Antibiotic treatment of overactive bladder: scoping review

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Introduction

Overactive bladder (OAB) is a non-specific symptom syndrome characterised by "urgency, with or without urinary incontinence, usually with increased daytime frequency and nocturia", and is a diagnosis of exclusion [1]. Urine infection has long been implicated in the pathophysiology of OAB, with proponents suggesting that the infection-associated inflammatory response exaggerates bladder sensory signaling. In addition, it is also possible that bacteria can directly and indirectly sensitise the sensory neurons with locally acting toxins and metabolites, as well as promote urothelial shedding, leading to increased bladder permeability, which allows urine to directly affect nerves, elicit pain and lead to the origin of storage symptoms [2]. Antibiotic therapy leads to a decrease in the pro-inflammatory cytokines in urine which in some studies correlates with decreased severity of the OAB symptoms [2].

However, there is still considerable debate about the role of infection and antibiotic therapy in the treatment of these conditions. The aim of this study was to review the existing evidence for use of antibiotic therapy in female overactive bladder patients.

Methods and Materials

A systematic search of Embase, Medline, CINAHL, Scopus, Web of Science, CENTRAL, and a grey literature search was conducted for primary studies on long-term or full-dose antibiotics as treatment for female adult patients with OAB. The search was implemented in accordance with the JBI methodology for systematic reviews [3]. The methods, inclusion criteria, antibiotic regimen and effects of the interventions were analysed, and the existing gaps in knowledge and research were identified.

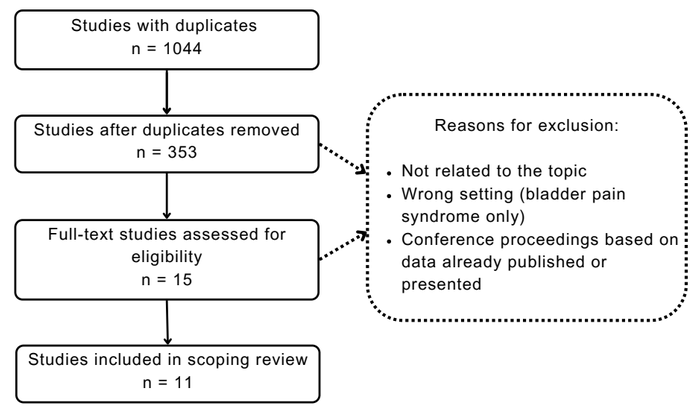

Chart 1. PRISMA-ScR flow diagram

Results

Seven published papers (table 1) and four conference proceedings were identified.
The identified studies were heterogenous in their design, inclusion and exclusion criteria, antibiotic treatment regimen, approach to the concurrent anticholinergic medications, follow-up period, methods, and measured outcomes. There was only one double-blind placebo controlled, non-comparative randomised control trial with a small sample size, and the largest study lacked study design. No retrieved study compared long-term antibiotic therapy with any OAB treatment currently recommended in international guidelines (anticholinergic medications or beta3-adrenergic drugs, intravesical onabotulinum toxin A, posterior tibial nerve stimulation or sacral neuromodulation). Only four out of 11 studies used antimuscarinics in study patients along the antibiotic treatment. Only three studies reported adverse events related to antibiotic use or antibiotic resistance.

Table 1. Published papers

Study	Inclusion criteria	Treatment protocol	Measured LUTS outcome	Results and limitations
Potts *et al*. 2000 Non-randomised cohort study **23 patients**	LUTS or pain and positive swabs for *U. urealyticum* or *M. hominis*	**Short-term antibiotics** **Anticholinergics**: not specified	**Primary**: improvement in symptoms' severity and 24-h voiding frequency	**Follow-up**: 6 months **Results**: 91% improvement in symptoms: frequency reduction from 9.2 to 6.8 times/24h
Lee *et al.* 2010 Multicentre non-randomised cohort study **29 patients**	Frequency and urgency and positive swab for *M. hominis* or *U. urealyticum* or *C. trachomatis*	**Short-term antibiotics** **Anticholinergics**: patients on anticholinergics excluded	**Secondary**: improvement in urgency episodes and changes in PPBC, ICIQ-FLUTS and PPTB.	**Follow-up**: 4 weeks **Results**: 87% reported improvement in ICIQ-FLUTS: frequency reduction from 10.6 to 8.1 times/24h, urgency episode reduction from 2.7 to 0.3 times/24h. Median PPBC score improvement from 4 to 2.
Vijaya *et al*. 2013 Non-randomised cohort study **35 patients**	Refractory OAB	**Long-term antibiotics**: 6 weeks of high-dose rotational antibiotics **Anticholinergics**: stopped for the study	**Secondary**: day-time frequency, nocturia, urgency score and PPBC score	**Follow-up**: 6 weeks **Results**: decrease in daytime urinary frequency, nocturia, PPBC and PPIUS scores. 57% had major improvement in PPBC scores.
Gill *et al*. 2018 Observational cohort study **24 patients**	OAB symptoms with or without urgency urinary incontinence	**Long-term antibiotics** if pyuria on the urine dip **Anticholinergics**: yes (drug not specified)	**Secondary**: ICIQ-LUTS, Whittington Urgency and Pain Scores	**Follow-up**: 48 weeks – 12 visits each 4 weeks **Results**: secondary lower urinary tract symptoms not reported. It is mentioned in the discussion that whilst there was an improvement in symptoms. Scores never fell to those of untreated controls
Swamy *et al.* 2018 Non-randomised case series **624 patients**	Chronic LUTS and pyuria (including OAB, IC/BPS, voiding symptoms and recurrent UTIs)	**No protocol** **Long-term full-dose antibiotics** until the symptoms and pyuria were resolved **Adjuncts**: Methenamine Hippurate **Anticholinergics**: not specified	**Outcomes not defined but reported**: LUTS questionnaire with urinary urgency and lower urinary tract pain subscales	**Mean treatment length**: 383 days **Results**: overall reduction in LUTS (PGI-I data), pain, frequency, and urgency. 84% improvement in PGI-I scores.
Swamy *et al*. 2018 Non-randomised case series **221 patients**	Heterogenous group – women from the study above who had an unplanned long-term antibiotic treatment cessation for five weeks	Patients were reviewed an average of 58 days before clinic closure, the service was closed for 5 weeks and patients were first reviewed in an average of 68 days after the closure. The last review within a year of suspension was at mean of 284 days after clinic closure.	**Outcomes not defined but reported**: deterioration of symptoms after cessation of treatment, improvement of symptoms on reiterating treatment	**Mean follow-up**: 284 days **Results**: 90% of patients reported deterioration. Symptom scores increased after cessation and recovered on reinitiating treatment – from 8 to 10.5 and back down to 9.0 (out of 39)
Chen et al. 2020 Double-blinded randomised non-comparative placebo-controlled trial 36 patients, **24 randomised to treatment**	Women > 50yo with refractory urge incontinence	**Long-term antibiotics**: 6 weeks of rotational antibiotics vs placebo **Anticholinergics**: Darifenacin 15 mg daily	**Primary**: volume of incontinence losses measured by 24-h pad test **Secondary**: change in frequency and urgency incontinence episodes on 3-day bladder diary; urgency severity (PPIUS); QOL improvement on ICIQ and overactive bladder questionnaire (OAB-q)	**Follow-up**: at 6 weeks and 6 months **Results**: reduction of pad weight (by 75g in treatment group vs. 35g in placebo group. Improvement in urge incontinence – cure of urgency incontinence (≤ 8g on 24h pad test) in 48% in treatment group vs. 17% in placebo group. No difference in PPIUS scores between the groups during the follow-up period.

PPBC – Patient Perception of Bladder Condition
ICIQ-FLUTS – International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms Modules
PPIUS – Patient Perception of Intensity of Urgency
IC/BPS – Interstitial Cystitis / Bladder Pain Syndrome
PGI-I – Patients Global Impression of Improvement for Incontinence
VAS score – Visual Analogue Score

Discussion

There was a lack of adequate study design of a standardised duration, characterisation of patients for inclusion and poorly defined outcomes. Apart from one RCT, there was no use of either placebo or conventional treatment comparators. The published studies were largely comprised of small-scale cohort studies with short follow-up periods. The inclusion and exclusion criteria varied significantly, and the pre-existing treatment for OAB was variably stopped or continued. The treatment strategies varied between full-dose repeated antibiotic courses and long-term full-dose rotational antibiotics and lacked a standartised approach. Reporting of adverse events and treatment safety was poor, with only three studies addressing adverse events related to antibiotic use and antibiotic resistance.

Conclusions

Given the potential adverse events associated with long-term antibiotics, concerns about microbial resistance and wide availability of other conventional treatment of overactive bladder, we conclude that there is no compelling evidence base to support the routine use of antibiotic therapy as chronic treatment of OAB in the absence of a documented urinary infection, as defined by contemporary clinical criteria.

References

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