

Editorial Comment

Results of previous studies support the importance of neovascularity in tumor growth and that cyclooxygenase 2 expression may be an important regulator of neovascularity in renal cell carcinoma. The authors of this study found that there is no significant difference between cyclooxygenase 2 expression in normal and pyelonephritic kidney tissues. It is indicative of differences in the mechanism of inflammation in pyelonephritis (infectious agents) and peritumoral inflammation occurring around the tumor due to anti-tumor immune response, which could induce cyclooxygenase 2 expression. The authors pointed out that the peritumoral kidney tissue inflammation seems to have different molecular characteristics than inflamed kidney tissue in pyelonephritis, such as increased cyclooxygenase 2 expression. Although preclinical and in the experimental setting, this paper opens new avenue in the treatment of renal cell carcinoma, that is the use of cyclooxygenase 2 inhibitors.

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RECONSTRUCTIVE UROLOGY

Botulinum Toxin Injections for Neurogenic and Idiopathic Detrusor Overactivity: A Critical Analysis of Results

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Objective: In recent years there has been an increasing use of the botulinum neurotoxins for the management of conditions characterised by detrusor overactivity. Early studies showed promising results in an area where few options previously existed between pharmacotherapy and surgery. This has led to an urgent need to assess the wide range of techniques and therapies available, as well as the efficacy and tolerability of the treatment. We performed a critical analysis of the numerous clinical studies for this novel treatment option in the management of neurogenic and idiopathic detrusor overactivity, with a view to directing further research and assisting urologists in the management of these conditions.

Methods: A systematic review of the literature, as well as a search for abstracts presented to relevant peer-reviewed meetings, was performed. All articles from 1988 onwards were included, prior to which no articles describing urologic use of botulinum neurotoxins had been published, although the majority of the articles have been published since 2000.

Results and Conclusions: Although many of the studies were small, overwhelming evidence supports the efficacy, safety, and tolerability of the botulinum toxins, specifically serotype A, for the management of these conditions. Before this is accepted as a widespread treatment modality, good-quality evidence from large-scale randomised controlled trials is needed. These studies should identify not only the most appropriate patients to treat but also the best dose, administration technique, and frequency for treatment.

Editorial Comment

The use of botulinum toxin in the treatment of both idiopathic detrusor overactivity (IDO) and neurogenic detrusor overactivity (NDO) is well-established clinical practice. However, as it is not an approved treatment option its use still is off label.

Schurch et al. were the first to describe the potential of botulinum toxin in the field of urology (1). In their pioneering work they were able to show botulinum toxin to be an effective, minimally invasive approach in the treatment of detrusor sphincter dyssynergy.

Two recent papers by Schulte-Baukloh et al. and by Patel et al. respectively provide the most comprehensive overview of the state of the art of the field.

Schulte-Baukloh also includes a critical assessment of Capsaicin and Resiniferatoxin (RTX) as possible alternatives to botulinum toxin. However, both drugs will probably play no more than minor roles in future long-term treatments, especially due to their limited availability as released drugs.

Patel gives the most complete overview to date of all published studies on the different types of botulinum toxin.

Both papers assess, summarize and highlight the treatment effectiveness of botulinum toxin over the past 18 years. However, emphasis must again be drawn to the fact that botulinum toxin is still unlicensed and therefore off label in the field of urology.

All studies on botulinum toxin to date have found overwhelming evidence of its efficacy, safety and tolerability. Even more, its use has demonstrably led to significant improvements in the patients' quality of life - an aspect often overlooked or forgotten. On top of that, it should be noted that NOB major surgeries, in particular, can be avoided or at least be delayed through use of botulinum toxin.

Despite of all this positive evidence a lack of worldwide, multi-center, double blind, placebo-controlled clinical trials inhibits the use of botulinum toxin from being more generally accepted. Only 3 placebo-controlled studies (2 on NDO, 1 on IDO) are mentioned by Patel attesting to the urgent need of carrying out accordingly designed studies.

Consequentially, several such trials have been initiated or are under way right now. Until they will have been completed the drug should primarily be used at designated centers to increase our understanding of its properties and applications.

Comparison of the different types of botulinum toxin is difficult because of variations in their individual molecular structures and mechanisms of action. The precise mechanism underlying the effects on smooth muscle cells and the nervous system is still not fully understood - as opposed to the well-studied effect guiding the onset of action in the striated muscle - opening further fields of study.

References

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Neuromodulatory Therapies in Female Pelvic Medicine and Reconstructive Surgery: Biological Agents

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In recent years, important improvements in the management of patients with neurogenic or non-neurogenic detrusor overactivity and urge incontinence have been brought about by the introduction of vanilloids and botulinum toxins in urology. In this review we introduce the new therapeutic options, provide basic information, and summarize the results experienced so far.

Neobladder Emptying Failure in Males: Incidence, Etiology and Therapeutic Options

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Purpose: Neobladder reconstruction is considered the best option for patients requiring cystectomy. Limited information is available about incidence, etiology and therapeutic options for neobladder emptying failure in males.

Materials and methods: In a retrospective study we analyzed the data of a consecutive series of 655 male patients (age range 23 to 82 years, median 63; followup range 0 to 208 months, median 36.5) who received an ileal neobladder following radical cystectomy at our institution. All patients had a complete followup until death or until December 2003. Data on all diagnostic and therapeutic procedures performed for neobladder emptying failure were collected.

Results: Of 655 patients 75 (11.5%) had at least 1 episode of failure emptying the neobladder requiring some form of therapy during followup. Failure was due to dysfunctional voiding in 23 patients (3.5%) and mechanical obstruction in 52 patients (8%). Causes of mechanical obstruction were benign strictures of the neovesicourethral anastomosis (23 patients, 3.5%) or the anterior urethra (11 patients, 1.7%), neoplastic obstruction by local tumor recurrence (13 patients, 2.0%) or a nonurological malignancy (1 patient, 0.2%), and obstruction by mucosal valves (3 patients, 0.5%) or a foreign body (1 patient, 0.2%). In 38 of 52 patients with mechanical obstruction of the neobladder outlet emptying was fully restored with endourological procedures, while in 14 of 52 patients long-term catheterization was necessary. Catheterization was the therapy of choice for all patients with dysfunctional voiding.

Conclusions: Neobladder emptying failure is of major concern but is not an argument against orthotopic diversion. The overall rate of transient or permanent neobladder emptying failure in males is high but most of the mechanical causes can be managed endoscopically, while the rate of patients with long-term catheterization for dysfunctional voiding is relatively low.

Editorial Comment

The authors report on the emptying problems in their vast experience in male patients with an orthotopic neobladder. 75 of 655 patients (11, 5%) had problems with emptying of the neobladder requiring therapy after follow up of up to 208 months. The biggest group of patients were those with a stricture of the neovesicourethral anastomosis (3, 5%) followed by a local tumour recurrence (2, 0%) and urethral strictures (1, 7%). In the recent literature with six major retrospective publications who analyzed this issue, a rate of outlet obstruction, mainly

as anastomotic strictures was found in 4.5 – 17.5% within 6 – 8 months after the surgery. Compared to these data, the authors have only 3.5% of anastomotic strictures, which is at the lower end.

The good message about the report of these problems is that the majority of patients did regain volitional voiding, generally after one endoscopic treatment (with the exception of pelvic tumour recurrences). This led to the conclusion by the authors that despite a fairly large emptying failure in this series most of these problems were of mechanical origin and could thus be managed endoscopically.

It is of note, too, that apparently none of the anastomotic tumor recurrences was treated either surgically or by radiotherapy. One can speculate that the anastomotic tumour recurrences were a consequence of a more cranial pelvic recurrence. It may, however, also have been possible that due to the omission of endoscopy during the follow up a recurrence was only diagnosed at a time when surgery was not a possibility anymore.

From this large series one can also see that a neobladder valve obstructing the outlet can be found in male patients as well. We have seen and published obstructing ileal valves as a possible reason of urinary retention in female patients. Obstructing ileal valves seem to be a possibility in male patients as well and are leading to the same therapeutic consequence, i.e. transurethral valve resection (1). The similar observation in male patients was seen with dysfunctional voiding: It was present in 2% of male patients and almost always led to long term catheterization.

Altogether a nice series of a not so rare problem in both male and female neobladder patients. For those performing such a procedure and those dealing with these patients during follow up it is definitely a recommendable manuscript.

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UROLOGICAL ONCOLOGY

Cystectomy for Transitional Cell Carcinoma of the Bladder: Results of a Surgery Only Series in the Neobladder Era

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Purpose: We studied the effect of radical cystectomy for transitional cell carcinoma of the bladder on survival and failure patterns when the 2 surgical standards cystectomy and neobladder were combined, when possible. **Materials and methods:** A consecutive series of patients undergoing radical cystectomy with pelvic lymph node dissection for transitional cell carcinoma of the bladder with curative intent was analyzed. Patients with neoadjuvant radiotherapy/chemotherapy were excluded. Pathological characteristics based on the 2002 TNM system, recurrence-free/overall survival and metastatic patterns were determined.