

comments

INTRODUCTION

There was a time when TURP was the 'standard' treatment for prostatic obstruction; then came Caine *et al.* [1], and others, who relieved the symptoms of prostatic obstruction using pharmacological agents. They showed that prostatic obstruction comprised two separate components, i.e. an active component from increased muscle tone of the prostate, distal bladder and prostatic urethra, that responds to sympathetic stimulation, and a second component from prostatic bulk obstruction. Caine *et al.* identified the receptors and neurotransmitters that were responsible for the active obstruction. They used α -sympathetic antagonists to reduce active obstruction and thus open the prostatic urethra and allow the patient to void urine. The urological fraternity and their patients owe a colossal debt to Marco Caine.

A further refinement added a 5α -reductase inhibitor, which prevents the conversion of testosterone to the active metabolite dihydrotestosterone (DHT). DHT is responsible for prostatic enlargement and scalp hair loss. This work developed from a simple clinical observation in a Caribbean island community. 5α -reductase inhibitors reduce the growth of prostate epithelial tissue but there is as yet no agent to reduce the growth of prostatic stromal tissue.

Medical therapy that combines α -adrenergic receptor blockade and a 5α -reductase inhibitor is probably the new 'standard' treatment in the First World [2,3]. However, there is one caveat; the 'association' between long-term 5α -reductase use and the development of aggressive cancer of the prostate needs further investigation and clarification.

There are two principal problems with combined therapy in the Third World, i.e. costs

THE MANAGEMENT OF BENIGN PROSTATIC OBSTRUCTION: A VOICE FROM THE THIRD WORLD DEEN P. SHARMA – Woodlands

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and patient compliance. Combined therapy costs just over US\$ 1000 per year; the treatment is life-long. A 55-year-old man can be asked to pay US\$ 20 000 for a lifetime's supply of drugs. Annual income per capita in the Third World is less than US\$ 1000. There is a tradition in the Third World that once a patient feels better he stops using the therapy and does not return to see the doctor [4]. These same men are also using other pharmaceuticals, e.g. anti-diabetics, antihypertensives, aspirin, etc., and they often have some degree of memory loss. They are easily confused about which tablet to take when. Combined medical treatment in the absence of the supporting structures of the First World health system adds to their memory burden.

TURP costs just under US\$ 1000 and is a 'one-off' procedure. Tissue is obtained for histological study and a more critical assessment of any prostatic 'remnant' can be made at the end of the procedure. Patients after TURP need a minimal follow-up. TURP-associated bleeding is the principal adverse event; bleeding can be severe enough to require a blood transfusion.

We use intraprostatic vasopressin (IPVP) for resecting the largest prostates; IPVP considerably reduces blood loss and we almost never need to use a blood transfusion [5]. IPVP also reduces irrigant absorption, thus permitting the safe use of cheap boiled water as the TURP irrigant. We do not see the TUR syndrome [6].

Thus I suggest some simplified guidelines for managing BPH in the Third World:

(i) Acute retention of urine (AUR); men who present with AUR are offered urgent TURP; 75% of the TURPs I conduct are for AUR, and haemoglobin, blood urea nitrogen, creatinine, electrolyte levels, an electrocardiogram, and blood group are assessed before surgery. The patient is specifically asked about bleeding after dental extraction; prolonged bleeding after dental extraction identifies a patient who will bleed aggressively after TURP. Such a patient (very few) is more safely placed on combined therapy. Early TURP relieves the patient of catheter drainage and reduces the risk of urinary sepsis. The anaesthetist gives a bolus of 80 mg gentamycin into the i.v. line before starting spinal anaesthesia. Ciprofloxacin is continued for 5 days, and the catheter is removed within 24 h after TURP.

(ii) Men aged >55 years with severe bother, i.e. and IPSS moderately or severely symptomatic are treated by TURP.

(iii) Men aged >75 years, especially with severe comorbidities, are treated with combined pharmacotherapy. These men are often dependent on their family or an institution, both of which can cope with the additional tablets.

(iv) Young men aged <55 years and mildly symptomatic on the IPSS are treated by watchful waiting or combined therapy. In this group the preservation of sexual function is a principal consideration. Some men in this group wish to start a second family. Sexual function is more predictably preserved by combined pharmacotherapy. Retrograde ejaculation is almost invariable after TURP. In

time these men may prefer and can be offered a TURP.

In the Third World TURP will remain the treatment of choice for most men with symptomatic BPH.

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Abbreviations: DHT, dihydrotestosterone; IPVP, intraprostatic vasopressin; AUR, acute retention of urine.

PHOSPHODIESTERASE-5 INHIBITORS HELP CLIMBERS TO ACHIEVE NEW HEIGHTS

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INTRODUCTION

The human body has to adjust physiologically to hypobaric hypoxia when climbing to altitudes above 2500 m. Failure to acclimatise to these conditions can result in a condition known as acute mountain sickness (AMS). This syndrome can lead to two potentially life-threatening conditions; high altitude pulmonary oedema (HAPE) and high altitude cerebral oedema (HACE). The symptoms of HAPE include dyspnoea at rest, tachycardia, cough, decreased exercise performance, orthopnoea and even haemoptysis. HAPE is a noncardiogenic pulmonary oedema, the crucial factor in the development of which is an excessive rise in pulmonary artery pressure (PAP) resulting from a greater than normal hypoxic pulmonary arterial vasoconstriction [1]. Coupled with oedema, these two processes combine to restrict adequate gas exchange. As a further consequence, sustained hypoxia leads to pulmonary hypertension. This is the result of the muscularization and deposition of connective tissue in the pulmonary arterioles and right ventricular hypertrophy.

Animal models have shown that nitric oxide (NO) production is important for maintaining low pulmonary vascular resistance [2]. In hypoxia there is a reduced NO availability and it is this feature that causes the excessive rise in PAP in HAPE. The vasorelaxant effects of NO are mediated via cGMP, which also inhibits vascular smooth muscle growth. Intracellular concentrations of cGMP and its effects are regulated by the phosphodiesterases (PDE). *In vitro* studies have shown that the subtype PDE-5 is responsible for cGMP metabolism in the lung [3]. PDE-5 is widely expressed throughout pulmonary vascular smooth muscle [4].

Apart from oxygen and descent to lower altitudes there is no definitive treatment for HAPE. Whilst oxygen may increase the partial pressure of alveolar oxygen, it does little to decrease the elevated PAP. Recent studies assessed sildenafil for preventing HAPE. Sildenafil was the first licensed oral drug for the treatment of erectile dysfunction (in October 1998), and is a potent selective inhibitor of the isoenzyme PDE-5. The effects of cGMP are terminated by PDE-5, which

converts cGMP to inactive GMP. With PDE-5 being found throughout lungs it is not surprising that attention has turned to sildenafil for preventing HAPE.

Initial experiments were carried out with animal models; these earlier studies involved the prophylactic treatment of rats before exposure to hypoxia. E4010, a selective PDE-5 inhibitor, reduced the PAP but the haemodynamic response was recorded from one measurement in anaesthetized rats at the end of the experiment [5]. More sophisticated studies using sildenafil as the pretreatment PDE-5 inhibitor showed a dose-dependant reduction in the rise of PAP after exposure to hypoxia. Moreover, sildenafil also attenuated pulmonary hypertension when given 14 days after the onset of hypoxia. As well as reducing the rise in PAP, sildenafil reduced the muscularization of the pulmonary arterioles and the remodelling process seen in the mice chronically exposed to hypoxia [4,6]. Zhao *et al.* [6] also assessed 10 healthy male volunteers in a randomized, double-blind study. After 30 min of breathing 11% oxygen there was a decrease in arterial oxygen saturation and an increase in PAP. Although the arterial oxygen saturation remained the same, the increase in PAP was virtually abolished in the group pretreated with sildenafil. Two independent trials have, albeit with small samples, found that sildenafil protects against HAPE in humans [7,8]. Also, both groups found that sildenafil improved exercise performance at altitude. Further evidence for the beneficial use of sildenafil with HAPE was presented at the VI World Congress on Mountain Medicine last year in China; work by Kojonazarov *et al.* [9] showed not only that sildenafil reduces PAP in the acute setting but that 30 days of sildenafil (50 mg three times daily) in a patient with HAPE significantly improved the quality of life and increased tolerance to exercise capacity. Quality of life was assessed not on sildenafil's original licensed action but on the Kansas City cardiomyopathy questionnaire. The action of sildenafil may go beyond reducing PAP in hypoxic conditions. A recent study on cultured human pulmonary artery smooth muscle cells showed that sildenafil has an antiproliferative effect [10].

The evidence for the use of sildenafil in preventing or treating HAPE is compelling. PDE-5 is found in abundance in lung tissue. Selective inhibition of PDE-5 prevents the rise in PAP seen in hypoxic conditions. Sildenafil

not only prevents HAPE from occurring but can also reduce the rise in the acute setting. Furthermore, exercise tolerance is increased with sildenafil at altitude. Continued therapy with sildenafil could prevent pulmonary vascular remodelling, as seen with its antiproliferative effects. The ability to increase exercise capacity in severe hypoxic conditions gives weight to a commercial use. Continued use of PDE-5 inhibitors could allow climbers or trekkers to work more efficiently at altitude for longer periods. However, sustained use may increase the risk of adverse effects. In erectile dysfunction, sildenafil need only be effective for a short period; obviously, climbing at altitude may take longer than the average tryst. Therefore it may be reasonable to assess other PDE-5 inhibitors such as tadalafil, with a longer duration of action. Tadalafil is given as a single dose that can act on the penis for a potential of ≥ 24 h. A potential indication of what is possible was reported by Ghofrani *et al.* [11]; they compared the short-term impact of three PDE-5 inhibitors (sildenafil, tadalafil and vardenafil) on the haemodynamics and gas exchange in patients with pulmonary hypertension. All three caused significant pulmonary vasorelaxation with vardenafil being the quickest to provide the maximum effect. However, sildenafil and tadalafil were more selective for the pulmonary circulation. It is clear from these studies that sildenafil is effective in reducing the rise in PAP at altitude. Further trials are needed, and with tadalafil, before sildenafil is licensed for preventing HAPE. Only then will climbers be able to last longer and achieve greater peaks... at altitude.

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Abbreviations: AMS, acute mountain sickness; HAPE, high altitude pulmonary oedema; HACE, high altitude cerebral oedema; PAP, pulmonary artery pressure; NO, nitric oxide; PDE, phosphodiesterase.

ANTI-EMETIC THERAPY: UPDATING UROLOGICAL CANCER-CARE PROVIDERS

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INTRODUCTION

In recent years there have been several advances in the treatment of locally advanced bladder cancer and hormone-resistant prostate cancer. The Cochrane review of neoadjuvant chemotherapy for the treatment of invasive, clinically nonmetastatic bladder cancer has led some authors to advocate its use as the new standard of care [1,2]. Similarly, the arrival of taxanes (docetaxel) has sparked new interest in systemic chemotherapy for patients with hormone-resistant prostate cancer. Two trials, SWOG 99–16 and TAX 327, showed a survival benefit for patients treated with docetaxel-based chemotherapy [3–5]. The role of radiotherapy in treating testicular and prostatic tumours is well established, and currently the role of chemoradiation in treating bladder cancer is being investigated [6]. There is therefore little

doubt that chemo- and radiotherapy will play an ever-increasing role in the daily practice of surgeons treating patients who have cancer. Urologists need to be aware not only of the benefits of these new therapies, but also of the associated toxicities and their management.

Despite recent advances in anti-emetic therapy, chemotherapy-induced nausea and vomiting (CINV) and radiotherapy-induced nausea and vomiting (RINV) are consistently rated as two of the most distressing side-effects of cancer therapy [7]. However, since the introduction of 5-hydroxytryptamine (HT)₃-receptor antagonists, nausea is often reported as more distressing to the patient than vomiting. Furthermore, the incidence of both symptoms, particularly in the delayed phase (>24 h after therapy), is still underestimated by both physicians and

TABLE 1 Risk of developing CINV; based on MASCC guidelines from <http://www.mascc.org> [8]

Risk of emesis, % of patients	Chemotherapeutic agent
High, >90	Cisplatin Cyclophosphamide
Moderate, 30-90	Carboplatin Ifosfamide
Low, 10-30	Paclitaxel Methotrexate Mitoxantrone
Minimal, <10	Bleomycin Vinblastine Vincristine

nurses. If untreated or inadequately controlled, CINV and RINV can result in physically damaging conditions such as dehydration, electrolyte imbalance and malnutrition. These not only affect the patient's quality of life but might also result in termination of treatment or lead to a delay in surgery.

The mechanisms behind CINV and RINV are not fully understood. Early research indicated a role for dopamine as a neurotransmitter in the emetic response. However, investigations involving the dopamine receptor antagonist, metoclopramide, indicated that a blockade of serotonin 5-HT₃ receptors is responsible for the anti-emetic effects of this agent when administered at high doses. The subsequent development and use of 5-HT₃ receptor antagonists for anti-emetic therapy has revolutionized the treatment of CINV and RINV, confirming the role of serotonin in the emetic response to cytotoxic treatments. However, recent investigations with neurokinin-1 receptor antagonists (which block the effects of substance P) highlighted the complexity of the emetic process. Current opinion supports a role for serotonin in the early part of the emetic response, followed by a delayed, substance P-mediated phase; however, the release of these two transmitters is thought to differ between cisplatin-based chemotherapy, non-cisplatin-based chemotherapy and radiotherapy regimens. The emetic effects of a particular treatment depends on the individual chemotherapy agents or the radiotherapy treatment schedule involved. Some chemotherapy agents are classified as highly emetogenic,

Risk group	Acute onset CINV	Delayed onset CINV
High	5-HT ₃ antagonist + dexamethasone + apretitant	Dexamethasone + apretitant
Moderate	5-HT ₃ antagonist + dexamethasone	Dexamethasone
Low	Low-dose corticosteroid	As required
Minimal	No prophylactic anti-emetic	As required

All anti-emetic medication needs to be administered before starting chemotherapy.

TABLE 2 Best recommended management of CINV according to risk groups; based on MASCC guidelines from www.mascc.org [8]

and likely to induce emesis in >90% of patients, whereas others are less so, or unlikely to induce an emetic response [8] Table 1. For radiotherapy, the irradiated volume, treatment site, radiation dose per fraction and total radiation dose affect the risk of developing RINV [7], and combined chemotherapy-radiotherapy regimens, might incur a higher risk of nausea and vomiting than the risk from the individual chemotherapy or radiotherapy schedules alone. Furthermore, the severity of the emetic response might depend on whether the chemotherapy-radiotherapy is implemented sequentially or concomitantly. Additionally, individual patient-related factors, e.g. female sex, younger age and previous history of nausea and vomiting, can all affect the risk of both CINV and RINV.

Current anti-emetic guidelines, endorsed by the Multinational Association for Supportive Care in Cancer (MASCC) in association with the American Association of Clinical Oncology and several other international oncology groups, recommend the prophylactic use of a 5-HT₃ receptor antagonist in combination with a corticosteroid for preventing CINV and RINV after moderate-to-high risk therapy [8] (Table 2). Additionally, the recently introduced neurokinin-1-receptor antagonist, apretitant, is recommended for use in combination with a 5-HT₃ receptor antagonist and dexamethasone after highly emetogenic chemotherapy [7]. It is important that these guidelines are fully adhered to, but when considering which anti-emetic regimen is the most appropriate for a particular patient, it is also important to consider individual patient-related factors. Furthermore, some patient groups, e.g. the young or the elderly, might need special consideration because of age-related factors that might influence

treatment decisions. The precise role of urologists in this process will no doubt depend on the individual and on regionally local arrangements. Nonetheless, to facilitate smooth delivery of modern oncological services, urologists need to be aware of the problems of patients with cancer who are receiving chemotherapy and/or radiotherapy, at least to be able to counsel them.

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Abbreviations: **(CI)(RI)NV**, (chemotherapy-induced) (radiotherapy-induced) nausea and vomiting; **MASCC**, Multinational Association for Supportive Care in Cancer.

TECHNIQUES FOR THE INTRADETRUSOR ADMINISTRATION OF BOTULINUM TOXIN

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INTRODUCTION

The current use of botulinum toxin (BTX) is increasing in clinical medicine. Although still unlicensed for use in the urinary tract, urologists are beginning to realise its potential in treating many aspects of lower urinary tract dysfunction. Most urological studies using BTX now focus on detrusor overactivity (DO) [1–3]. The original description of the use of BTX for treating patients with neurogenic DO (NDO) was of BTX-A being injected through a collagen-based flexible needle using a rigid cystoscope [4]. Since then the details of the method have developed but the way in which the toxin is administered into the bladder has not been standardized, and indeed practice varies around the world. In this comment we discuss the various techniques and the development of a minimally invasive local-anaesthetic technique that is now widely used in the UK.

TECHNIQUES OF INTRADETRUSOR INJECTIONS TO TREAT DO

The rationale for using BTX injections into the bladder in preliminary studies was based on its known effect of blocking the parasympathetic release of acetylcholine, akin to its mechanism of action in skeletal muscle [4]. In the initial experience with BTX-A and NDO, the trigone was avoided, as it was thought that paralysing the trigonal muscle

might induce VUR. Since then there has been mounting evidence that BTX may also affect sensory nerves [5], and as afferent mechanisms have an important role in the pathophysiology of DO, some investigators in the USA have advocated injecting the trigone [6], thinking that trigonal injections would affect the region with the highest density of afferent nerve fibres [7,8]. These authors did not formally assess patients for VUR, but reported no episodes of symptomatic pyelonephritis in the treated patients. To resolve the issue as to which method is more effective for treating DO, trials of trigonal vs non-trigonal injections of BTX are eagerly awaited.

An open-label study using BTX-A for both patients with NDO or idiopathic DO (IDO) was started in 2002. Initially BTX was injected using a rigid cystoscope with the patients under sedation. Thereafter, the clinicians involved, led by Prokar Dasgupta at the National Hospital for Neurology and Neurosurgery, London (NHNN), began exploring an alternative method using a flexible cystoscope and an ultra-fine 4 mm flexible needle for the injection (Olympus, Keymed, UK). The objective was to ensure that the toxin could be delivered at an optimum depth into the submucosa or detrusor muscle, but not beyond. Experiments were carried out which involved injecting oranges under water using the ultra-fine needle, but it was soon realized that the needle was not steady

enough to pierce the fruit's tegument. To overcome this, a fine sheath (27 G) was introduced through the working channel of the cystoscope and the ultra-fine needle was passed through this sheath. The sheath not only provided the necessary stability to the needle, resulting in excellent operator control and precise injection, but also protection to the flexible cystoscope in case of inadvertent puncture whilst feeding the needle down the channel. This was soon translated into clinical practice, and has since become known as the 'Dasgupta technique', a minimally invasive day-case procedure performed under local anaesthesia [9].

Prophylactic antibiotics and 20 mL of 2% lignocaine intraurethral gel are administered before the procedure. The injections are evenly distributed among the dome, posterior, right and left lateral walls of the bladder, avoiding the trigone. The technique has obvious benefits in terms of cost and ease of administration, particularly in those with advanced neurological disease or significant comorbidity who are unfit for general or spinal anaesthesia. In addition, the needle length is such that injection beyond the bladder is unlikely. Furthermore, as an ultra-fine needle is used the chance of backflow of the toxin after removing the needle is reduced. These two factors may detract from the technique when a longer and wider collagen needle is used with rigid cystoscope injections, as traditionally used in mainland Europe and the USA.

The 'Dasgupta technique' is quick, the procedure taking on average 20 min. It is also well tolerated; 75 patients treated at the NHNN were asked to score the discomfort experienced on a verbal 11-point box scale (between 0 and 10). The mean (SD) scores obtained were 3.2 (0.3) and 3.3 (0.4) in 44 patients with NDO and 31 with IDO, respectively [10]. Patients who have a good response to treatment are willing to undergo repeat injections when their symptoms recur, which provides the firmest evidence of the technique's acceptability. In the very few patients who tolerated the procedure poorly, instillation of 40 mL of 2% lignocaine for 30 min before injection was beneficial to that treatment and subsequent ones. The initial results of the open-label study using this technique have been extremely promising for subjective (voiding diary outcomes) and clinical (urodynamic) variables, independent of the cause of DO [10].

TABLE 1 The technique and outcome with intradetrusor BTX injections

Reference	Study group (N)	Technique/ injections	Anaesthesia	Toxin type/ dose (units)	Duration of effect, weeks	Outcome
Schurch <i>et al.</i> [4]	NDO (21)	RC/FN; 20 or 30 at 10 U/mL/site	Not stated	A (200 or 300)	Up to 36	At 6 weeks 17/19 continent. At 16 & 36 weeks, 7/11 continent. Improvement in MCC, RV, PVR, MDPV, BC at 6, 16 and 36 weeks
Reitz <i>et al.</i> [14]	NDO (200)	RC/FN; 30 at 10 U/mL/site	LA/SA/GA	A (300)	Up to 36	At 12 weeks 132/180 continent. At 36 weeks 72/99 continent. Improvement in MCC, RV, MDPV, BC at 12 & 36 weeks
Schurch <i>et al.</i> [15]	NDO (59) RCT placebo- controlled	RC/FN; 30 at 1 mL/site	LA/SA/GA	A (200 vs 300 vs placebo)	Up to 24	Significant reduction in incontinence episodes with both doses of BTX for study period (24 months) except 12 and 18 weeks in the 200 U group. Vs placebo difference between groups significant in favour of 300 U at 2 & 6 weeks and in 200 U group at 24 weeks. Improvement in MCC, RV, MDPV at all times and in QoL using I-QOL questionnaire at all times with both doses
Kuo <i>et al.</i> [16]	NDO (12)/ IDO (8)/ DO with previous BOO (10)	RC + 23-G IN; 40 at 5 U/0.2 mL/site	GA	A (200)	Follow-up data at 2 and 12. Mean efficacy 5.3 months	8/30 continent; 14/30 had improvement in symptoms; 8/30 treatment failures. Success considered if patients continent with no voiding difficulty, IPSS improved >50%, or incontinence improved by ≥1 grade on scale of 0–3. Symptom scores improved vs baseline at 2 and 12 weeks (except emptying symptoms at 2 weeks) and MCC, BNOT, MDPV, Q _{max} , PVR, VE improved at 2 but not 12 weeks, except MDPV
Smith <i>et al.</i> [6]	NDO (21), IDO (17)	RC + IN; 30–40 for NDO and 10 for IDO at 0.5–1 mL/ site	Sedation	A (100–300)	Up to 36	In patients with MS and detrusor hyper- reflexia 12/18 reported subjective favourable response, similar ratio of improvement reported in IDO group but no data presented. Grouped data of baseline vs 6 months show significant changes in frequency episodes (32), and MCC (22) but not in MDPV
Rapp <i>et al.</i> [17]	Symptoms of OAB (35) (six with history of neurological disease)	RC + collagen IN; 30 at 10 U/0.1 mL/ site	Sedation	A (300)	Up to 36	12/35 reported complete resolution of symptoms, 9/35 slight improvement and 14/35 no improvement. Improvement in QoL at 3 weeks and 6 months (data on 24 patients). Significant pad reduction in those with urge incontinence
Werner <i>et al.</i> [18]	IDO (26)	RC + 23-G Bard IN; 30 at 3.33 U/mL/ site	SA/GA	A (100)	Up to 36 Only two patients re-injected so far (efficacy reported as lasting for 5 and 10 months)	Significant reduction in frequency and nocturia at 4 and 12 weeks. Significant improvement in MCC at 4 and 12 weeks and increase in PVR at 4 weeks. 12/26 continue to have DO at 4 weeks and 7/20 at 12 weeks. Follow-up at 36 weeks in five patients only, therefore no statistics performed. At 4 weeks 18/26, at 12 weeks 16/20 and at 36 weeks 1/5 was continent. Significant subjective improvement in all urge-related items evaluated by the KHQ at 4 and 12 weeks.
Popat <i>et al.</i> [10]	NDO (44)/ IDO (31)	FC/ultra-FN down FC sheath; 30 for NDO and 20 for IDO at 10 U/mL/ site	LA	A (300) NDO (200) IDO	Up to 16	At 4 weeks 25/39 (NDO), 13/24 (IDO) and at 16 weeks 16/29 (NDO) and 8/14 (IDO) were continent. Two patients unchanged in incontinence. Significant improvement in all clinical (frequency, urgency, urge incontinence) and urodynamic variables at 4 and 16 weeks in both IDO and NDO. Improvement similar between groups except NDO significantly better for urgency.
Rajkumar <i>et al.</i> [19]	IDO (15)	FC or RC (not specified); 30 at 10 U/mL/site	GA	A (300)	Mean efficacy 24 (range 10–52)	At 6 weeks DO eliminated in six, MCC increased in 10. Frequency, BFLUTS and KHQ scores significantly improved at 6 weeks. Seven patients had residual >90 mL (range 90–350) after injections.

(R)FC, (rigid) flexible cystoscopy; IN, injection needle; FN, fine needle; LA, GA, SA, local, general or spinal anaesthetic; MCC, maximum cystometric capacity; RV, reflex volume; PVR, postvoid residual volume; MDPV, maximum detrusor pressure on voiding; BC, bladder compliance; QoL, quality of life; BNOT, bladder neck opening time; Q_{max}, maximum urinary flow rate; VE, voiding efficiency; KHQ, King's Health Questionnaire, BFLUTS, British Female LUTS Questionnaire.

This minimally invasive technique has been adopted by some clinicians in the USA to treat patients with refractory overactive bladder, using 100 U of BTX-A [11]. Ten injections are used and delivered submucosally into the bladder base and trigone only. In their series of 10 patients the efficacy was similar to that after their older rigid cystoscopic technique involving 30 injection sites. The added benefit appears to be that no patient developed urinary retention or a high postvoid residual volume with the use of a reduced dose of BTX-A and this modified technique.

It was suggested that clinicians using the technique for the first few injections and for teaching or demonstration purposes might add a dye to the reconstituted BTX, e.g. indigo carmine [12] or methylene blue, to help identify injected areas and facilitate placing further injections. Care should be taken whilst doing this, as redox reagents like methylene blue can detoxify BTX by photo-oxidation [13].

As there are no standardized guidelines or outcome measures of what constitutes 'success' and 'failure' with this form of therapy, evaluating which of the currently used techniques is superior is therefore made difficult. Further trials and perhaps direct comparisons of rigid vs flexible cystoscopic techniques, with the same outcomes being measured, will establish whether the technique of administration has a role in the efficacy of treatment. Certainly injecting the trigone systematically will not be easily achieved using a flexible cystoscope. It is reassuring that the results obtained using the flexible technique are comparable to and in some cases surpass those published globally using rigid cystoscopy. Table 1 [4,6,10,14–19] shows the results of various studies using BTX to treat DO, and the techniques used.

MENTORSHIP AND REPRODUCIBILITY OF THE 'DASGUPTA TECHNIQUE'

Apart from efficacy, for a technique to be a 'success' it should be simple to reproduce and widely adopted in the hope of becoming 'standard practice' for all clinicians offering the therapy. Results from the use of BTX in the treatment of intractable DO show remarkable efficacy, thereby prompting increasing interest and awareness amongst the urologists and urogynaecologists of the UK and indeed worldwide.

Through a research grant from the Multiple Sclerosis Society of Great Britain and Northern Ireland, the team in the department of Uro-Neurology at NHHN provided a service to all those clinicians and nurses requesting some form of training in the 'Dasgupta technique'. The visiting consultants and trainees attended the department for a demonstration of counselling patients before treatment, reconstitution of BTX-A, the injection technique, and instruction about the follow-up. The visitors were able to learn the technique and ask questions on the indications, efficacy, side-effects and pitfalls of its use. However, the most important thing demonstrated to them by interacting with the patients was the extraordinary improvement in quality of life that this treatment provides.

To date 36 senior urologists and urogynaecologists have been trained in the minimally invasive technique, and have completed a standardized questionnaire about their current practice. Everyone who attended their training day found it to be helpful and the technique easily reproducible. About a third are currently treating patients with BTX, and all of them are using the flexible cystoscopic method, although two of the consultants are using general anaesthesia. Two consultants, in their experience, found that patients with IDO did not tolerate the procedure as well, and offer rigid cystoscopy under general anaesthesia to this group, but continue to use the minimally invasive technique for their patients with NDO. The commonest reason for those who are not using injection is local lack of agreed funding.

It seems highly likely that the possibility to give such effective treatment for DO by the minimally invasive day-case 'Dasgupta technique' will have a major impact on urological practice.

CONFLICT OF INTEREST

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Abbreviations: **BTX**, botulinum toxin; **(I)(N)DO**, (idiopathic)(neurogenic) detrusor overactivity; **NHNN**, National Hospital for Neurology and Neurosurgery.