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Intravesical Capsaicin as a Therapeutic Option for Bladder Sensory Disorders

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ABSTRACT

Intravesical capsaicin has been used as a treatment for detrusor overactivity and bladder pain syndromes due to its desensitizing effect on C-fiber afferents. However, patient responses vary widely in both efficacy and tolerability. As a therapeutic option, intravesical capsaicin has largely been replaced by botulinum toxin. However, the drug may still be considered in select cases of refractory disease or within the context of research protocols.

Introduction

The first vanilloid (capsaicin) receptor, TRPV1, was cloned in 1997,[1] which became the starting point for studies of the importance of this receptor for normal bladder function and dysfunction. Based on animal in vivo models, showing that intravesical capsaicin induces a reversible concentration-dependent detrusor hyperactivity that could be assessed by cystometry, intravesical capsaicin has been widely used in rats to study OAB/DO, painful bladder syndrome/interstitial cystitis (PBS/IC), neurogenic detrusor overactivity (NDO), and bladder outlet obstruction (BOO)-related OAB/DO.[2] Even if these conditions are associated with abnormal afferent nerve activity and urgency,[3,4] the underlying pathophysiology connecting these entities remains poorly understood. Still, a central hypothesis explaining the urgency and pain is the hypersensitization of bladder afferent pathways, resulting in the activation of silent C-fibers via TRPV1 receptors[5].

The basis for the use of capsaicin in the above-mentioned disorders is the selective desensitization of C-fiber afferents via the TRPV1 receptor,[6,7] making it a potential therapeutic agent when administered intravesically.[8] Despite promising mechanistic rationale, intravesical capsaicin has yielded inconsistent clinical outcomes.[2] Some patients experience marked symptom relief, while others report little benefit or discontinue treatment due to severe discomfort. This variability in response has decreased its clinical use. Thus, no clinical reports could be identified via PubMed or Embase over the last 10-year period. Recent systematic reviews of current intravesical NDO treatments [9,10] did not include capsaicin, and the drug has been replaced by intravesical botulinum toxin. Capsaicin and botulinum toxin (BoNT) are both used for treating OAB, NDO, and IC/BPS) due to their effects on sensory nerves.[11-13] However, they work via different mechanisms and have distinct advantages and disadvantages (Tables 1 and 2).

Table 1. Factors of relevance for the use of capsaicin and botulinum toxin in bladder sensory disorders

	Capsaicin	**Botulinum Toxin (BoNT-A)**
Mechanism	TRPV1 desensitization (sensory only)	Neurotransmitter inhibition (sensory & motor)
Onset of action	Slow (days–weeks)	Fast (within 1–2 weeks)
Duration of effect	Months (shorter than BoNT)	6–12 months
Administration	Intravesical instillation	Cystoscopic injection
Side effects	Burning pain, bladder irritation	Urinary retention, UTI, injection-site pain
Cost	Low	High
Availability	Limited	Widely available and approved

Figure 2. Advantages and disadvantages of using capsaicin and botulinum toxin in bladder sensory disorders

	Factor	**Capsaicin**	**Botulinum Toxin**
Patient Characteristics	Age	May affect sensory nerve sensitivity	Older patients more prone to urinary retention
	Pain threshold/tolerance	Low threshold limits capsaicin use due to burning pain	Usually better tolerated; procedural pain manageable
	Previous treatment history	Desensitized nerves may blunt response	Repeated injections may lead to antibody resistance
	Comorbidities (e.g., neuropathy, MS)	May reduce nerve responsiveness	Catheterization may be difficult for some patients
	Cognitive/functional status	Must tolerate procedure and post-treatment pain	Mixed sensory-motor dysfunction →better response
Disease-Specific Features	Degree of sensory nerve involvement	Greater sensory dominance → better response	Effective for both sensory and motor symptoms
	Detrusor overactivity	Less effective if motor involvement is significant	Chronic inflammation may affect diffusion or efficacy
	Bladder compliance/inflammation	Inflammation may increase irritative response	More broadly effective across OAB, IC, neurogenic bladder
	Underlying pathology (e.g., IC vs OAB)	More effective in sensory-predominant BPS/IC	Injection site number, depth, and dose influence effect
Procedural Variables	Technique of administration	Bladderinstillation technique affects distribution	Requires cystoscopy and sometimes sedation
	Pre-procedure preparation	Requires local anesthesia for tolerability	High doses increase efficacy but also retention risk
	Dose and concentration	High doses increase the risk of irritation. Pain management important for tolerability	Monitoring for retention, managing UTI risk

It may be questioned whether intravesical capsaicin/resiniferatoxin and analogues remain valid options in the treatment of OAB, NDO, and bladder pain syndromes. This narrative review aims to analyse 1) why the use of this mode of treatment has declined and 2) whether further understanding and consideration of patient- and treatment-specific factors that influence outcomes can restore its place in the therapeutic arsenal.

Methodology

Pubmed and Embase have been searched for articles related to the field published between 1990 and 2025.

Factors influencing the response to intravesical vanilloids

For more than three decades, intravesical administration of capsaicin/resiniferatoxin has been used as a treatment for bladder sensory disorders, such as NDO, OAB, and IC/BPS. [2,8,14] However, the clinical response to vanilloids varies considerably among patients [2] and is influenced by a combination of neurophysiological, pathological, and technical factors.

NEUROPHYSIOLOGICAL FACTORS

A key determinant of treatment response is the expression and distribution of transient receptor potential vanilloid 1 (TRPV1) receptors on C-fiber afferents in the bladder.[15] Capsaicin/resiniferatoxin selectively target these receptors, leading to defunctionalization of sensory nerves and subsequent symptom relief, [16,17] Variability in TRPV1 density, whether due to genetic polymorphisms,[18] chronic inflammation, or disease progression, may therefore contribute significantly to the heterogeneity in therapeutic outcomes.

Vanilloid treatment changes the gene expression profile in the bladder. Lepiarczyk et al. performed a transcriptomic characterization of the porcine urinary bladder trigone following intravesical administration of resiniferatoxin.[19] Using multistep bioinformatics they identified 129 differentially expressed genes (DEGs), 54 upregulated and 75 downregulated. DEGs can be involved in nerve degeneration processes, but can also be implicated in the initiation of neuroprotective mechanisms. Analysis indicated that resiniferatoxin treatment influences the signaling pathways regulating nerve growth, myelination, axon specification, and elongation. Intravesical instillation of the drug induces changes in the expression of genes involved in synaptic plasticity and neuromodulation, including those related to 5-HT, H2S, glutamate, and GABA transmission. This suggests that resiniferatoxin may exert a therapeutic, antinociceptive effect not only by acting on TRPV1 receptors.[20]

PATHOLOGICAL FACTORS

Patient-related factors, including pain sensitivity, age, sex, and genetic makeup, polymorphisms in the TRPV1 gene,[18] may influence treatment responses. Elderly patients may have altered neural responsiveness or urothelial permeability,[21] further complicating treatment outcomes.

The etiology of the bladder disorder plays a critical role in the response to vanilloids. Intravesical capsaicin is most consistently effective in patients with NDO, particularly following spinal cord injury, where C-fiber hyperactivity is a well-established pathophysiological mechanism.[8, 22-24] OAB and IC/BPS, which may involve additional mechanisms such as urothelial dysfunction, mast cell activation, and central sensitization, often show more variable or limited responses.[2] The urothelium normally acts as a protective barrier, [21,25] and in individuals with intact epithelium, capsaicin penetration to the suburothelial nerve plexus may be limited, reducing efficacy.

In patients with epithelial disruption—commonly seen in IC/BPS—drug permeability increases, which can enhance capsaicin's effects but also predispose to increased discomfort or pain during instillation.[21] If influenced by prior treatments such as botulinum toxin A, neuromodulation, or chronic inflammation, the sensitization state of afferent pathways can modulate the response to capsaicin. Pre-sensitized or desensitized nerves may respond less predictably, underscoring the importance of individualized evaluation before treatment.

TECHNICAL FACTORS

Dose, concentration, and formulation significantly affect capsaicin's efficacy and tolerability.[2,8] High doses can achieve profound desensitization, but are often associated with adverse effects such as burning, urgency, and discomfort during administration. The use of intravesical anesthetics (e.g., lidocaine) before capsaicin instillation has been shown to improve tolerability without impairing therapeutic action.[26, 27]

Other technical aspects—including instillation technique, volume, dwell time, and prior bladder preparation—can alter drug distribution and mucosal contact time, affecting clinical results.[2, 8] Ensuring consistent administration protocols is essential for reducing procedural variability.

Conclusion

A multifactorial interplay of bladder pathology, neural receptor expression, individual biological characteristics, and procedural techniques can modulate the response to intravesical capsaicin. Although intravesical capsaicin has shown potential in desensitizing C-fiber afferents and alleviating symptoms of bladder hypersensitivity, its clinical use is now rare due to significant tolerability issues, limited availability, lack of regulatory support, and the emergence of more effective alternatives. Intravesical capsaicin has largely been replaced by botulinum toxin, but may still be considered in select cases of refractory disease or within the context of research protocols.

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