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PENTOLINIUM FOR CONTROL OF REFLEX HYPERTENSION IN SPINAL CORD INJURED PATIENTS

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Abstract. Ganglioplegia was produced by intravenous infusion of pentolinium tartrate 5 mg to control reflex hypertension in 29 patients with chronic spinal cord injuries undergoing 32 elective surgical procedures. The patient group with lesions above the first thoracic segment (T1) demonstrated significant but moderate intraoperative elevation of both systolic and diastolic pressure whether pentolinium was given prior to or during surgical stimulation. Patients with lesions below T1 had no significant pressure elevations with either mode of therapy. Pentolinium ganglioplegia can safely maintain blood pressure within reasonable limits in these patients; some increase in dosage may be required in patients with lesions above T1.

Key words: Pentolinium; Reflex hypertension; Spinal cord injury.

Introduction

AUTONOMIC hyperreflexia (AH) may produce paroxysmal arterial hypertension in spinal cord injured patients undergoing perineal, urinary bladder, or orthopaedic surgery (Guttman and Whitteridge, 1947; Kurnick, 1956; Caron and Bors, 1970; Johnson *et al.*, 1975; Guttman, 1976, Snow *et al.*, 1977). The severity of the potential stigmata of throbbing headache, convulsion, and cerebrovascular accident requires that the intraoperative management of these patients permit control of reflex-mediated vasoconstriction. Although general anaesthesia and subarachnoid block have been advocated for prevention of AH (Rocco and Vandam, 1959; Caron and Bors, 1970), susceptible patients generally have complete cord transection with loss of sensation below the lesion, and do not require anaesthesia with its attendant hazards. In this study, we have reviewed our experience with a ganglioplegic drug, pentolinium tartrate (Ansolysen) and evaluated its effectiveness in controlling AH when given before and during surgery.

Methods

The intraoperative records of 29 adult male patients with chronic, complete cord transection who had undergone a total of 32 surgical or diagnostic procedures from April 1975 through February 1977 (Table I) were analysed retrospectively. Hospital documents specified the levels of the cord lesions, all of which occurred at least 4 months prior to surgery, usually as a result of trauma from automobile accidents or gunshot. Lesions above the first thoracic segmant (range C4–C8 were defined as 'high lesions; all others were 'low' lesions (range T2–T8). No

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patients studied were receiving antihypertensive medications prior to surgery; all were given narcotic and/or tranquilisers intramuscularly for premedication.

Intraoperative vital signs were obtained from the patients' anaesthesia records, having been measured and recorded by anaesthetists using arm cuff sphygmomanometer and an electrocardiogram. 'Control' values represent vital signs upon initiation of monitoring, with the patient supine upon the operating table, prior to pentolinium or surgery. In 22 procedures, the patients had been 'pre-treated': 5 mg of pentolinium were given intravenously (IV) 5 or 10 min prior to surgery at the discretion of the anaesthetist or surgeon. This has been a frequent practice with these patients at our hospitals. In the remaining ten procedures ('empirical' treatment), pentolinium had been given in 1 to 5 mg increments IV during surgery in an attempt to titrate the drug against increases in blood pressure.

For patients who had been pretreated, the 'response to pentolinium' represents

TABLE I

Patient and lesion characteristics

Patient age (yr)	Patient weight (kg)	Sensory level of lesion	Age of lesion (mos)	Surgical procedures
17	99	C7–T1	24	Ext. sphincterotomy
18	64	C5–C6	8	Cystoscopy
18	55	C4–C5	12	Cystoscopy
17	60	C5	11	Ext. sphincterotomy
19	36	C5–C6	10	Cystoscopy
42	68	C6–C7	264	Ext. sphincterotomy
35	99	C5–C6	144	Cystoscopy
20	87	C4	22	Ext. sphincterotomy
21	91	C6–C7	4	Gluteal flap
28	63	C4–C5	5	Cystoscopy
20	68	C5–C6	9	Cystoscopy
35	114	C5–C6	120	Penile prosthesis
19	unknown	C5–C6	4	Cystoscopy
28	55	C6	17	Cystoscopy, circumcision, repair ureterocutaneous fistula
23	50	C7	6	Ext. sphinct., cystoscopy
16	unknown	C5–C6	6	Ext. sphinct., cystoscopy
50	80	C7	7	Ext. sphincterotomy
36	75	C7	6	Ext. sphincterotomy
19	59	T2	11	Ext. sphincterotomy
20	61	T3–T4	66	Cystoscopy
28	80	T4	43	Cystoscopy Abscess drainage
53	64	T4	252	Ext. sphinct., cystoscopy
59	53	T3–T4	372	Cystoscopy
30	58	T7–T8	45	Ext. sphincterotomy
46	63	T7–T8	264	Ext. sphincterotomy
28	59	T2–T4	24	Cystoscopy
27	59	T6–T7	84	Closure suprabubic stoma
39	50	T4–T5	96	Inguinal exploration
24	unknown	T5	24	Debride. sacral ulcer

vital signs 5 min after IV bolus infusion of pentolinium 5 mg, prior to surgery. Vital signs subsequently recorded as 'surgical maximum' for these patients were those observed at the point of peak systolic pressure elevation during surgery or cystoscopy, prior to any supplemental pentolinium. For patients treated empirically, 'surgical maximum' represents vital signs observed at the point of peak systolic pressure after a cumulative dose of 5 mg pentolinium had been given intraoperatively.

No patient had sensation below the lesion, and no anaesthetics or other antihypertensives were used during these procedures. Additional increments of pentolinium were given to some patients as indicated by clinical considerations.

Statistical evaluation of the transcribed blood pressures and heart rates consisted of calculation of mean values and standard error, and *t*-test comparisons. A *P* value of 0·05 or less was the criterion of significance.

Results

The control systolic and diastolic pressures for all patients studied were 121·0 ± 4·4 mmHg and 75·3 ± 2·5 mmHg, respectively, mean ± S.E.; control heart rate was 90·2 ± 3·0 beats/min. Control values for the patients with high lesions were comparable to those for the low lesion group (Table II). Although the low lesion patients demonstrated small numerical increases in both systolic and diastolic pressure during maximum surgical stimulation, neither of these changes proved to be significant when compared to control values. In contrast, patients with high cord lesions had statistically-significant elevations of blood pressure during surgery: systolic and diastolic pressure elevations were significantly greater for the high lesion patients than those observed for the low lesion group.

The mode of pentolinium therapy did not change the cardiovascular response

TABLE II

Systolic and diastolic arterial blood pressure and heart rate in response to surgery for patients with high (above T1) and low (below T1) spinal cord lesions

	All high lesions (n = 20)		All low lesions (n = 12)
Systolic pressure (mm Hg) mean ± S.E.			
Control	124·0 ± 5.4	NS	116·1 ± 7·9
Surgical maximum	164·5* ± 6·6	$P<0.005$	131·2 ± 9·7
Change with surgery	+40·5 ± 6·2	$P<0.005$	+15·2 ± 6·6
Diastolic pressure (mm Hg) mean ± S.E.			
Control	75·0 ± 3·1	NS	74·8 ± 4·4
Surgical maximum	98·5* ± 4·6	$P<0.01$	79·2 ± 6·3
Change with surgery	+23·5 ± 4·4	$P<0.005$	+3·3 ± 4·4
Heart rate (beats/min) mean ± S.E.			
Control	91·4 ± 4·1	NS	88·1 ± 3·5
Surgical maximum	93·4 ± 5·2	NS	89·2 ± 2·7
Change with surgery	+2·0 ± 5·6	NS	+1·1 ± 2·3

NS, differences between high and low lesion values not significant.
* Significant difference from control, $P<0.05$.

to surgical stimulation. In the five empirically-treated patients with high lesions (Fig. 1, solid black triangles), surgical stimulation produced significant elevation of both systolic and diastolic pressures. The 15 high-lesion patients who had been pre-treated with pentolinium (open triangles) also demonstrated a significant increase during surgery, but this followed a significant drop in pressure after pentolinium infusion. The mean maximum values for systolic and diastolic pressure of the pre-treated group were numerically smaller but statistically indistinguishable from the corresponding values of the empirically-treated group.

The pre-treated low-lesion patients had mean systolic and diastolic pressures during surgical stimulation which were essentially identical to the control values (Fig. 2). Although the blood pressures of the five empirically treated patients were numerically higher than control, they were not significantly different from control values or from the respective values for pre-treated patients. Unlike high lesion patients, there was no drop in blood pressure after pentolinium infusion. Heart rates were essentially unchanged in both treatment groups.

The mean total dose of pentolinium given to high lesion patients was $7{\cdot}9 \pm 0{\cdot}7$ mg, significantly more than the $5{\cdot}5 \pm 0{\cdot}5$ mg required by patients with low lesions ($P < 0{\cdot}005$). Sixty per cent of the patients with high lesions required additional pentolinium beyond the original 5 mg, while only 33 per cent of the low-lesion group required more pentolinium for clinically adequate control of pressure. The

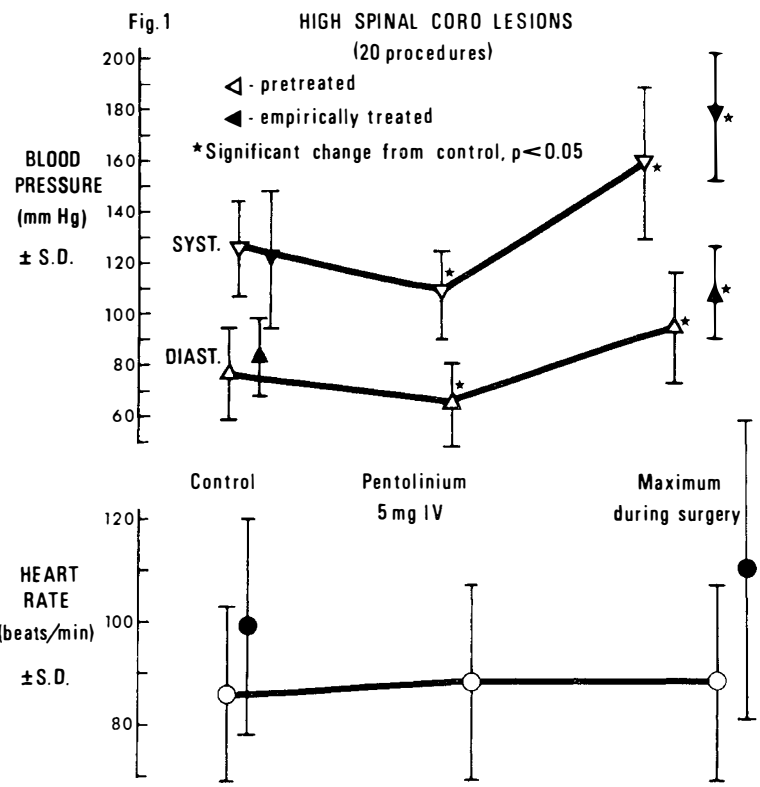

FIG. 1.

Cardiovascular response to pentolinium and surgery, spinal cord lesions above T1. Open figures represent pretreated group, closed figures, the empirically-treated group.

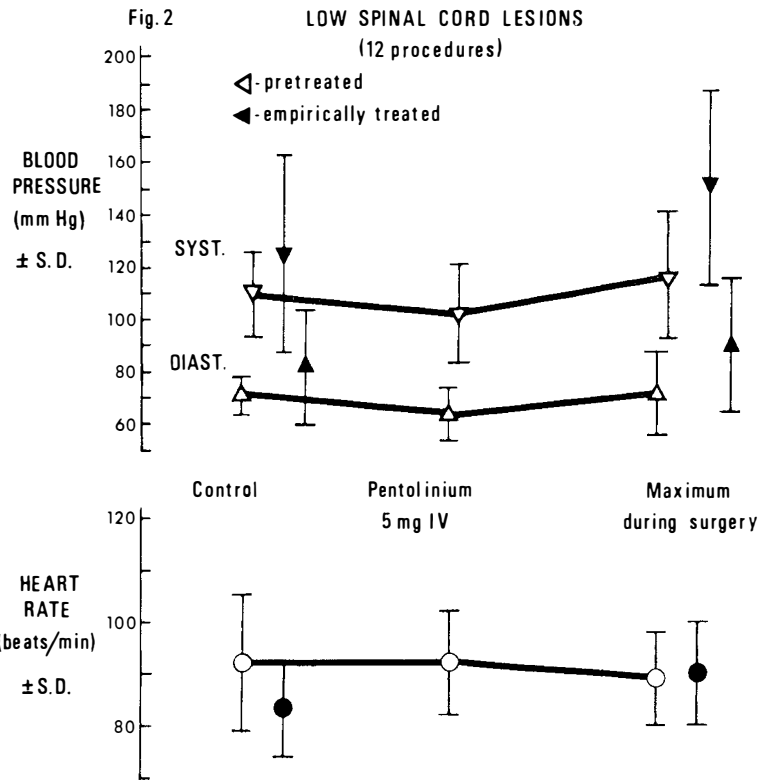

FIG. 2.

Cardiovascular response to pentolinium and surgery, spinal cord lesions below T1. Open figures represent pre-treated group, closed figures, the empirically-treated group.

duration of surgery for high- and low-lesion patients was $64{\cdot}5 \pm 7{\cdot}7$ and $76{\cdot}1 \pm 7{\cdot}9$ minutes, respectively, $P > 0{\cdot}05$. The high-lesion patient group had a lower mean age ($25{\cdot}7 \pm 2{\cdot}4$ years *vs.* $33{\cdot}9 \pm 4{\cdot}0$ years) and a greater mean body weight ($72{\cdot}8 \pm 5{\cdot}2$ kg *vs.* $60{\cdot}6 \pm 2{\cdot}5$ kg) than the low-lesion group, both parameters showing differences of possible statistical significance ($P < 0{\cdot}05$ and $P < 0{\cdot}025$, respectively). No patient developed the clinical manifestations of the fully developed syndrome of autonomic hyperreflexia.

Discussion

The acute cardiovascular changes which are the major stigmata of the syndrome of autonomic hyperreflexia were first clearly described by Guttmann and Whitteridge, 1947, 30 years after Head and Riddoch described the symptoms of diaphoresis, nasal congestion, agitation, and severe throbbing headache (Head and Riddoch, 1917). The neuroanatomic basis of the syndrome was defined by Kurnick, 1956. Autonomic hyperreflexia occurs in patients who have had spinal cord transection involving the lateral spinothalamic tracts and dorsal columns; when the lesion level is midthoracic or higher, the preganglionic sympathetic neurons originating below the transection are removed from inhibitory influences which descend from higher cord and brain stem centers. Thus, if distension of a hollow viscus produces strong afferent input which enters the intact cord below the lesion, an autonomic

spinal reflex arc with uninhibited efferent activity is completed. Uncontrolled sympathetic ganglion activity then occurs in those areas of the body deriving their sympathetic innervation from cord segments below the transection. Intense arteriolar constriction in skin and viscera can produce severe arterial hypertension with pounding headache and a bradycardia mediated by the carotid sinus reflex arc. The incidence of this phenomenon in untreated, susceptible patients may be as high as 90 per cent (Johnson *et al.*, 1975; Snow *et al.*, 1977).

Subarachnoid block and general anaesthesia suppress or prevent AH, but both approaches have limitations when applied to the paraplegic patient. Lumbar puncture is often difficult because of abnormalities of soft tissue and the vertebral column (Desmond, 1970). General anaesthesia is almost always associated with some degree of postoperative respiratory depression, a situation poorly tolerated in patients with chronic paralysis of the accessory muscles of respiration who are already at high risk for the development of atelectasis and pneumonia (Rocco and Vandem, 1959).

An alternative technique for control of AH has been ganglioplegia with agents such as hexamethonium (Rocco and Vandam, 1959), guanethidine (Shea *et al.*, 1973), trimethaphan (Snow *et al.*, 1977) or, recently, pentolinium tartrate (Basta *et al.*, 1977; Textdr *et al.*, 1976). Pentolinium is believed to act at ganglionic receptor sites for acetylcholine by stabilising the resting potential of the post-synaptic membrane. Blockade of ganglionic transmission interrupts the efferent limb of the reflex pathway responsible for the acute, severe hypertension of AH. Ganglioplegia may cause bladder and bowel atony, cycloplegia, and xerostomia, but persistent postural hypotension is the most significant complication. All patients in our study were kept at complete bed rest for 6 hours after receiving pentolinium to prevent postural hypotension, and were given intravenous fluids until the day after surgery in anticipation of the expected gastrointestinal atony. One patient developed a generalised urticarial eruption 45 min after pentolinium injection; this appeared to be an allergic reaction, and responded to treatment with an antihistaminic agent, diphenhydramine.

Conclusions and Summary

In our study, the effectiveness with which pentolinium controlled reflex hypertension in spinal cord injured surgical patients was related to the level of the lesion. Pentolinium 5 mg IV prevented significant elevation of blood pressure intraoperatively in the group of patients with lesions below T1; prophylactic administration of pentolinium appeared to give slightly better control than did empirical treatment.

Patients with cord transections above T1 had a more dramatic cardiovascular response to pentolinium infusion and to surgical stimulation than did low lesion patients. Pentolinium 5 mg IV prior to surgery produced a ganglioplegia that was of sufficient intensity to cause an initial decrease in blood pressure, but not adequate to prevent an elevation of systolic pressure during surgery. The empirically treated patients with high lesions demonstrated similar elevations of blood pressure, but in neither group was the bradycardia of the fully developed syndrome of autonomic hyperreflexia (Cole *et al.*, 1967; Guttmann, 1976) apparent.

We conclude that with appropriate adjustment of dosage, pentolinium ganglioplegia is a suitable technique for safe, convenient control of the cardiovascular stigmata of autonomic hyperreflexia. For comparable degrees of surgical stimulation, the effectiveness of a given dose of pentolinium appears to be a function

of the level of the spinal cord lesion, and to a lesser extent, the time of administration.

RÉSUMÉ

Le tartrate de pentolinium (Ansolysen) par voie intaveneuse est un moyen efficace de baisser les poussées d'hypertension associées avec l'hyperréfiexie autonome. On a trouvé, chez 29 malades avec la moelle traumatisée à un niveau inférieur à Dl, a suffit pur prevenir des poussées de la pression arterielle pendant la chirurgie. Chez les maldes avec lesions supérieures à Dl, des doses supplementaires de pentolinium par voie intraveneuse étaient requises pour controller la tension arterielle. L'efficacité d'une dose donnée de pentolinium, pour le même degré de stimulation chirurgicale, semble être une fonction du niveau de la lesion de la moelle.

ZUSAMMENFASSUNG

Hochdruck, hervorgerufen durch autonome Hyperreflexa, kann durch entsprechende Dosierung von Pentolonium i.v. vermieden werden. In 24 Patienten mit Rückenmarksschädigung, deren Verletzung unterhalb T1 lag, konnte ein signifikanter Blutdruckansteig durch intravenöse Verabreichung von 5 mg Pentolonium verhindert werden. Patienten mit Rückenmarksverletzungen oberhalb T1 benötigten zusätzliche Gaben von Pentolonium zur Blutdruckkontrolle. Bei vergleichbarer chirurgischer Stimulierung scheint die Effecktivität einer gegebenen Dosis von Pentolonium von der Höhe der Rückenmarksläsion abzuhängen.

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