Comparative study between Percutaneous Posterior Tibial Nerve Stimulation Versus Propiverine Hydrodchloride for Treatment of Overactive Bladder

Thesis

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LIST OF ABBREVIATIONS

Abbrev.	Meaning
ACh	Acetylcholine
BOO	Bladder outlet obstruction
BTX	Botulinum toxin
CICS	Clean intermittent self-catheterization
CNS	Central nervous system
CYP450	Cytochrome P450
DO	Detrusor overactivity
ER	Extended release
ICS	International Continence Society
IR	Immediate release
LUTS	Lower urinary tract symptoms
OAB	Overactive bladder
OTG	Oxybutynin chloride topical gel
PAG	periaqueductal gray matter
PBS	Painful bladder syndrome
PMC	Pontine micturition center
PNE	Peripheral nerve evaluation
PTN	Posterior tibial nerve
PTNS	Percutaneous tibial nerve stimulation
RCT	Randomized controlled trial
SANS	Stoller Afferent Nerve Stimulations
SNS	Sacral nerve stimulation
TENS	Transcutaneous electrical nerve stimulation
UUI	Urinary urge incontinence

Introduction:

Overactive bladder (OAB) refers to a complex of urinary symptoms defined by the International Continence Society (ICS) as urgency, with or without urgency incontinence, usually accompanied by frequency and nocturia and without proven infection or other obvious pathology . The symptom complex is suggestive of detrusor overactivity, which can be further defined as being of unknown cause (idiopathic detrusor overactivity or due to a neurological condition (neurogenic detrusor overactivity), **(Abrams et al, 2002).**

Overactive bladder (OAB) symptoms (urgency, frequency, nocturia and urge incontinence) are frequent complaints of patients attending urology and gynecology clinics. In many patients, the cause for these symptoms is detrusor overactivity (DO) which in most cases is idiopathic with no obvious underlying neurological abnormality. Patients with DO also suffer from sleep disturbance, psychological distress and disruption of social and work life. Quality of life scores are consistently reduced in this group of patients **(Govier FE et al, 2001).**

There are a variety of treatment options available for the treatment of OAB. The simplest involve advice on fluid intake. Encouraging an adequate but not excessive fluid intake (1.5 L per day). Bladder retraining (bladder drill) is often beneficial in short term but many patients relapse. Supervised pelvic floor muscle

training can reduce particularly urgency in some patients (**NICE Clinical Guideline No 40, 2006).**

The mainstay of treatment currently is the use of anticholinergic drugs. Although there has been considerable development in these drugs over the last decade, with more bladder specific preparations available, many patients even if they find them effective can struggle with side-effects. These commonly include dry mouth, constipation and heartburn. Of particular concern in the elderly, is possible cognitive side-effects seen with some drugs such as confusion or memory loss which may limit their use. New approaches such as using a transdermal route of administration may be helpful in reducing the side-effects although skin irritation can be a problem **(Brazelli M et al, 2006).**

Propiverine is a well established antimuscarinic agent with a mixed mode of action in the treatment of symptoms associated with overactive bladder (OAB). As well as blocking muscarinic receptors in the detrusor muscle, the drug also inhibits cellular calcium influx, thereby diminishing muscle spasm. In patients with symptoms of OAB resulting from idiopathic detrusor overactivity (IDO) or neurogenic detrusor overactivity (NDO), propiverine demonstrated dose-dependent efficacy and tolerability, with adverse events consistent with those associated with all antimuscarinic agents. In adults with IDO, propiverine demonstrated similar efficacy to that of other antimuscarinic

agents (including solifenacin, tolterodine, oxybutynin and imidafenacin) and, in adults with NDO, propiverine and oxybutynin demonstrated similar efficacy. Propiverine was generally well tolerated in these patient populations, with a lower incidence of dry mouth than that associated with oxybutynin, **(Madersbacher et al, 2001).**

Newer second line treatment options include the use of intravesical botulinium toxin, sacral nerve stimulation and percutaneous posterior tibial nerve stimulation. **(Casanova N et al, 2006).**

Percutaneous posterior tibial nerve stimulation (PTNS) is a technique that was developed a decade or more ago but which does not appear to have become widely adopted into clinical practice. It is currently enjoying much interest with improved equipment and marketing. At a time when conservative and non-surgical treatment options are being encouraged for the management of many conditions, it seems reasonable to consider PTNS. The mechanism of action is not well understood and most of our knowledge comes from studying sacral nerve stimulation. There may be different modes of action in different clinical conditions. Some may involve the gate theory, by restoring control at the spinal segment gate as well as some supra spinal sites. Others may involve restoration of the balance between

inhibitory and excitatory control systems both centrally and peripherally **(Van Balken MR et al, 2007).**

Side-effects appear almost negligible, being limited to minor discomfort at the needle insertion site. Another problem seems to be the need for maintenance treatment after the initial 12 week course of therapy **(Van der Pal F et al, 2006).**

Aim of the work:

The aim of this study is focused on comparative study between the efficacy of percutaneous posterior tibial nerve stimulation (PTNS) versus propiverine hydrochloride for the treatment of the overactive bladder.

Anatomy :

The lower urinary tract can be divided into the bladder and urethra. At the junction of these two continuous, yet discrete, structures lies the vesical neck. This hybrid structure represents that part of the lower urinary tract where the urethral lumen traverses the bladder wall before becoming surrounded by the urethral wall. It contains portions of the bladder muscle, and also elements that continue into the urethra. The main function of the lower urinary tract is to store and expel urine. The urinary bladder is a hollow organ with strong muscular wall, the detrusor muscle, which functions as a reservoir. When empty, the bladder is entirely located within the pelvis. As it fills, it can contain about 500 cc or more while it rises into the abdominal cavity. The bladder neck, urethra and pelvic floor form the bladder outlet and facilitate urine evacuation. From both sides the ureters penetrate the bladder in its posterolateral wall after tunneling the bladder wall obliquely over a 1-2 cm long to end as the ureteral orifices. The posterolateral angles formed by the ureters orifices and the internal orifice of the urethra form a triangular area: trigone **(Groat de W, 1993)**.

The bladder consists of the detrusor muscle, covered by an adventitia and serosa over its dome, and lined by a submucosa and transitional cell epithelium. The muscular layers of the

detrusor are not discrete; nevertheless, in general, the outer and inner layers of the detrusor musculature tend to be longitudinal, with an intervening circular–oblique layer. The mucosa is continuous with the lining membrane of the ureters and renal pelvis, and below with that of the proximal urethra. The areolar tissue of the submucosa connects the mucosa only slightly; it makes the bladder look wrinkled when contracted. Over the trigone the mucous membrane is firmly attached to the muscular coat, and thus looks smooth and flat. The outer tunica serosa is derived from the peritoneum **(Gray H, 1995)**.

The physiological internal sphincter maintains continence by closure of the bladder neck and proximal urethra. **(Steers W, 1998)**.

Trigone

Within the bladder there is a visible triangular area known as the vesical trigone. The two ureteral orifices and the internal urinary meatus form its apices. The base of the triangle, the interureteric ridge, forms a useful landmark in cystoscopic identification of the ureteric orifices. This triangular elevation is caused by the presence of a specialized group of smooth muscle fibers that lie within the detrusor, and arise from a separate embryologic primordium. They are continuous above with the ureteral smooth muscle; below, they continue down the urethra.

Urethra

The urethra holds urine in the bladder and is therefore an important structure that helps determine urinary continence. It is a complex tubular viscus extending below the bladder.

Striated urogenital sphincter

The outer layer of the urethra is formed by the muscle of the striated urogenital sphincter (which is Striated urogenital sphincter) which is found from approximately 20% to 80% of the total urethral length (measured as a percentage of the distance from the internal meatus to the external meatus)

(figure 1). In its upper two-thirds, the sphincter fibers lie in a primarily circular orientation; distally, they leave the confines of the urethra and either encircle the vaginal wall as the urethrovaginal sphincter or extend along the inferior pubic ramus above the perineal membrane (urogenital diaphragm) as the compressor urethrae**, (Delancey et al, 1986).**

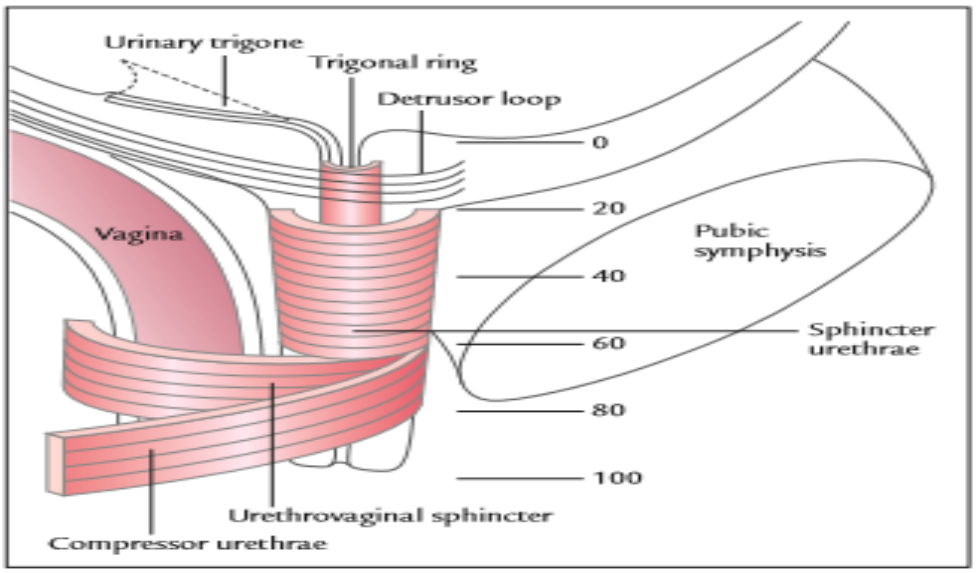

Fig. 1 *Striated urogenital sphincter muscle and trigonal musculature within the bladder base and urethra (cut in sagittal section). The ruler indicates the locations of structures along the urethral length.*

(John and Delancey, 2006)

Urethral smooth muscle

The smooth muscle of the urethra is contiguous with that of the trigone and detrusor, but can be separated from these other muscles on embryologic, topographical and morphologic grounds. It has an inner longitudinal layer, and a thin outer circular layer, with the former being by far the more prominent of the two . The layers lie inside the striated urogenital sphincter muscle, and are present throughout the upper four- fifths of the urethra. The configuration of the circular muscle suggests a role in constricting the lumen, and the longitudinal muscle may help to shorten and funnel the urethra during voiding.