AUTONOMIC HYPERREFLEXIA:
INTRAOPERATIVE CONTROL WITH PENTOLINIUM TARTRATE

J. W. BASTA, K. NIEJADLIK AND V. PALLARES

SUMMARY

Autonomic hyperreflexia (AH) is an episodic clinical syndrome associated with the development of severe hypertension. It usually occurs in patients who have high-level chronic spinal cord injury, and in response to stimuli associated with the distension of a hollow viscus. Protection against AH by the prophylactic use of pentolinium tartrate (Ansolysen) in doses of 10–15 mg was evaluated in a controlled study of unanaesthetized patients who were either quadriplegic or paraplegic and who underwent rectal and bladder surgical procedures. When compared with the control group, the systolic and diastolic arterial pressures during operation were significantly less \( (P < 0.05) \) and remained near normal in the pretreated patients. The use of pentolinium to prevent or control AH during surgical procedures in patients with chronic spinal cord damage is a simple alternative to spinal or general anaesthesia.

Autonomic hyperreflexia (AH) is a clinical syndrome developing episodically in up to 85% of patients with chronic spinal cord injury, particularly if such injury results in quadraplegia or high-level paraplegia (levels of T5 or above) (Kurnick, 1956; Arief, Tigay and Pyzik, 1962; Johnson et al., 1975). The syndrome consists of the paroxysmal onset of symptoms including sweating, flushing, pilo-erection and severe headache. The clinical signs may include marked increases of the systemic arterial pressure, bradycardia, alterations in the level of consciousness, and possibly convulsions or cessation of respiration (Johnson et al., 1975). The increase in arterial pressure is often precipitous and is the major cause of morbidity (myocardial infarction, retinal artery haemorrhage or cerebrovascular accident) (Johnson et al., 1975).

Stimuli related to distension of a hollow viscus are particularly effective in eliciting the response, therefore AH is a common problem of management during urological procedures in patients with spinal cord damage. Afferent impulses from bladder distension and pressure enter the spinal cord via the pelvic and pudendal nerves and elicit unmodulated reflex autonomic output over the splanchnic outflow (Kurnick, 1956; Arief, Tigay and Pyzik, 1962).

Many methods have been proposed for the control of AH. Spinal (Ciliberti, Goldfein and Rovenstine, 1954) or general (Drinker and Helrich, 1963) anaesthesia is effective. Ganglionic blockade with hexamethonium was reported as successful by Kurnick in 1956. This drug, however, is no longer available. The present study was undertaken to determine whether ganglionic blockade with pentolinium could be successfully used to prevent or control the signs and symptoms of AH in susceptible patients undergoing operations on the urinary tract or on the colon and rectum.

PATIENTS AND METHODS

Sixteen consecutive quadriplegic or paraplegic patients aged 22–52 yr with stable neurological deficits (levels ranging between C6 and T6), and who were undergoing surgery of the type described above were divided into two groups. The nature of the anaesthetic management was explained and informed consent was obtained on the night before surgery. One group was treated prophylactically with pentolinium tartrate and the other group (control) was treated with pentolinium only if an increase in arterial pressure occurred during operation. The prophylactically treated group consisted of six patients; three of these gave a history of severe headache occurring upon accidental obstruction of a urinary catheter or during previous urological procedures. Half of these patients therefore, were known to be susceptible to viscerovascular reflex phenomena. The control group consisted of 10 patients; two had a specifically related history of previous hypertension and headache during bladder distension. The remaining eight patients had spinal injury levels high enough (C5–T9) to place them at risk for autonomic hyperactivity.
The patients were not premedicated. Upon arrival in the operating room, an i.v. infusion was started, an arterial pressure cuff applied and electrocardiograph monitoring established. Diazepam 5–10 mg or small doses of sodium thiopentone were administered i.v. to produce only minimal sedation. No other anaesthetics were used. The prophylactically treated patients were also given 10–15 mg of pentolinium (0.15–0.20 mg kg⁻¹) i.v. approximately 10 min before the beginning of surgery. The control group was given pentolinium i.v. if the arterial pressure increased excessively (systolic > 140 mm Hg) during the procedure. The prophylactically treated group was given additional pentolinium according to the same criteria.

Measurements of arterial pressure and heart rate were recorded on entrance to the operating room, after pretreatment with pentolinium, just before the beginning of the operation (“initial” values) and finally at the time of maximum cardiovascular response to surgical stimulation. A non-parametric statistical analysis was carried out on the data. The values within each group were analysed by the signed-rank test. The initial and maximum response values of the individual groups were compared by the Mann–Whitney U test.

RESULTS
The results of the study in the control group are presented in table I. The initial mean heart rate was 77 beat min⁻¹, the arterial pressure was 119 mm Hg systolic and 74 mm Hg diastolic. Within 10 min of the start of surgical manipulation the heart rate had increased to 109 beat min⁻¹, and the systolic pressure had increased by an average of 73 mm Hg, to a mean of 193 mm Hg. The diastolic pressure increased by 12.5 mm Hg to an average of 86 mm Hg. These changes were statistically significant at the 5% level for diastolic pressure and at the 1% level for heart rate and arterial systolic pressure.

When the patient’s systolic pressure exceeded 140 mm Hg, treatment was begun with an i.v. injection of 2–5 mg doses of pentolinium and all patients required this therapy. The average dose needed to control the arterial pressure was 15.5 mg and all patients responded to this therapy alone. Arterial pressure returned to within normal limits within an average of 14 min and remained at that level for the duration of the surgery.

In the prophylactically treated group (table II) the initial mean heart rate was 93 beat min⁻¹, the arterial systolic pressure 108 mm Hg and the diastolic pressure was 62 mm Hg. These patients had received an average of 13 mg of pentolinium 10 min before surgery and their cardiovascular response to surgical stimulation was attenuated markedly. In the pretreated group the maximum increase in heart rate was to 107 beat min⁻¹ and the systolic pressure increased by an average of 17.5 mm Hg to a mean of 125 mm Hg. The diastolic pressure increased by an average of 5 mm Hg to a mean of 67 mm Hg. Only the change in systolic pressure was statistically significant (P = 0.05). The time required from the beginning of the surgical stimulus to the maximum change in vital signs was 9 min.

In comparing the two groups it should be noted that there was no significant difference between the initial values for systolic or diastolic pressure. Prophylactic administration of pentolinium did not produce a significant change in arterial pressure in these recumbent patients. The initial heart rate, although not excessively fast, was increased significantly in the pretreated group. During operation two of the six prophylactically treated patients had an increase in systolic pressure to 140 mm Hg or greater. In the control group all patients had excessive increases in arterial pressure and required pentolinium. In both groups the maximum change in vital signs occurred within 10 min of the start of surgery. At the time of maximum change there was no significant difference in the mean heart rate values. The maximum systolic and diastolic pressures in the two groups, however, were significantly different (fig. 1).

None of the prophylactically treated patients complained of any discomfort during the procedures. This symptomatic relief was one of the important
### Table I. Control group

<table>
<thead>
<tr>
<th>Operation</th>
<th>Initial heart rate (beat min⁻¹)</th>
<th>Heart rate at maximum pressure (beat min⁻¹)</th>
<th>Initial systolic pressure (mm Hg)</th>
<th>Maximum systolic pressure (mm Hg)</th>
<th>Initial diastolic pressure (mm Hg)</th>
<th>Maximum diastolic pressure (mm Hg)</th>
<th>Total dose of pentolinium (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perineal urethostomy</td>
<td>60</td>
<td>90</td>
<td>120</td>
<td>180</td>
<td>80</td>
<td>100</td>
<td>10</td>
</tr>
<tr>
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<td>80</td>
<td>100</td>
<td>100</td>
<td>160</td>
<td>65</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>Transurethral prostatectomy</td>
<td>80</td>
<td>110</td>
<td>110</td>
<td>160</td>
<td>60</td>
<td>80</td>
<td>25</td>
</tr>
<tr>
<td>Suprapubic cystolithotomy</td>
<td>70</td>
<td>110</td>
<td>120</td>
<td>210</td>
<td>60</td>
<td>80</td>
<td>17.5</td>
</tr>
<tr>
<td>Sphincterotomy</td>
<td>70</td>
<td>150</td>
<td>110</td>
<td>170</td>
<td>70</td>
<td>90</td>
<td>20</td>
</tr>
<tr>
<td>Cystolithotomy</td>
<td>80</td>
<td>120</td>
<td>130</td>
<td>210</td>
<td>80</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>Cystolithotomy</td>
<td>100</td>
<td>120</td>
<td>130</td>
<td>210</td>
<td>90</td>
<td>90</td>
<td>15</td>
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<tr>
<td>Polypectomy (colon)</td>
<td>90</td>
<td>90</td>
<td>120</td>
<td>220</td>
<td>80</td>
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<td>2</td>
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<tr>
<td>Haemorrhoidectomy</td>
<td>65</td>
<td>100</td>
<td>130</td>
<td>200</td>
<td>80</td>
<td>90</td>
<td>15</td>
</tr>
<tr>
<td>Cystolithotomy</td>
<td>75</td>
<td>100</td>
<td>120</td>
<td>210</td>
<td>70</td>
<td>70</td>
<td>10</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>77 ± 12</td>
<td>109 ± 18</td>
<td>119 ± 10</td>
<td>193 ± 23</td>
<td>74 ± 10</td>
<td>86 ± 10</td>
<td>15.5 ± 7</td>
</tr>
</tbody>
</table>

*P* < 0.05; **P* < 0.01; † see table II; ‡ see table II.

### Table II. Prophylactically treated group

<table>
<thead>
<tr>
<th>Operation</th>
<th>Total dose of pentolinium (mg)</th>
<th>Pre-pentolinium heart rate (beat min⁻¹)</th>
<th>Post-pentolinium heart rate (beat min⁻¹)</th>
<th>Heart rate at maximum pressure (beat min⁻¹)</th>
<th>Pre-pentolinium systolic pressure (mm Hg)</th>
<th>Post-pentolinium systolic pressure (mm Hg)</th>
<th>Maximum systolic pressure (mm Hg)</th>
<th>Post-pentolinium (initial) diastolic pressure (mm Hg)</th>
<th>Maximum diastolic pressure (mm Hg)</th>
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</thead>
<tbody>
<tr>
<td>Cystoscopy</td>
<td>10</td>
<td>85</td>
<td>85</td>
<td>85</td>
<td>140</td>
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<tr>
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<td>100</td>
<td>105</td>
<td>125</td>
<td>120</td>
<td>95</td>
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<td>Internal sphincterotomy</td>
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<td>100</td>
<td>140</td>
<td>55</td>
<td>65</td>
</tr>
<tr>
<td>Transurethral prostatectomy</td>
<td>10</td>
<td>100</td>
<td>100</td>
<td>110</td>
<td>140</td>
<td>140</td>
<td>150</td>
<td>70</td>
<td>85</td>
</tr>
<tr>
<td>Cystoscopy and sphincterotomy</td>
<td>15</td>
<td>75</td>
<td>85</td>
<td>90</td>
<td>100</td>
<td>100</td>
<td>120</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>13 ± 3</td>
<td>89 ± 11</td>
<td>93 ± 10†</td>
<td>107 ± 16</td>
<td>117 ± 21</td>
<td>108 ± 18†</td>
<td>125 ± 16‡</td>
<td>62 ± 11</td>
<td>67 ± 13‡</td>
</tr>
</tbody>
</table>

*P* = 0.05. Compared with table I; † *P* < 0.05; ‡ *P* < 0.01.
advantages of the technique. There were no anaesthetic complications, hypotensive or hypertensive sequelae or problems in the recovery room with any of the patients.

DISCUSSION

The control of reflex autonomic hyperactivity in quadriplegic patients can be especially troublesome during manipulative procedures of the urinary tract or bowel. To prevent patient discomfort and morbidity from systemic hypertension, spinal (Ciliberti, Goldfein and Rovenstine, 1954) or general (Drinker and Helrich, 1963) anaesthesia has been used with success to suppress this hyperactivity. The use of general anaesthesia reduces autonomic activity by obtunding the entire central nervous system, but management can be difficult technically because of the precipitous nature of the arterial pressure changes (Desmond, 1970). Spinal anaesthesia, while being a less extreme approach, must be carried out under circumstances in which the technical problems with lumbar puncture may be significant and adequate monitoring of the level of spinal block is difficult (Desmond, 1970).

The use of ganglionic blockade to provide direct control of the arterial pressure was reported by Kurnick in 1956. Others have suggested the use of trimethaphan (Vandam and Rossier, 1975). Ganglionic blockers, however, vary with respect to pharmacodynamics.

An appropriate agent for control of autonomic hyperreflexia during operation should be effective, easily administered, rapid in onset, and the duration of action should be long enough to provide a stable and nearly complete level of ganglionic blockade for 45–60 min. Pentolinium tartrate satisfies these requirements.

In doses of 15–20 mg, pentolinium produces physiologically significant ganglionic blockade within 3–5 min (Enderby, 1954; Larson, 1964). Ninety per cent recovery from the effect on arterial pressure occurs within 102 min after i.v. administration (Fahmy and Laver, 1976). In this study, doses of pentolinium in excess of 20 mg were unnecessary and are not recommended for routine use during short operative procedures. If hypertension should occur after the use of 20 mg, careful elevation of the head of the operating table can provide additional control of arterial pressure. Pentolinium lasts longer than does hexamethonium (Enderby, 1954) and its pharmacodynamics allow for a smoother control of episodic hypertension than is possible with trimethaphan (Thorn-Alquist, 1975) or general anaesthesia (Ciliberti, Goldfein and Rovenstine, 1954; Drinker and Helrich, 1963). The fundamental advantage of pentolinium is its ability to provide a sustained level of ganglionic blockade which is effective in preventing autonomic hyperreflexia during operation while producing minimal clinical effects on heart rate and arterial pressure in normotensive supine subjects (Enderby, 1954).

Certain precautions in the use of pentolinium should be observed. Pentolinium may produce the transient signs common to ganglionic blockade. Orthostatic hypotension should be kept in mind and the arterial pressure should be monitored carefully if the patient’s position is changed. Initial administration of the drug should be in 2–5 mg increments to avoid overdosage in more sensitive individuals. If significant hypotension occurs, change of position, augmentation of the circulating blood volume and adrenergic stimulation (with phenylephrine or epinephrine) are useful.

REFERENCES


HYPERREFLEXIE AUTONOME: CONTRÔLE INTRAOPÉRATOIRE À L'AIDE DE TARTRATE DE PENTOLINIUM

RESUME
L'hyperreflexie autonome (AH) est un syndrome clinique associé au développement d'une hypertension grave. Elle se produit généralement chez les malades souffrant d'une blessure chronique grave à la moelle épinière et en réponse aux incitations motrices associées à la distension d'une viscére creuse. On a évalué la protection que prodigue l'usage prophylactique du tartrate de pentolinium (Ansolysen) en doses de 10–15 mg contre l'AH, au cours d'une étude contrôlée effectuée sur des malades non anesthésiés, qui étaient soit quadriplegiques soit paraplégiques, et qui étaient soumis à des procédures chirurgicales au rectum ou à la vessie. Lorsqu'on les a comparés au groupe témoin, les pressions systoliques et diastoliques artérielles pendant l'opération ont été substantiellement inférieures (P<0,05) et sont demeurées près de la normale sur les malades prétraités. L'usage du pentolinium pour empêcher ou contrôler l'AH pendant toute intervention chirurgicale sur les malades ayant la moelle épinière endommagée est une alternative simple à l'anesthésie générale ou à la rachianesthésie.

AUTONOME HYPERREFLEXION: KONTROLLE WAHREND DER OPERATION DURCH PENTOLINIUMTARTRAT

ZUSAMMENFASSUNG

HIPERREFLEXIA AUTONOMICA: CONTROL INTRAOPERATORIO CON TARTRATO DE PENTOLINIO

SUMARIO
La hiperreflexia autonómica (HA) es un síndrome clínico asociado con el desarrollo de una severa hipertensión. Generalmente ocurre en pacientes que sufren de una lesión crónica de alto nivel a la médula espinal y en respuesta a estímulos asociados con la dilatación de una víscera hueca. Se evaluó la protección contra HA mediante el empleo profiláctico de tartrato de pentolínio (Ansoliseno) en dosis de 10–15 mg, en un estudio controlado de pacientes no anestesiados, quienes sufrían ya fuera de cuadriplejia o de paraplejia y quienes estaban sometidos a procedimientos quirúrgicos al recto y vejiga. En comparación con el grupo de control, las presiones arteriales sistólicas y diastólicas durante la operación resultaron significativamente menores (P<0,05) y permanecieron casi normales en los pacientes pretratados. El empleo de pentolínio para evitar o controlar HA durante procedimientos quirúrgicos en pacientes que sufren lesiones a la médula espinal constituye una alternativa sencilla a una anestesia espinal o general.