side effects were transient.

The side effect profile of gabapentin across these studies is minimal, with few patients requiring discontinuation. However, long-term follow-up, especially in children, is needed to document the safety profile of gabapentin.

The limitations of our review include a limited number of RCTs, with the majority of studies exhibiting a moderate risk of bias. Additionally, we were unable to conduct a meta-analysis due to variations in methodology, dosage of gabapentin, and follow-up protocols across the included studies.

Even though the usage of gabapentin for overactive bladder has been explored since 2004, there are not many studies defining the criteria for usage, dosage recommendations, or estimating the proportion of patients who may be non-responsive. However, combined results from studies, whether gabapentin is used alone or in conjunction with anticholinergics, have consistently shown significant improvement in symptoms and changes in urodynamic parameters. It's important to note that there is a subset of patients who may not respond to gabapentin, similar to other medications, and may require second-line management options such as botulinum toxin injection. Our review will definitely shed light on future studies with RCTs, promoting uniformity in reporting findings and addressing the need for standardized criteria for gabapentin usage, optimal dosage recommendations, and strategies for identifying non-responsive patients.

CONCLUSIONS

Although a definitive conclusion supporting gabapentin may not be drawn due to differences in dosages and treatment duration across studies, along with the limited number of high-quality studies, the majority of the included studies demonstrated a positive response to gabapentin, whether used alone or in combination with other drugs. High-quality randomized controlled trials comparing gabapentin with other medications and investigating factors related to non-responsiveness would be valuable for future endeavours.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

FUNDING

This research received no external funding.

ETHICS APPROVAL STATEMENT

The ethical approval was not required.

REGISTRATION AND PROTOCOL

Prospero CRD42024540949.

References

1. Leron E, Weintraub AY, Mastrolia SA, Schwarzman P. Overactive Bladder Syndrome: Evaluation and Management. Curr Urol. 2018; 11: 117-125.
2. Dash V, Bawa M, Mahajan JK, Kanojia RP, Samujh R, Rao KL. Role of gabapentin and anticholinergics in management of neurogenic bladder after repair of spina bifida- a randomized controlled study. J Pediatr Surg. 2016; 51: 2025-2029.
3. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Int J Surg. 2021; 88: 105906.
4. Barker TH, Stone JC, Sears K, et al. Revising the JBI quantitative critical appraisal tools to improve their applicability: an overview of methods and the development process. JBI Evid Synth. 2023; 21: 478-493.
5. Barker TH, Stone JC, Sears K, et al. The revised JBI critical appraisal tool for the assessment of risk of bias for randomized controlled trials. JBI Evid Synth. 2023; 21: 494-506.
6. Barker TH, Habibi N, Aromataris E, et al. The revised JBI critical appraisal tool for the assessment of risk of bias for quasi-experimental studies. JBI Evid Synth. 2024; 22: 378-388.
7. Munn Z, Barker TH, Moola S, et al. Methodological quality of case series studies: an introduction to the JBI critical appraisal tool. JBI Evid Synth. 2020; 18: 2127-2133.
8. Ansari MS, Bharti A, Kumar R, Ranjan P, Srivastava A, Kapoor R. Gabapentin: A novel drug as add-on therapy in cases of refractory overactive bladder in children. J Pediatr Urol. 2013; 9: 17-22.
9. Cakici OU, Kaya C, Sanci A, Gencler OS, Mammadkhanli O, Cindas A. Gabapentin add-on therapy for patients

with spinal cord injury associated neurogenic overactive detrusors that are unresponsive to combined anticholinergic and beta-3 adrenergic therapy. Cent European J Urol. 2021; 74: 547-551.

10. Carbone A, Palleschi G, Conte A, Bova G, Iacovelli E, Bettolo CM, et al. Gabapentin treatment of neurogenic overactive bladder. Clin Neuropharmacol. 2006; 29: 206-214.

11. Kim YT, Kwon DD, Kim J, Kim DK, Lee JY, Chancellor MB. Gabapentin for overactive bladder and nocturia after anticholinergic failure. Int Braz J Urol. 2004; 30: 275-278.

12. Chua ME, See MC, Esmeña EB, Balingit JC, Morales ML. Efficacy and Safety of Gabapentin in Comparison to Solifenacin Succinate in Adult Overactive Bladder Treatment. Low Urin Tract Symptoms. 2018; 10: 135-142.

13. Chincholkar M. Gabapentinoids: pharmacokinetics, pharmacodynamics and considerations for clinical practice. Br J Pain. 2020; 14: 104-114.

14. Loutochin O, Afraa TA, Campeau L, Mahfouz W, Elzayat E, Corcos J. Effect of the anticonvulsant medications Pregabalin and Lamotrigine on urodynamic parameters in an animal model of neurogenic detrusor overactivity. Neurourol Urodyn. 2012; 31: 1197-1202.

15. Ziganshina LE, Abakumova T, Hoyle CHV. Gabapentin monotherapy for epilepsy: A review. Int J of Risk Saf Med. 2023; 34: 243-286.

16. Delgado-Garcia G, Lapidus S, Talero R, Levy M. The patient journey with NMOSD: From initial diagnosis to chronic condition. Front Neurol. 2022; 13: 966428.

17. Gupta S, McColl MA, Smith K, McColl A. Prescribing patterns for treating common complications of spinal cord injury. J Spinal Cord Med. 2023; 46: 237-245.