OXYBUTYNIN CHLORIDE (DITROPAN)— CLINICAL USES AND LIMITATIONS

MOSHE ELYAKIM BROOKS, M.D. and ZVI F. BRAF, M.D.

Neurolurologic Clinic, Sir Ludwig Guttmann Spinal Cord Injury Center; The Chaim Sheba Medical Center; Sackler School of Medicine, Tel-Aviv University, Tel Hashomer, Israel

Abstract. Eighteen patients treated with oxybutynin chloride are presented. The effect of the drug on the hyperactive detrusor is shown and discussed. Side effects and limitations are described and related to treatment.

Keywords: Pharmacology; Neurogenic bladder; Cystometrogram.

Introduction

THE problem of the hyperactive detrusor (Andersen & Bradley, 1977) of varying aetiologies is a very common urologic occurrence. Many various pharmacologic agents are available for management of this distressing situation. Oxybutynin chloride (Ditropan) is the latest in a long series of attempts to find an agent which will have greater specificity for the detrusor muscle with fewer systemic effects. This drug has been shown to have two main mechanisms of action: (1) cholinergic blockade, and (2) direct spasmolytic activity on smooth muscle (Frederichs *et al.*, 1975). Dickno and Lapidès (1972) have shown the clinical effectiveness of oxybutynin chloride. Their findings have been supported by Mulcahy, James and McRoberts (1977), and Thomson and Lauvetz (1976). We have treated 18 patients who suffered from hyperactive detrusor reflexes using oxybutynin chloride. We present our findings and discuss the uses and limitations of this agent.

Methods

Eighteen patients, nine male and nine female, between the ages of 9 and 74 with a mean age of 47 ± 18.7 years are included in this report. Seven of these patients had documented injury to the spinal cord with neurologic findings of complete or incomplete spinal cord injuries. In seven cases the bladders, as shown by cystometrogram, were of the spastic upper motor neurone type. Three patients had brain damage; one patient a brain concussion, and the other two patients cerebral vascular accidents. Two patients had small capacity bladders as a result of long-standing indwelling catheter drainage. The remaining six patients had hyperactive detrusors with varying complaints of urgency, frequency, and nocturia (Table I). Pre-examination medications in all spinal cord injured patients included Hypprex and vitamin C for urine acidification. One patient in this group with indwelling catheters received benactyzine methylbromide (Paragone), an anticholinergic agent, 25 mg three times daily. This was stopped prior to the institution of oxybutynin chloride. All other patients received no medication prior to examination. Four patients had indwelling catheters, one brain injured, two with spinal cord injury, and one with a hyperactive detrusor of unknown aetiology.

All examinations were performed with a carbon dioxide cystometer. Patients

TABLE I
Personal data and diagnosis

Patient	Age	Sex	Diagnosis or Complaint	Bladder type
A	35	F	D6 incomplete paraplegia	Hyperactive detrusor
B	68	M	Lt. mid. cereb. art. thromb.	Hyperactive detrusor
C	48	F	Frequency, urgency	Hyperactive detrusor
D	59	M	L1 incomplete paraplegia	Hyperactive detrusor
E	9	F	Frequency, incontinence	Hyperactive detrusor
F	28	M	Brain concussion	Hyperactive detrusor
G	67	F	Urgency	Hyperactive detrusor
H	72	M	Prostatism, bladder tumour	Hyperactive detrusor
I	21	M	L2 spina bifida	Hyperactive detrusor
J	51	F	Frequency	Hyperactive detrusor
K	44	M	Frequency	Hyperactive detrusor
L	29	M	L4-5 dissection	Hyperactive detrusor
M	53	F	Nocturia	Hyperactive detrusor
N	63	M	Lt. mid. cereb. art. thromb.	Hyperactive detrusor
O	56	F	D11 complete paraplegia	Hyperactive detrusor
P	23	F	L2 incomplete cauda equina	Hyperactive detrusor
Q	40	M	D4 complete paraplegia	Hyperactive detrusor
R	74	F	Urgency	Hyperactive detrusor

voided and then were catheterised with sterile technique using the non-touch method (Guttmann, 1973). Residual urines were drained and measured, and then CO₂ was introduced at a flow rate of 120 ml per min. Patients were asked to report the first urge to void which was recorded as the first sensation of filling (FSF). Patients were then instructed to tolerate the increasing feeling of fullness and urgency until they were absolutely unable and then to urinate. With a rise in intrabladder pressure 30 cm H₂O above the initial bladder pressure, either voluntarily or involuntarily, the examination was terminated. This point was used to determine the total bladder capacity (VOL). Oxybutynin chloride in the dosage of 5 mg three times daily was then instituted, and after 1 month of therapy, repeat examinations were performed. Bladder types were classified according to Anderson and Bradley (1977).

Results

Twelve of the 18 patients tolerated oxybutynin chloride easily. In all cases the chief complaints of frequency and urgency markedly subsided. Patients reported a decrease in nocturia or an ability to function for longer periods between voiding. Three patients showed large increases in residual urines. Of the four patients with indwelling catheters prior to the institution of therapy, only 1 patient, patient R, was able to achieve a catheter-free state. Patient Q had a penile scrotal fistula resistant to surgical closure and requiring a suprapubic catheter. Patient O could not tolerate the drug and patient B died soon after the follow-up from a second cerebral vascular insult (see Table II).

Table III shows the improvement in FSF and VOL. Mean initial was 83 ± 43 ml and the mean initial VOL was 147 ± 72 ml. Follow-up studies in 13 patients showed a mean FSF of 141 ± 53 ml and a mean VOL of 290 ± 87 ml.

TABLE II
Residual urine volumes (ml)

Patient	Initial	Follow-up
A	160	40
B	catheter	catheter
C	10	0
D	20	30
E	85	135
F	0	0
G	0	255
H	75	35
I	20	250
J	0	—
K	0	10
L	0	—
M	0	—
N	0	0
O	catheter	catheter
P	0	110
Q	catheter	catheter
R	catheter	0

TABLE III
CO₂ cystometrogram volumes (ml)

Patient	Initial		Follow-up	
	FSF	VOL	FSF	VOL
A	200	240	200	400
B	160	160	160	360
C	50	170	130	220
D	55	100	150	225
E	50	85	120	130
F	80	80	40	250
G	50	210	95	360
H	150	160	110	300
I	40	40	130	180
J	60	160	—	—
K	60	220	160	400
L	80	240	—	—
M	100	340	—	—
N	40	140	100	210
O	80	120	—	—
P	75	75	270	380
Q	70	100	—	—
R	100	160	165	350
Mean	83	141	147	290
S.D. $\pm$	43	53	72	87

In all cases an improvement in follow-up VOL was noted as compared to the initial VOL. Patient E is a 9-year-old girl whose total bladder capacity certainly is much less than the normal adult volume. Patient B is a man with a large prostate gland who was on catheter drainage. Five patients had no follow-up study. Four of these patients stopped therapy for various reasons as discussed below. The fifth man, patient Q, had a suprapubic catheter inserted as described above.

Six of the 18 patients were unable to tolerate oxybutynin chloride. Table IV shows the varying reasons for this. Four of the patients complained of symptoms seemingly related to the anticholinergic effects of the drug. The other 2 patients complained of direct allergic reactions. Two of the patients who stopped the drug, patients C and D, did show improvement in bladder function before being forced to interrupt treatment.

Discussion

Our results in this study are in agreement with those shown in previous publications (Mulcahy, James & McRoberts, 1977; Thomson & Lauvetz, 1976). We note a 77 per cent improvement in the FSF with oxybutynin chloride and a 97 per cent improvement in the VOL with this drug (Table III). While not as dramatic an improvement as shown by Thompson and Lauvetz (1976) because of the heterogeneity of the group, this certainly is a significant change. In conjunction with this improvement in objective findings, we also noted a marked decrease in subjective complaints. Although three patients did have a marked increase in residual urines, these residual volumes were reduced by better emptying techniques. There is no doubt that oxybutynin chloride is an excellent addition to the pharmacologic management of the hyperactive detrusor.

Most disturbing to us, however, is the finding that 33 per cent of our patients could not tolerate oxybutynin chloride. Their complaints as listed in Table IV were severe enough in all six cases to cause the patient to stop the drug ingestion without consulting the physician. Four of the patients had typical systemic effects of anticholinergic agents. In the cases of patients J and O, where the side effects were typical of all anticholinergic drugs, *i.e.* abdominal discomfort, fullness, and constipation, no amount of reassurance or explanation could convince these patients to reduce the dosage and continue therapy. Two other patients had direct allergic reactions of itching and pain in surgical scars. This may be related to histamine release and the stimulation of fibroblasts. In both these cases, the symptoms subsided completely after cessation of the drug. Contrary to the reports cited above (Diokno & Lapides, 1972; Thompson & Lauvetz, 1976;

TABLE IV
Side effects

Patient	Complaint
C	Flushing, facial burning sensation
D	Itching
J	Abdominal discomfort
L	Painful surgical scars
M	Weakness, sensation of heat
O	Abdominal pain, dysphagia, constipation

Mulcahy, James & McRoberts, 1977), we feel that the side effects of oxybutynin chloride are severe enough to cause immediate withdrawal of therapy. The direct allergic reactions, described above, raise the question of additional sites of action of oxybutynin chloride in addition to its known pharmacologic properties.

RÉSUMÉ

Dix-huit patients traités au chlorure d'oxybutynine sont présentés. L'effet de médicament sur le détresseur hyperactif est montré et discuté. Les effets secondaires et les limites d'application.

ZUSAMMENFASSUNG

Achtzehn Patienten, die mit Oxybutyninchlorid behandelt wurden, werden beschrieben. Die Wirkung des Mittels auf den hyperaktiven Blasenmuskel wird beschrieben und diskutiert. Seiteneffekte und Anwendungsbeschränkungen werden beschrieben.

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