I.V. PRACTOLOL DURING MICROLARYNGOSCOPY. EFFECT ON ARTERIAL PRESSURE, HEART RATE, BLOOD GLUCOSE AND LIPOLYSIS

O. WERNER, J. MAGNUSSON, R. FLETCHER, P. NILSSON-EHLE AND O. PAHLM

SUMMARY
Twenty-five patients undergoing microlaryngoscopy were anaesthetized with thiopentone and nitrous oxide with suxamethonium as a muscle relaxant. Thirteen received practolol 0.4 mg kg\(^{-1}\) and atropine 1.5 mg i.v. shortly before anaesthesia. During anaesthesia practolol 0.2 mg kg\(^{-1}\) was given. Twelve (control) received atropine 0.5 mg before anaesthesia. Practolol reduced the frequency of tachycardia and arrhythmia. The treatment group had a greater reduction in systolic arterial pressure during induction. The hypertensive response to laryngoscopy was not significantly attenuated by practolol. A weak hyperglycaemic response to microlaryngoscopy was not affected, nor was the plasma concentration of glycerol.

I.v. \(\beta_1\) selective adrenoceptor blockade has been tried to combat the circulatory response to laryngoscopy and tracheal intubation. Although there is a good effect in limiting tachycardia and arrhythmia, conflicting results have been obtained in respect of protection against increases in arterial pressure. Prys-Roberts and others (1973) used practolol (Eraldin, I.C.I.) in hypertensive subjects, and found a significant attenuating effect. Similar results were obtained by Ryhänen and others (1977). Siedlecki (1975) found no effect on the hypertensive response. However, different types of anaesthesia were used in those three studies and the assignment of patients to treatment or control groups was, apparently, not strictly randomized.

Microlaryngoscopy causes a similar but more lasting cardiovascular response (Weigand, 1970). We describe a randomized trial on the cardiovascular effects of i.v. practolol during microlaryngoscopy. To test whether the procedure leads to a metabolic stress response and whether this response can be attenuated by practolol, we measured blood-glucose and plasma glycerol concentrations. The latter is considered to be the most sensitive indicator of adipose tissue lipolysis (Havel, 1965).

PATIENTS AND METHODS
Twenty-five patients undergoing microlaryngoscopy were studied. Those with diabetes, obstructive lung disease, inspiratory difficulties, congestive heart failure, second or third degree A-V block, moderate or severe heart enlargement on chest x-ray were excluded, as were patients receiving digitalis or antihypertensive treatment, including beta-blockers. Informed consent was obtained from the patients.

The patients were fasted from midnight. In the morning, a 12-lead e.c.g. was taken and arterial pressure measured after 10–15 min of rest. A portable e.c.g. recorder (SRA, Sweden) was attached. One lead (modified V\(_6\)) was used. The patients were premedicated with morphine and hyoscine i.m. according to age (table I). On arrival at the operating theatre, the patient lay recumbent for 10–15 min, after which blood was sampled through a plastic i.v. cannula. E.c.g. leads were attached for oscilloscope monitoring. Allocation to practolol or saline (control) treatment was random. The anaesthetist, but not the person measuring arterial pressure, knew the nature of the treatment given. Immediately before injections systolic arterial pressure was measured by radial artery palpation. The same cuff (width 12 cm) and anaeroid manometer were used for all patients. The manometer had been checked against a mercury manometer and been found to be correct within 4 mm Hg in the range 0–260 mm Hg. All patients were first given atropine sulphate 0.5 mg i.v. so that the heart rate response would not reveal which drugs were given subsequently. Thereafter, either saline (controls) or atropine 1.0 mg (treatment group) was given. Practolol 0.4 mg kg\(^{-1}\) or saline was administered during 4 min, starting 1 min after the injection of atropine. Two minutes later, thiopentone was
TABLE I. Some comparisons of the two groups. Values are given as mean ± 1 SD (when applicable). ML = microlaryngoscopy

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males/females</td>
<td>13/0</td>
<td>11/1</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>58 ± 12</td>
<td>50 ± 16</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>77 ± 12</td>
<td>78 ± 17</td>
</tr>
<tr>
<td>Resting arterial pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>139 ± 16</td>
<td>135 ± 24</td>
</tr>
<tr>
<td>Diastolic</td>
<td>77 ± 9</td>
<td>80 ± 11</td>
</tr>
<tr>
<td>Heart rate at rest (beat min⁻¹)</td>
<td>66 ± 9</td>
<td>59 ± 10</td>
</tr>
<tr>
<td>Premedication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine (mg)</td>
<td>8.4 ± 3.1</td>
<td>9.3 ± 3.8*</td>
</tr>
<tr>
<td>Hyoscine (mg)</td>
<td>0.34 ± 0.12</td>
<td>0.37 ± 0.12</td>
</tr>
<tr>
<td>Induction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiopentone (mg kg⁻¹)</td>
<td>4.2 ± 0.4</td>
<td>4.7 ± 0.6</td>
</tr>
<tr>
<td>Suxamethonium (mg kg⁻¹)</td>
<td>1.1 ± 0.2</td>
<td>1.1 ± 0.2</td>
</tr>
<tr>
<td>Time intervals (min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premedication–anaesthesia</td>
<td>75 ± 34</td>
<td>78 ± 25</td>
</tr>
<tr>
<td>Induction–intubation</td>
<td>2.8 ± 0.6</td>
<td>2.9 ± 0.6</td>
</tr>
<tr>
<td>Intubation–start of ML</td>
<td>5 ± 2</td>
<td>5 ± 2</td>
</tr>
<tr>
<td>Start–end of ML</td>
<td>14 ± 10</td>
<td>14 ± 7</td>
</tr>
<tr>
<td>End of ML–extubation</td>
<td>5 ± 4</td>
<td>6 ± 4</td>
</tr>
<tr>
<td>Subjects receiving fentanyl</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Mean dose of fentanyl in these subjects (mg)</td>
<td>0.12</td>
<td>0.15</td>
</tr>
</tbody>
</table>

* One subject received diazepam 5 mg i.m. instead.

injected over approximately 1 min, followed by suxamethonium. The lungs were ventilated with 5–10 breaths of oxygen, after which the trachea was intubated with the aid of a Macintosh laryngoscope. The tube (cuffed Portex 6.5) was lubricated with tetracaine gel; otherwise, no topical anaesthesia was given. Subsequently, the lungs were ventilated manually with nitrous oxide 70% in oxygen. A suxamethonium infusion (2 mg ml⁻¹ in Ringer solution) was started when the patient showed signs of recovering from the initial paralysis. During the induction of anaesthesia systolic arterial pressure was measured and recorded every 30–45 s. Thereafter arterial pressure was measured every minute throughout the procedure. No fentanyl was given before or during induction. During microlaryngoscopy fentanyl 0.1 mg was given if the systolic pressure was 200 mm Hg or greater, for at least 2 min. A further 0.1 mg was given if arterial pressure was greater than 225 mm Hg. Practolol 0.2 mg kg⁻¹ or saline was given slowly between 12 and 14 min after the end of the first injection, about 10–12 min after the start of anaesthesia. Blood was sampled 20 min after the start of anaesthesia. The arterial pressure measurements continued at 1-min intervals until 2 min after extubation.

Analyses. Electrocardiograph tapes were replayed on a computer system (Pahlim et al., 1978). Significant events, such as injections, were identified with a marker pulse. An e.c.g. record covering the whole procedure was written on paper (25 mm s⁻¹). Arrhythmia was evaluated from the e.c.g. record by an observer who was unaware of the treatment. Heart rate was measured from e.c.g. every 20 s beginning 1 min before the injection of atropine. The blood samples were immediately placed in ice. Samples for analysis of blood-glucose were drawn in tubes containing sodium fluoride and analysed within 6 h by an enzymatic-colorimetric method (Marks, 1959). Blood samples for glycerol analysis were drawn in tubes containing EDTA. Plasma was separated by centrifugation immediately after operation, and stored at −20 °C. Glycerol concentrations were measured by an enzymatic-fluorimetric method (Laurell and Tibbling, 1966).

Statistics. The Mann-Whitney (two-sided) rank sum test for unpaired data was used for between-group comparisons. The Wilcoxon (two-sided) rank sum test for paired data was used for within-group comparisons. Probability values <0.05 were considered to indicate statistical significance.

RESULTS

There were no notable differences between the groups in respect of resting arterial pressure, weight, premedication, anaesthetic drugs given and duration of the procedure, except that the controls received slightly more thiopentone (table I).

Systolic arterial pressure. Mean arterial pressure at rest immediately before injection of atropine was similar in the two groups. Compared with the initial pressure, no significant change in systolic arterial pressure occurred during or after the first injection of practolol or saline in either group. Minimum arterial pressure during induction was less in the practolol group (P < 0.05) (fig. 1). Maximum arterial pressure within 2 min after laryngoscopy and intubation was greatest in the control group. However, a large increase in arterial pressure occurred in the treatment group, so that the difference between groups was not statistically significant. Usually the arterial pressure decreased during the few minutes before microlaryngoscopy, but when microlaryngoscopy began, arterial pressure increased, remaining increased in both groups during the rest of the procedure, and also after repeated injection of saline or practolol 0.2 mg kg⁻¹.
Arterial pressure (mmHg)

200
150
100
50

• Practolol (n=13)
○ Control (n=12)

1. Systolic arterial pressure before and during microlaryngoscopy (group mean and 1 SD). A = Immediately before injections; B = 1 min after injection of atropine and practolol (saline). Patient still awake; C = Smallest value recorded during induction (this always occurred before intubation); D = Greatest value within 2 min after laryngoscopy and intubation; E = Greatest value during microlaryngoscopy; F = Mean value during microlaryngoscopy; G = 2 min after repeated injection of practolol 0.2 mg kg⁻¹ or saline. SD in panel A was calculated directly from the recorded values, while panels B–G show the standard deviation of the change in relation to A.

Heart rate. The tape recording failed for various technical reasons in three subjects of each group. In the remaining subjects, no significant differences between groups were found immediately before atropine (fig. 2). Compared with the initial heart rate, the increase after atropine was greater in the treatment group (who received 1.5 mg) than in the other group (0.5 mg), although the difference was not significant. The heart rate decreased more after practolol than after saline, so that heart rates were again nearly equal 1 min after practolol or saline injection. Induction of anaesthesia and intubation caused very little response in the treatment group, while the maximum heart rate in the other group was significantly greater in relation to the initial heart rate (P<0.01). The controls also had significantly greater maximum heart rates during microlaryngoscopy (P<0.01) and during awakening and extubation (P<0.05) and there was greater variation in heart rate during the procedure (fig. 2).

Arrhythmia. Among 10 e.c.g. tapes from the practolol group, one showed a total of three ventricular extrasystoles during and shortly after injection of practolol. Otherwise, no arrhythmia was seen except sinus tachycardia in some cases.

Among nine tapes from the controls, three showed junctional rhythm during intubation, while other disturbances of rhythm were observed shortly after atropine in two patients (marked sinus arrhythmia and ventricular extrasystoles respectively). One patient already had ventricular extrasystoles before atropine. These persisted and increased in number during microlaryngoscopy.

Blood-glucose and plasma glycerol. Blood-glucose increased slightly during anaesthesia in both groups (table II). The increase was significant only in the practolol group (P<0.05). The difference in blood-glucose between the groups was not significant. The initial mean plasma glycerol concentrations were slightly greater than the upper reference limit (100 μmol litre⁻¹). In the control group, plasma

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
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<tbody>
<tr>
<td>Before</td>
<td>During</td>
</tr>
<tr>
<td>Blood-glucose (mmol litre⁻¹)</td>
<td>5.6 (0.7)</td>
</tr>
<tr>
<td>Plasma glycerol (μmol litre⁻¹)</td>
<td>122 (46)</td>
</tr>
</tbody>
</table>
Heart rate and contractility are stimulated via beta adrenoceptors, mainly \( \beta_1 \) (Carlsson et al., 1977). The degree of blockade of cardiac beta adrenoceptors appears to be closely related to the plasma concentration of the beta blocker (Vaughan Williams et al., 1975). The relation between plasma concentration and antihypertensive effect is less direct. Thus, a single dose of beta blocker does not greatly reduce arterial pressure (Tarazi and Dustan, 1972). The full effect is seen only after a few hours or days of treatment (Conway and Amery, 1975). Likewise, a single dose suppresses the tachycardia associated with mental stress, but has little effect on the hypertensive response (Nyberg, Graham and Stokes, 1977). The same applies to the effects of beta blockers on the circulatory response to isometric exercise (Sangvik et al., 1975) and to the effects during direct stimulation of the defense—alarm area of the dog brain (Åblad et al., 1975). Thus, except for dynamic exercise, short-term administration of beta blockers does not greatly attenuate the hypertensive response associated with many types of stress. However, they do reduce heart rate.

Since acute administration is rather ineffective in the awake subject, it is far from evident that beta blockers are effective antihypertensive agents during anaesthesia. One thing is to be expected, namely interaction between the beta blocker, external stimuli and the anaesthetic, which always exerts its own effects on the cardiovascular system. The present findings support this concept. The greater decrease in systolic arterial pressure during induction in the treatment group may be explained by such interaction. Thiopentone seems to cause a pooling of blood in the systemic capacitance vessels, by depression of medullary centres. This reduces cardiac output and, usually, arterial pressure (Conway and Ellis, 1969). An additional effect of practolol, further reducing cardiac output and arterial pressure, is likely. During laryngoscopy and intubation, the central depressant action of thiopentone is strongly counteracted. This may explain why practolol did not significantly attenuate the hypertensive response—paralleling the lack of effect of beta blockers in awake subjects under stress.

Carruthers and others (1974) showed a rapid reduction in plasma concentration of practolol after i.v. injection. This is not an explanation for the lack of significant antihypertensive effect during intubation or microlaryngoscopy. In both cases, plasma concentrations were obviously great enough to inhibit tachycardia. Also, the arterial pressure was not much less among those treated than among those not treated 2 min after a repeated injection of practolol (saline).

We followed the recommendation of Prys-Roberts and others (1973), to give a generous dose of atropine before practolol in order to avoid bradycardia. We do not believe that practolol without atropine would have been more effective against the hypertensive response, although heart rates would, of course, have been slower. Our belief is based on the studies cited in the first paragraph of this discussion. As mentioned, acute beta blockade (without atropine) reduced stress-induced tachycardia, but had little effect on the hypertensive response.

The present results agree with those of Siedlecki (1975), who used the same type of induction and did not find any attenuation by practolol of the arterial pressure response to intubation. Superficially, the results contradict those of Prys-Roberts and others (1973), who studied hypertensive subjects intubated under halothane—nitrous oxide anaesthesia, and those of Ryhänen and others (1977), who used thiopentone combined with halothane—nitrous oxide in a mixed group of normo- and hypertensive patients. They found that i.v. practolol did reduce the arterial pressure response to laryngoscopy and intubation. We believe that the discrepancy may be explained by the type of anaesthesia used. Thus, halothane has potent cardiovascular effects, particularly as a myocardial depressant (Prys-Roberts et al., 1972). Practolol may have potentiated the effect of halothane. This explanation may seem difficult to reconcile with the findings by Slogoff and others (1977) who found, in experiments on dogs under isoprenaline challenge, that halothane does not potentiate the haemodynamic effects of propranolol. Also propranolol actually increased the mean aortic pressure in these experiments, although cardiac output decreased. However, the beta stimulation by isoprenaline is probably not analogous to the sympathetic stimulation caused by laryngoscopy. Furthermore, propranolol is non-selective and therefore counteracts the systemic vasodilator effects of \( \beta_2 \) stimulation.

Our conclusions are that beta blockade, instituted shortly before or during anaesthesia, does not...
effectively counteract the hypertensive response to laryngoscopy, unless other agents are also given which are potentiated by the beta blocker. Deep general anaesthesia (King et al., 1951) or thorough topical analgesia (Stoelting, 1977) would seem to give more predictable effects. In order to reduce the hypertensive response to microlaryngoscopy, we prefer to complement thiopentone-nitrous oxide anaesthesia with fentanyl 0.2-0.5 mg and to give naloxone after the procedure, if necessary. This seems to reduce the arterial pressure response. At the time of these studies, however, the practice at our hospital was to use fentanyl sparingly and it was used about equally often in both groups (Table 1). The comparison between the groups ought not to have been affected, therefore.

In contrast to its effect on hypertension, a single dose of beta blocker is certainly effective against tachycardia during anaesthesia and operation. This was the case in the present study and several previous ones (Ryder, Charlton and Gorman, 1973). The effect on stress-induced arrhythmia is also striking (Katz and Bigger, 1970). However, for the latter purpose, much smaller doses are needed than those employed in the present study.

Non-selective beta blockade has been shown to attenuate the hyperglycaemic and lipolytic response to stress (Taggart and Carruthers, 1972). In the present study, a weak hyperglycaemic response to microlaryngoscopy was obtained, which was not affected by practolol. Perhaps surprisingly, the procedure had no significant effect on plasma glycerol concentrations. Also, there was no significant difference in lipolytic response between the groups. The last result is consistent with the observations of Gibbons and others (1976), who found that practolol does not affect the basal level of lipolysis, but has a weak inhibitory effect on isoprenaline-induced lipolysis.

ACKNOWLEDGEMENT

We thank Drs N. Dahlgren and K. Messeter for showing us their data on pretreatment with fentanyl before intubation.

REFERENCES


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**INJECTION INTRA-VEINEUSE DE PRACTOLOL PENDANT UNE MICROLARYNGOSCOPIE. EFFET SUR LA PRESSION ARTERIELLE, LA FREQUENCE CARDIAQUE, LA GLUCOSE DU SANG ET LA LIPOLYSE**

**RESUME**

Vingt-cinq patients soumis à une microlaryngoscopie ont été anesthésiés au thiopentone et au protoxyde d'azote, auxquels on a ajouté un agent de relaxation des muscles: le Suxaméthonium. Treize patients ont reçu du practolol à raison de 0,4 mg kg\(^{-1}\) et de l'atropine à raison de 1,5 mg peu avant l'anesthésie. Pendant l'anesthésie, on leur a administré du practolol à raison de 0,2 mg kg\(^{-1}\). Douze témoins ont reçu 0,5 mg d'atropine avant l'anesthésie. Le practolol a réduit la fréquence de la tachycardie et de l'arythmie. La pression artérielle systolique a été considérablement réduite pendant l'induction chez le groupe soumis au traitement. Le practolol n'a pas atténué de façon significative la réaction hypertensive à la laryngoscopie. Une faible hyperglycémie due à la microlaryngoscopie n'a pas été affectée et il en a été de même pour la concentration de glicérol dans le plasma.

**PRACTOLOL INTRAVENOS WÄHRENTH MIKROLARYNGOSKOPIE. AUSWIRKUNG AUF ARTERIELLEN DRUCK, PULSZAHL, BLUTZUCKER UND LIPOLYSE**

**ZUSAMMENFASSUNG**

Fünfundzwanzig Patienten wurden für Mikrolaryngoskopie mit Thiopentone und mit Stickoxyd mit Suxamethonium als Muskelenlspannungsmittel narkotisiert. Dreizehn davon erhielten kurz vor der Narkose 0,4 mg kg\(^{-1}\) Practolol und intravenös 1,5 mg Atropin. Während der Narkose wurden 0,2 mg kg\(^{-1}\) Practolol verabreicht. Zwölf Kontrollpatienten erhielten vor der Narkose 0,5 mg Atropin. Durch Practolol wurde die Häufigkeit von Tachykardie und Arrhythmie verringert. Die Behandlungsgruppe zeigte eine geringere Verringerung des systolischen arteriellen Druckes während Narkoseeinleitung. Die hypertensive Reaktion auf Laryngoskopie wurde durch Practolol nicht wesentlich erhöht. Eine schwache Hyperglykämische Reaktion auf Mikrolaryngoskopie wurde nicht beeinträchtigt, auch nicht die Plasmakonzentration von Glycerol.

**PRACTOLOL I.V. DURANTE MICRO-LARYNGOSCOPIA. EFECTO SOBRE LA PRESION ARTERIAL, EL RITMO CARDIACO, LA GLUCOSA SANGUINEA Y LA LIPOLISIS**

**SUMARIO**

A 25 pacientes sometidos a microlaringoscopia, se les administró tiopentona y óxido nitroso junto con suxametónio como relajante muscular. Trece recibieron 0,4 mg kg\(^{-1}\) de practolol y 1,5 mg de atropina i.v. poco antes de la anestesia. Se administró 0,2 mg kg\(^{-1}\) de practolol durante la anestesia. Doce (controles) recibieron 0,5 mg de atropina antes de la anestesia. El practolol redujo la frecuencia de la taquicardia y de la arritmia. El grupo tratado experimentó una mayor reducción de la presión arterial sistólica durante la inducción. El practolol no atenuó significativamente la respuesta hipertensiva a la laringoscopía. No hubo efecto en la respuesta hiperglicémica debido a la microlaringoscopía ni tampoco en la concentración de glicérol en el plasma.