THE AUTONOMIC NERVOUS SYSTEM AND THE BLADDER DURING SPINAL SHOCK—AN EXPERIMENTAL STUDY

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INTRODUCTION

WHILE it is well recognised clinically that drugs, which modify the action of the bladder and its sphincters, are not effective during spinal shock to allow bladder evacuation, little information is available about the action of these drugs immediately after spinal cord injury. This experimental study was carried out on dogs, immediately after division of the spinal cord, *i.e.* during the period of spinal shock.

MATERIALS AND METHODS

Seven adult female dogs weighing between 8 and 14 kg. were used which were neither pregnant nor postpartum. Each dog was anaesthetised with intravenous sodium pentobarbital (Nembutal® 30 mg./kg.).

Intravesical Pressure Recording. Under aseptic conditions a vesicostomy was carried out as described by Lapidès *et al.* (1960). This allowed a 3-way Fr. 16 Foley catheter to be passed into the bladder. The irrigating channel was connected to a Statham² transducer (Model P23) and thence to a Grass³ polygraph (Model 5B). The bladder was emptied and 50 ml of 1 : 5000 chlorhexidine (Hibitane®) was instilled.

Intraurethral Pressure Recording. Two No. 4 ureteric catheters were placed under X-ray control in the proximal and middle thirds of the urethra to record intraurethral pressures U₁ and U₂, respectively (fig. 1). These catheters were shortened to be 10 cm. long, filled with 1 : 5000 chlorhexidine (Hibitane®) and connected to syringes driven by a Harvard pump, adapted to deliver 1 ml./hour and thence to Statham transducers, from which the intraurethral pressures were recorded on the Grass polygraph.

Drug Administration. Drugs were administered through a cannula in the external jugular vein. The drugs were suspended in 50 ml. of five per cent dextrose and infused over two minutes.

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FIG. 1

X-ray showing the position of the recording catheters, in the proximal and middle thirds of the urethra. The bladder is outlined with Hypaque and the Aliss forceps are applied to the mucosa adjacent to the external meatus.

Arterial Pressure Recording. A second cannula was inserted percutaneously in the femoral artery and connected to a transducer and thence to the polygraph to record blood pressure.

Spinal Cord Transection. After baseline studies which allowed each animal to act as its own control, the catheters were left in place, but disconnected from the transducers and the animal turned prone. A 10 cm. longitudinal incision was made over the spinous processes between T₉ and T₁₁. Two adjacent spinous processes were excised. This exposed the laminae which were removed to reveal the spinal cord. After the spinal cord had been elevated with umbilical tape, the cord was divided.

FIG. 2

Alpha adrenergic stimulation causes an immediate and sustained rise of U₁, U₂ and blood pressure, but no change in the intracystic pressure (ICP).

FIG. 3

During spinal shock alpha adrenergic blockade combined with beta adrenergic stimulation produces an impressive fall of U₁ and U₂. A Credé manoeuvre (C) allows effective bladder emptying.

RESULTS OF PHARMACOLOGICAL EXPERIMENTS DURING SPINAL SHOCK

During spinal shock there was no intrinsic activity of the bladder. There was some activity at U₁ but marked activity at U₂.

Effect of Alpha Adrenergic Stimulation. 0.1 mg. of phenylephrine hydrochloride (Neo-synephrine®) produced a very marked rise of U₁ and U₂ (fig. 2). No change in bladder pressure was noted. This was a very striking finding and frequently the pressures would rise from a resting pressure of 20 cm. of water to over 100 cm. of water.

Effect of Alpha Adrenergic Blockade. Five mg. of phentolamine (Regitine®) was used. This produced a marked fall in U₁ and U₂. The fall would be dependent on the resting urethral pressure, the higher the resting pressure, the greater would be the fall. Frequently, the pressure would fall from 25 to 5 cm. of water. Neosynephrine® would not produce such a marked rise in U₁ and U₂ when phentolamine had previously been given. Phentolamine had no effect on resting bladder pressure.

FIG. 4

During spinal shock urecholine produces a small rise in ICP, but a very marked rise in U₂.

Effect of Beta Stimulation. 0.1 mg. of isoprenaline hydrochloride (Isuprel®) produced falls of U₁ and U₂ pressures, but no changes in bladder activity.

Effect of Alpha Blockade combined with Beta Stimulation. This produced complete relaxation of U₁ and U₂ (fig. 3). It was then possible to empty the bladder almost completely with Credé manoeuvre. However, it was unfortunately noticed that this also produced a marked fall in the blood pressure to about 60/20 mm.Hg.

Effect of Parasympathetic Stimulation. 0.5 mg. of bethanechol chloride (Urecholine®) induced some bladder activity but no micturition contractions during spinal shock. The most interesting effect noted was a very marked rise in U₂ pressure to a pressure which was always greater than the bladder pressure (fig. 4).

DISCUSSION

Our experimental model differs in certain important respects from those of other investigators. To record intraurethral pressure Tanagho *et al.* (1969) used a large modified Enhörning catheter whereas Raz and Caine (1972) used the urethral profile as described by Brown and Wickham (1969) with a Fr. 12 catheter. Two No. 4 ureteric catheters occupy a far smaller cross section of the urethra and with the flow rate of 1 ml./hour, there would be as small a disturbance as possible to the true pressure. The importance of this is emphasised by Donker *et al.*

(1972) who found that the resting urethral pressure was proportional to the diameter of the recording catheter, but this has been disputed by Griffiths (1973).

Anaesthesia is an unfortunate necessity for this work, and there is no doubt that anaesthesia modifies cortical and spinal reflexes, so therefore the greatest caution must be taken in interpreting the results (Langworthy *et al.*, 1940).

Alpha stimulation during spinal shock has no effect on intravesical pressure but produces a very marked rise of U₁ and U₂ pressures. Alpha blockade does not affect the resting bladder pressure, but profoundly affects the urethral pressure. Edvardsen (1967) believed that an important component of the neurogenic bladder dysfunction in spinal shock was caused by excessive sympathetic activity. However excessive activity in the urethral 'internal sphincter' was not demonstrated in this study.

Beta stimulation relaxes the urethra. This has been supported by studies of urethral strips in muscle bath experiments (Raz *et al.*, 1972). It is interesting that in combination with alpha blockade it is so effective in relaxing the urethra and allowing bladder evacuation by the Credé manoeuvre. At present, this has no clinical application as the blood pressure fall is also catastrophic.

The results of parasympathetic stimulation are interesting. The urethral musculature regains its reactivity to drugs more rapidly than the detrusor, and it has been demonstrated by Rossier *et al.* (in print) that during spinal shock in spinal cord injury patients with an upper motor neuron lesion there was no bladder activity but a marked resistance in U₂. It is of interest that U₂ rises with parasympathomimetic drugs during spinal shock; it may explain why they are ineffective during spinal shock even though cystometric studies have shown enhanced detrusor activity; their use therefore ought to be contraindicated.

SUMMARY

During experimental spinal shock, the urethral muscle responded to drugs earlier than the detrusor muscle. Stimulation with parasympathomimetic drugs caused some rise in intravesical pressure, but an unexpected and much greater rise of intraurethral pressure. Bladder evacuation was achieved with the Credé manoeuvre during spinal shock with the combined effect of alpha adrenergic blockade and beta adrenergic stimulation.

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Discussion

CHAIRMAN: MR. J. COSBIE-ROSS. Thank you, Mr. Abel. Before opening these two papers for discussion, I should just like to put the records straight. This is a paper by Mr. Abel and Mr. Gibbon and all I have done is to provide them with the earlier series of cases. Naturally, this second paper, in particular, is of great interest to me because it does emphasise, I think, the point that we have made repeatedly that it is better to do too little than too much. You can always repeat the operation—it is quite easy to do so if it is necessary, but even in the incomplete cases an improvement is achieved. An improvement in that delicate balance that we try to achieve between the expulsive forces and the factors causing incontinence, and, of course, there are several other factors causing blockage as well as the external sphincter. I think that with this technique, as Mr. Abel has shown, it is possible to distinguish between the part that the external sphincter takes and to distinguish it from the part taken by the other factors in providing incontinence. Now, both these papers are open to discussion.

DR. H. L. FRANKEL (*G.B.*). I greatly admire Professor Rossier's paper. I should just like to ask him to clarify how acute this injury was—was it on the day of the laminectomy that the study was carried out or how long afterwards?

PROF. A. ROSSIER (*U.S.A.*). Not on the day—it was within the hour.

DR. FRANKEL. Were they still anaesthetised?

PROF. ROSSIER. No.

DR. FRANKEL. We have done some preliminary work on humans using the newer pharmacological agents, encouraged largely by the Scandinavian work on cat bladders which showed innervated parasympathetic areas by the sympathetic, and the only drug you can with reasonable safety administer to the human is, in fact, the Beta blocking of this group, and we found on some preliminary studies some beneficial effect to ease micturition on patients with lower motor neuron lesions of some months' duration. This encouraged me to think that it might, in fact, work in spinal shock. We have found no effect whatsoever during spinal shock. I would point out that our work was done purely on clinical grounds, we made no pressure measurements of any sort, we just attempted to induce micturition during spinal shock and we were quite unable to do so by this means.

PROF. ROSSIER. I have to correct what I told you, I said it incorrectly. The dogs, during the experiment, were, actually under anaesthesia. This, by the way, is a point which is very important for all these experiments in medicine. We cannot do these experiments without anaesthesia. We know, as has already been pointed out by Langworthy, that anaesthesia plays a major role and it is known that the depth of anaesthesia may influence bladder activity, therefore, we just try to be as light as possible, but we cannot avoid this technical feature.

DR. HACHEN (*Switzerland*). Much has been written in recent months about the possibility of influencing both the detrusor and the striated urethral sphincter with various pharmaceutical agents. I think it is very important to realise that in the situation in a patient emerging from spinal shock the external urethral sphincter is more responsive to parasympathetic stimuli than the bladder, in fact, it is perfectly possible to induce some bladder emptying but at the same time there is a very large danger of inducing a

reflux, and we have seen this currently in patients who could not be accepted in our department because we had no beds but were treated in other departments. Many urologists are now aware of this possibility of influencing neurogenic bladders with drugs and they are sometimes prescribing those drugs too early. So unless it's possible to perform fresh studies both in the bladder and around the striated sphincter and unless the ice water test is positive with the small amount of 90 ml. of ice water, I think one should wait a considerable time before one intervenes with pharmacological agents, otherwise the danger of bringing about a considerable reflux is quite significant.

CHAIRMAN. I am sure Professor Rossier would agree with that, wouldn't you?

PROF. ROSSIER. Absolutely. I believe it is in the main interests of these experiments to show that we are just increasing the activity of the external urethral sphincter during spinal shock.

MR. N. GIBBON (*G.B.*). I also was interested in Professor Rossier's paper. In the past we have all paid for too much attention to the striated muscle of the urethra and not nearly enough to the plain muscles of the urethra and I wonder whether we could shed light on the patient with a conus lesion who, although he has an open bladder neck and he strains to empty his bladder, has an obstruction at the external sphincter level. In the past the only satisfactory explanation of this was that advanced by Vincent of Belfast who suggested that on straining the weight of the bladder compressed the urethra longitudinally against the triangular ligament and this subtracted it. Alternatively, we had Dr. Dollfus's case showing angulation of the posterior urethra on the triangular ligament and how that could be relieved by elevation of the bladder and the prostate. But, I don't think this is a very common thing, it doesn't show on our cystograph very commonly. Unfortunately the conus cases are not as common as the upper motor neuron cases, but we had a patient who for six months was unable to void because of obstruction at the external sphincter. Even when he had virtually a flat electromyograph of the pelvic floor, and when he sat up the urethral pressure profile went very high and he was unable to void. But we discovered that this could be abolished by giving him an injection of 10 mg. of phentol. So it appears that in some cases at least it's an over-activity of the plain muscle of the urethra and not a mechanical effect of longitudinal compression by straining or the force of gravity. The only thing that remains to be looked into is to see far more cases of this type and to find out what the afferent limb of this reflex arc is because if the pelvic floor is in fact denervated it is the afferent limb where the sympathetic overactivity takes place.