84

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Title (type in CAPITAL LETTERS, leave one blank line before the text):

AN EXPERIMENTAL MODEL REPRODUCING THE RESPONSE OF URINE FLOW RATE TO PENILE CUFF PRESSURE OBSERVED IN MEN

Aim of study

One in three men will develop lower urinary tract symptoms (LUTS) in later life [1]. These symptoms can be attributed either to bladder outflow obstruction or to a weak bladder contraction. While conventional cystometry can in principle separate the two groups [2], such measurements are expensive, time consuming, uncomfortable and have some morbidity [3]. Therefore, prostatectomy is often undertaken on the basis of symptoms and flow-rate only. A quick, non-invasive means for measuring voiding function would be of considerable benefit to such patients [4].

We are investigating the use of an inflatable penile cuff to obstruct flow progressively during emptying of the bladder. We make continuous recordings of cuff pressure and urine flow rate, which give characteristic pressure-flow graphs for normal and obstructed subjects (fig 1). The flow typically maintains a fixed value to a knee-point pressure, beyond which it falls steadily to zero. We believe this characteristic conveys important information about the function of the bladder and outlet. The aim of this study was to determine the precise relevance of each feature of the pressure-flow characteristic, using a simple experimental model of the bladder-outlet-cuff system.

Methods

The bladder was represented by a fixed head of 120cm water, while the urethra was represented by sections of soft, thin-walled latex tube. The constriction at the prostatic urethra was modelled by a tube of 3.8mm diameter, while the penile urethra was 9.5mm in diameter.

In vivo, the penile cuff applies a compressive obstruction to the penile urethra [5]. The enlarged prostate may have a similar compressive effect on the prostatic urethra [6]. In our model, the prostatic and penile 'urethras' passed through separate airtight boxes. A pressure (p_{pros}) was applied to the first box to simulate the prostatic opening pressure, while a pressure (p_{cuff}) applied to the second box corresponded to the penile cuff pressure.

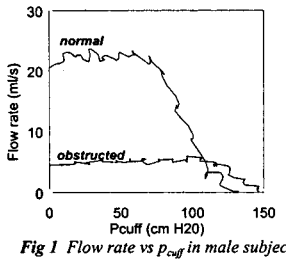

Fig 1 Flow rate vs p_{cuff} in male subjects

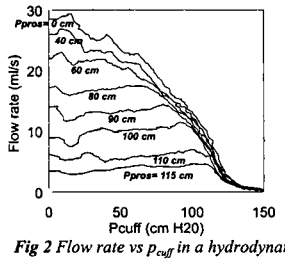

Fig 2 Flow rate vs p_{cuff} in a hydrodynamic model

Results

Fig 2 shows the relation of flow rate with cuff pressure (p_{cuff}), for a range of prostatic opening pressures (p_{pros}) in the model, and exhibits the following features. First, and irrespective of the value of p_{pros}, flow stops completely only when the simulated cuff pressure (p_{cuff}) exceeds the simulated bladder pressure of 120cm water. Second, flow is relatively constant while p_{cuff} is below a knee-point pressure approximately equal to p_{pros}, the pressure applied at the prostatic obstruction. Third, when p_{cuff} exceeds the knee pressure, a graph of $[flow\ rate]^2$ versus p_{cuff} gives a straight line whose slope is related to the minimum diameter of the urethral obstruction, here 3.8mm. These observations are supported by the underlying hydrodynamic theory [6,7]. The similarities between results in the model and in

humans are notable. By analogy with the model, we have therefore raised the following hypotheses for human subjects:

- *Only when penile cuff pressure exceeds bladder pressure will urine flow be stopped completely;*
- *The knee-point pressure at which flow begins to decrease corresponds to the prostatic opening pressure or opening pressure of the flow-controlling zone [6,7];*
- *Beyond the knee pressure, the flow/pressure relation can be used to estimate the minimum urethral diameter.*

Conclusion

We believe our findings may be of significant benefit in understanding and managing patients with outflow disorders, particularly the role of the putative flow-controlling zone. We now plan to test our hypotheses formally in a large group of both symptomatic and asymptomatic subjects.

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85A

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TOLERABILITY AND EFFICACY OF TROSPIUM CHLORIDE IN A LONG-TERM TREATMENT (52 WEEKS) IN PATIENTS WITH URGE-SYNDROME: A DOUBLE-BLIND, CONTROLLED, MULTICENTRE CLINICAL TRIAL

Aims of Study:

Trospium chloride (TCl) is already established as an efficacious anticholinergic in the treatment of urge-syndrome. To confirm also the positive safety results of former studies the primary objective of this study was to investigate the long-term tolerability and safety of trospium chloride over a treatment period of 52 weeks. Secondary objective was to investigate the efficacy of trospium chloride in these patients.

Methods:

As an active control group oxybutynin (Oxy) was chosen because placebo was not justified in this investigation of long-term application due to ethical reasons. Patients were assigned to TCl or Oxy in a randomisation ratio of 3:1. A treatment period of 52 weeks was planned with a follow-up period of 2 up to 4 weeks. Trial medication was 2 x 20 mg TCl daily or 2 x 5 mg Oxy daily, respectively. Main criterion for inclusion was the diagnosis: urge-syndrome or urge-incontinence, solely or associated with stress-incontinence or neurogenic detrusor hyperactivity. For safety evaluation data of adverse events, laboratory tests, physical examination, resting ECG and cardiovascular examinations were obtained. Additionally, the tolerability of the study drugs was assessed by the patient and the investigator. The main efficacy variable was the maximum bladder capacity (CCmax). Further urodynamic variables and data of the patients' diary (frequency of micturitions, incontinences and number of urgencies) were evaluated.