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Parkinsonism and Neurogenic Bladder

Experimental and Clinical Observations

S. Raz

Department of Surgery, Division of Urology, University of California School of Medicine, Los Angeles, California, U.S.A.

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Summary. In a group of patients suffering from Parkinson's disease, beside neurogenic bladder dysfunction, we have also found dysfunction affecting the external sphincter musculature. Treatment with L-Dopa probably improves the urethral symptoms by providing a relaxing effect on the urethral closure pressure together with better coordination of the pelvic floor and external sphincter Mechanism during micturition. The effect was parallel to the improvement in Parkinsonion symptoms. Experimental studies demonstrate the ability of L-Dopa to reduce urethral closure pressure and this effect was related to a central effect on the skeletal musculature.

Key words: Parkinsonism - Neurogenic bladder - L-Dopa.

The problem of urinary disturbance in a patient suffering from Parkinson's disease (PD) raises the question of the exact relationship between the two conditions.

Urinary symptoms in PD may be due to: A) Conditions unrelated to the neurogenic disease such as Benign Hypertrophy of the Prostate. B) Treatment of the neurological disease. For example one of the accepted methods of treatment of PD is the use of cholinolytic agents which may affect a the contractility of the bladder and lead to urinary symptoms. C) The neurological disease itself. This group of patients are discussed in this paper.

Although PD was described over 150 years ago, there are relatively few reports concerning urinary tract involvement in this disease (1, 2, 5, 6). Parkinson's disease is a clinical entity associated with a variety of pathological processes which involve the extrapyramidal system and produced by several different aetiological factors: 1. Drugs (phenothiazine), 2. Infections (encephalitis), 3. Vascular disease (atherosclerosis), and 4. Idiopathic. Neurologically this syndrome is a motor lesion characterized by an increase in tonus of the skeletal musculature, bradykinesia, tremor and a loss of the automatic reflexes with resultant postural instability.

Autonomic dysfunction is often present in Parkinson's disease (constipation, seborrhoea, sweating, urinary symptoms, etc.). The incidence of involvement of the urinary tract ranges between 37% (5) to 70% (6) and all the studies refer to bladder dysfunction. Patients are classified as hypoactive bladder or hyperactive bladder dysfunction according to the clinical symptoms, intravenous urogram and cystogram. Nevertheless, Parkinson's disease is a motor lesion of the nervous system affecting the basic tonus of the skeletal muscles. It seems logical to believe that the striated muscle of the external urethral sphincter and the pelvic floor will also be involved in this dysfunction. The same changes of increased tonus and loss of automatic reflexes may involve the pelvic floor muscles producing a relative urinary outflow obstruction due to dysfunction and lack of normal relaxation of the external sphincter during micturition.

The aim of this work is to present part of a study carried out in a group of Parkinson patients concerning this relative outflow obstruction. It is well-known that the improve-

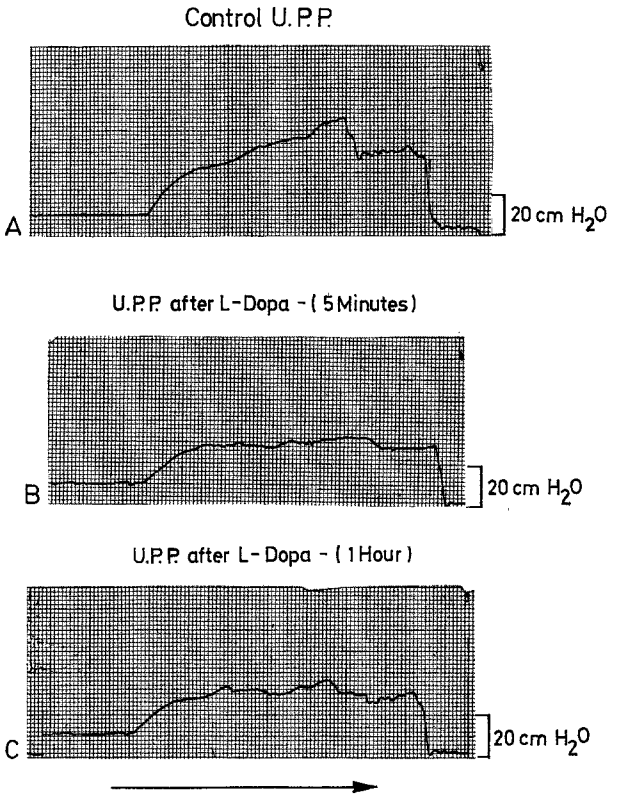

Fig. 1. Control urethral pressure profile in an anaesthetized dog. (A) Showing a closure pressure of the urethra of 53 cm H_2O. (B) 50 mg of L-Dopa intravenously produce a drop in closure pressure of the urethra to 30 cm H_2O. (C) The effect is prolonged after an hour

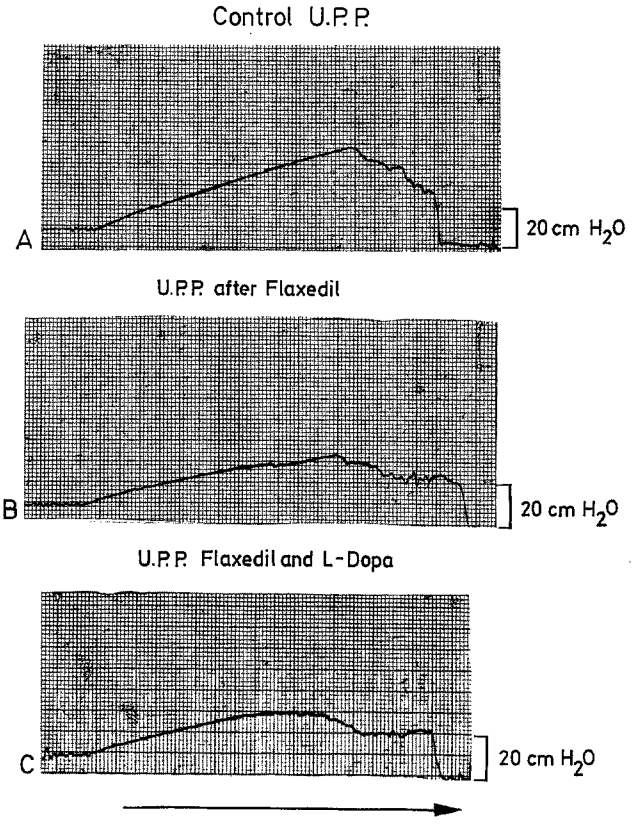

Fig. 2. Effect of Flaxedil on the closure pressure of the urethra (A & B). When 50 mg of L-Dopa were given, no further change in closure pressure of the urethra was found (C)

ment in urinary symptoms parallels the improvement in symptoms of Parkinson's disease following treatment. Since one of the most common drugs used in the treatment of Parkinson's disease is Laevo-Dopa (L-Dopa), we designed the present experimental (in-vivo and in vitro) study to determine the influence of this drug on the lower urinary tract.

EXPERIMENTAL STUDY 1. IN VIVO STUDY

Materials and Methods

Mongrel dogs, weighing 12-15 kg, were prepared with intravenous pentobarbitone general anaesthesia, an intravenous infusion and endotracheal intubation. Urethral pressure profile (U. P. P.) was performed using a modification of the Brown and Wickham technique (3). Pressures were recorded through a pressure transducer and Sanborn recorder. Immediately before the experiments, a fresh solution of L-Dopa, 250 mg in 500 cc of Normal Saline was prepared and 100 ml administered intravenously. In 6 of the 15 dogs studied Flaxedil (a curare-like skeletal muscle relaxant) was administered in the dosage of 1 mg/kg before L-Dopa was given.

Results

As seen in Fig. 1, the intravenous administration of 50 mg. of L-Dopa produced a rapid and persistent drop in closure pressure of the urethra as recorded by the change of the urethral pressure from 53 cm water in the control record (1 A) to 30 cm water after L-Dopa administration (1 B) . This change of pressure occurs mainly in the distal part of the urethra (external sphincter) and is very prolonged. After an hour we were able to record practically the same drop in urethral pressure (1 C).

As seen in Fig. 2, Flaxedil produced a marked drop in the closure pressure of the urethra from 50 cm water in the control (2 A) to 30 cm water (2 B). The further addition of 50 mg of L-Dopa intravenously did not change the closure pressure after Flaxedil, suggesting

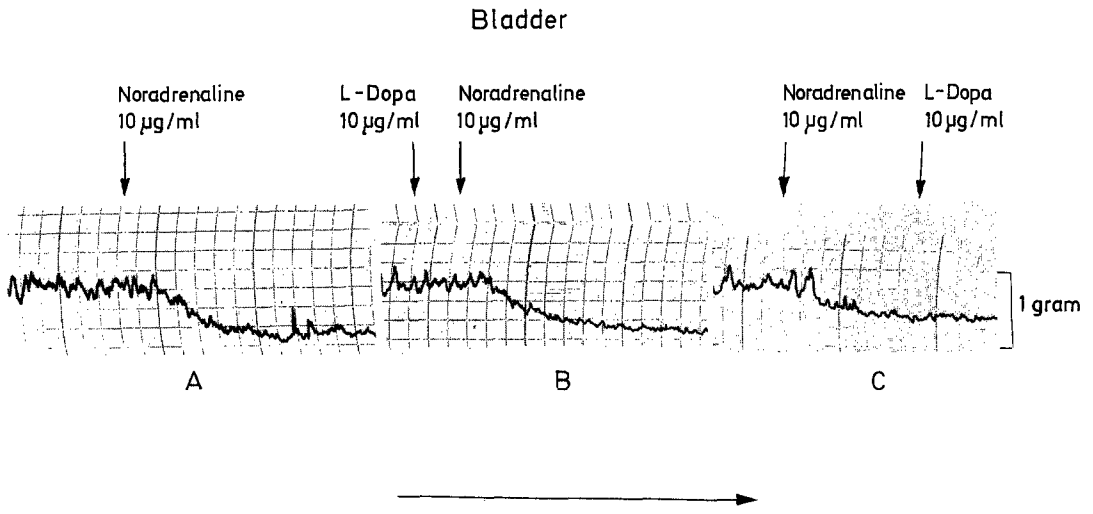

Fig. 3. Isometric study showing. (A) The inhibitory effect of Noradrenaline on bladder rhythmic activity and tonus. (B) L-Dopa added to the isometric bath before Noradrenaline. (C) After Noradrenaline

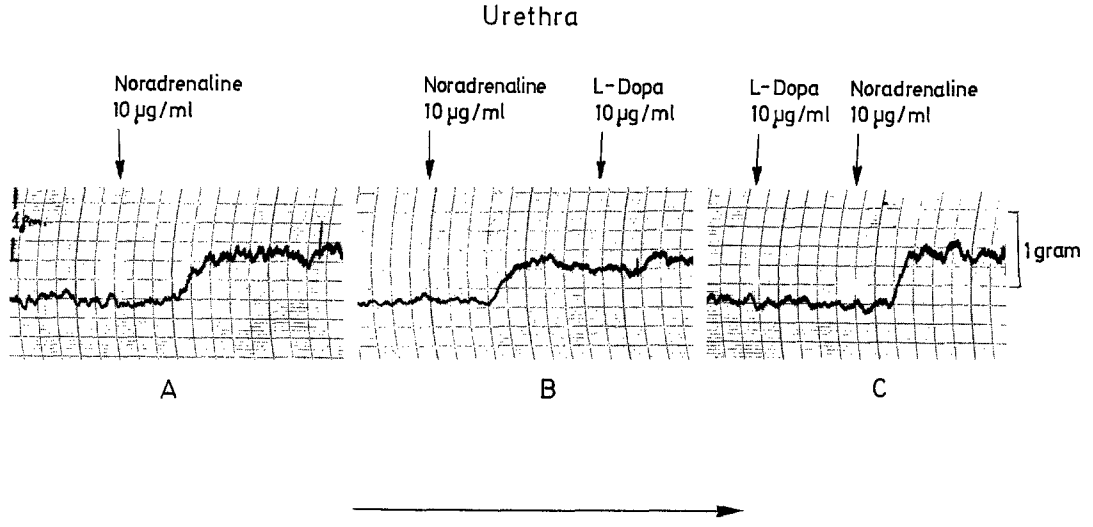

Fig. 4. Isometric study showing. (A) The stimulatory effect of Noradrenaline on the basic tone and activity of the urethra. (B) L-Dopa added after Noradrenaline. (C) Before Noradrenaline

that when compared to the above experiments, the relaxing effect of L-Dopa to the urethral closure pressure is related primarily to its effect on the striated muscle and L-Dopa probably does not affect the smooth muscle component of the urethral closure mechanism.

In order to investigate this theory further, another group of studies was performed using an in vitro technique which allowed the study of the smooth musculature component of the urethral wall.

EXPERIMENTAL STUDY 2. IN VITRO STUDY

Materials and Methods

The urethra and bladder of mongrel dogs were excised through a midline laparotomy under general anaesthesia, taking care to avoid stretching of the tissues. Separated pieces of bladder dome and urethral wall (transverse strips) were placed in Locke solution No. 2 at 4 degrees Centigrade. Using a 15 ml muscle chamber aerated with a 97% oxygen, 3% CO_2 mixture and maintained at 37 degrees Centigrade, the free pieces of tissue were examined using an isometric technique (10). Forty of these experiments were performed. Norepinephrine was used in a concentration of 10 µg/ml in the bath and a fresh concentrated solution of L-Dopa (in Locke solution No. 2) was used in a concentration of 10 µg/ml in the bath.

Results

As seen in Figure 3 (A) Noradrenaline inhibited the basic rhythmic activity and tone of the

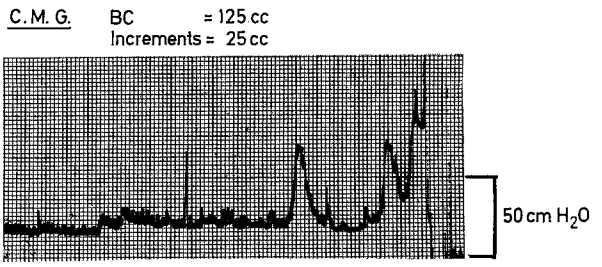

Fig. 5. Cystometrogram of a patient suffering from Parkinson's disease with signs of upper motor neurone lesion with characteristic shift to left

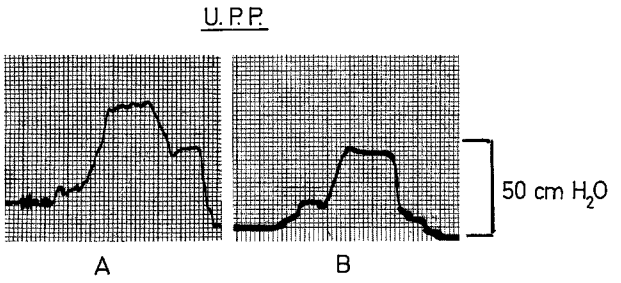

Fig. 6. U.P.P. before and after starting treatment with L-Dopa in a 47 year old patient suffering from PD, showing the decrease in closure pressure of the urethra after 3 weeks of treatment

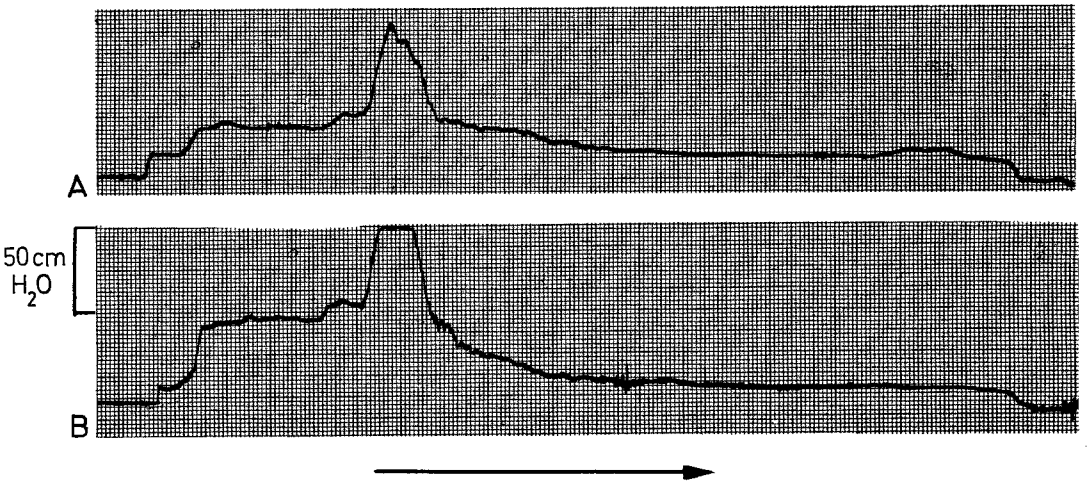

Fig. 7. U.P.P. (A) before and (B) after stopping the treatment of L-Dopa in a 52 year old patient suffering from PD, showing an increase in closure pressure of the urethra mainly in the region of the external sphincter

bladder (8). This response of the bladder smooth muscle to Noradrenaline was not changed by the previous addition of L-Dopa to the bath (3 B) or by the addition of L-Dopa to the bath after Noradrenaline (3 C).

Noradrenaline increased the basic tonus and rhythmic activity of the urethra (Fig. 4). This excitatory effect of Noradrenaline was not enhanced or blocked by the previous or subsequent addition of L-Dopa.

In vivo studies showed an inhibitory effect of L-Dopa on the urethral closure pressure as measured by urethral pressure profile. In addition the lack of any further decrease in urethral closure pressure after skeletal muscle blockade by a curare-like drug suggests that this effect of L-Dopa on the closure pressure of the urethra is probably related to its effect on the skeletal musculature. The blocking effect of L-Dopa as described was recorded mainly in the distal part of the urethra, (site of the external sphincter) supporting the impression that the urethral relaxing action of L-Dopa is probably related to an effect on the skeletal musculature. The in-vitro studies support the above theory. L-Dopa failed to produce any blocking or enhancing effect on the smooth musculature of the urethra or its reaction to Noradrenaline, suggesting that the inhibitory effect of L-Dopa as seen in the in-vivo studies was due to skeletal muscle inhibition.

CLINICAL STUDY

Materials and Methods

A group of 15 patients suffering from Parkinson's disease was studied. Beside the clinical history, physical examination and intravenous pyelogram, a complete neurourological examination was performed. This examination includes cystometrogram, cystoscopy, urethral

pressure profile, reflex activity of the external sphincter (7), iced water test (8), and neural blocks when necessary (9). Patients receiving other drugs like cholinolytic agents for treatment of Parkinson's disease were excluded from the study. Patients suffering from other diseases such as prostatic hypertrophy were also excluded. Nine patients were examined before and after starting treatment with L-Dopa and these patients were examined while on treatment and also after stopping the treatment for a week.

Results

Eleven of the 15 patients suffered from signs compatible with an upper motor neurone lesion of the bladder. They suffered clinically from frequency, urgency and urge incontinence, and interrupted stream of urine. CMG showed a small bladder capacity with a shift to the left of the pressure-volume curve (Fig. 5). The sensation of imminent micturition was felt very early in the cystometrogram study. Ice water test was positive in 9 patients. In 4 of the 15 patients obstructive symptoms were found with poor stream and hesitancy. CMG showed a shift to the right with increasing bladder capacity, delay in appearance of the first sensation to void and absent or poor voiding contraction. In 10 of the 15 patients, treatment with L-Dopa reduced the closure pressure of the urethra as measured by urethral pressure profiles (Fig. 6) can also be appreciated in patients already receiving L-Dopa and whose treatment was interrupted for a week (Fig. 7). We were able to see in these cases an increase in the closure pressure of the urethra.

DISCUSSION

The tonus of the skeletal muscles is regulated by a spinal arc called the gamma loop. The muscle spindles receive inflow regulatory impulses from the gamma neuron localized in the anterior horn of the spinal cord. The outflow sensory impulses from the spindles regulate the activity of the anterior horn alpha motor neurone. Several impulses can regulate and change the activity of this reflex arc. Parkinson's disease affects this basic tonic activity by facilitating this tonic reflex, with the subsequent increase in skeletal muscle tonus. The external sphincter and the pelvic floor musculature, as part of the skeletal system, do not appear to escape this hypertonic change. In Parkinson's disease there is impairment of the coordination of automatic reflex activities. Micturition is also an automatic reflex and this dysfunction is present in Parkinson's disease. Previous studies demonstrated bladder dysfunction in Parkinson's disease without stressing the importance of the pelvic floor and external sphincter dysfunction. In the initiation of normal micturition, one of the important stages is pelvic floor relaxation occurring prior to maximal bladder contraction. In Parkinson's disease can be a delay in the normal relaxation of the pelvic floor producing hesitancy and a slow stream in addition there is a delay in the normal reflex coordinated cessation of micturition and this delay can explain the terminal dribbling so common in Parkinsonian patients.

L-Dopa treatment improved the urinary symptoms in 12 of the 15 patients. There was a parallel between inprovement in urinary symptoms and other symptoms (tremor, hypertony and bradykinesia). L-Dopa produced a decrease in closure pressure of the urethra in 10 of the 15 patients. This effect, as demonstrated by the in-vivo and the in-vitro studies, is an effect on the striated muscle of the urethra, L-Dopa can improve the urinary obstructive symptoms not only by reducing the pelvic floor and external sphincter hypertonus but also by a better coordination of the micturition reflex. More investigation needs to be done in order to evaluate the correlation between Parkinson's disease and urinary dysfunction. Bladder dysfunction is a well established occurrence in Parkinson's disease but it is our impression that outlet dysfunction plays an important role in the symptomatology of Parkinson's disease and is due to external sphincter hypertonus, lack of coordination of the normal pelvic floor relaxation during micturition and by lack of normal external sphincter function during interruption of micturition.

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Shlomo Raz, M. D.
Dept. of Surgery, Division of Urology
University of California School of Medicine
Los Angeles, CA 90024
U. S. A.