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Does the choice of antihypertensive therapy influence haemodynamic responses to induction, laryngoscopy and intubation?†

J. W. SEAR, C. JEWKES, J.-C. TELLEZ AND P. FOËX

Summary

We have measured haemodynamic responses to induction of anaesthesia, laryngoscopy and intubation in 103 mild–moderate hypertensive patients (83 patients (diastolic pressures $\leqslant 110$ mm Hg) currently receiving one of four monotherapies (ACE inhibitors, group A; β adrenoceptor blocking drugs, group B; calcium channel antagonists, group C; diuretics, group D) and 24 were untreated hypertensive patients). Anaesthesia was induced with fentanyl 1.5–2.0 μg kg^{-1} and thiopentone 3–5 mg kg^{-1}. Tracheal intubation was facilitated by vecuronium 0.1 mg kg^{-1} and anaesthesia maintained with enflurane and nitrous oxide in oxygen. Systolic and diastolic pressures (SAP, DAP) were measured at 1-min intervals by a non-invasive oscillometric method and cardiac output (CO) and stroke volume (SV) by thoracic bioimpedance. Induction of anaesthesia was associated with a decrease in SAP, DAP and CO in groups A–D ($P < 0.05$). Heart rate (HR) decreased in groups A and D ($P < 0.01$) and systemic vascular resistance (SVR) decreased in groups A and B ($P < 0.05$). SAP and HR increased in all groups after laryngoscopy and intubation ($P < 0.01$) as did SVR in groups A, B and D ($P < 0.02$). CO was unaltered. Similar changes occurred in the untreated hypertensive patients, although nine of 24 patients exhibited HR $\geqslant 100$ beat min^{-1} after laryngoscopy and intubation. Comparison of the changes in SAP, DAP, CO and SVR with time showed no differences in the five treatment groups; changes in HR were significantly less in group B compared with the other groups ($P < 0.01$). We conclude that the pressor responses to laryngoscopy and intubation are unaffected by concurrent medication in mild–moderate hypertensive patients and changes of a similar magnitude are observed also in untreated hypertensive patients. (*Br. J. Anaesth.* 1994; **73**: 303–308)

Key words

Intubation tracheal, responses. Cardiovascular system, effects. Larynx, laryngoscopy.

Hypertension (defined by the WHO as systolic pressure $\geqslant 160$ mm Hg, or diastolic pressure $\geqslant 90$ mm Hg, or both) is a common clinical problem [1]. Although Goldman and Caldera reported that mild hypertension (diastolic arterial pressure < 100 mm Hg) was not a major risk determinant in the development of these complications [2], more recent data by Stone and colleagues have suggested that myocardial ischaemia and arrhythmias are more frequent in mild–moderate untreated hypertensive patients compared with treated patients receiving either single dose, acute β adrenoceptor block at the time of premedication or chronic β adrenoceptor block [3, 4]. However, although β adrenoceptor block obtunds the heart rate response to noxious stimulation during anaesthesia and surgery, it has little effect on the pressor response (which is mediated by α adrenergic mechanisms).

Similarly, calcium channel block has been shown to obtund the pressor response, but not the increase in heart rate, to laryngoscopy and intubation when given as premedication to either normotensive or hypertensive patients [5–7]; similar modifications of the responses to the noxious stimulus of aortic clamping in dogs have been described after treatment with nifedipine [8]. Although the effects of both acute and chronic β adrenoceptor blocking therapy in the peroperative management of these pressor responses in the hypertensive patient are well described [9], there are fewer data on the interactions between anaesthesia and mild–moderate hypertension (diastolic pressures < 110 mm Hg) in patients receiving chronic monotherapy in the form of angiotensin converting enzyme inhibitors or calcium channel blockers (alone or in combination with a diuretic), or diuretics alone.

Comparison of large numbers of patients using the thoracic electrical bioimpedance (TEB) method of cardiac output evaluation has been shown by Mickell and colleagues to improve the reliability of this non-invasive method [10]. Hence we have chosen to study larger groups of patients than in most other

J. W. SEAR, MA, BSC, PHD, FRCA, C. JEWKES, MB, BS, FRCA, J.-C. TELLEZ, MD, P. FOËX, MD, DPHIL, FRCA, Nuffield Department of Anaesthetics, University of Oxford, John Radcliffe Hospital, Headington, Oxford OX3 9DU. Accepted for publication: March 23, 1994.

Correspondence to J.W.S.

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reports in order to compare induction–intubation responses in patients receiving different treatment regimens.

Patients and methods

Patients were studied with informed consent and after approval of the Central Oxford Research Ethics Committee. The patients studied were either known hypertensive subjects receiving one of four monotherapies or were untreated or unknown hypertensives presenting with a minimum of three arterial pressures of between 160/90 and 200/105 mm Hg recorded in hospital before surgery.

The patients were grouped as follows: group A (angiotensin converting enzyme (ACE) inhibitors, $n = 16$); group B (β adrenoceptor blocking drugs, $n = 24$); group C (calcium channel antagonists, $n = 18$); group D (diuretics alone, $n = 21$). In addition, there were 24 untreated mild–moderate hypertensive patients (group U).

None of the patients had angina pectoris or ECG changes suggestive of active coronary artery disease; none had ECG evidence of left ventricular hypertrophy ($V_1 + V_6 > 40$ mm); and none had laboratory evidence of significant renal impairment (serum creatinine > 150 μmol litre^{-1}). All patients were undergoing surgery necessitating general anaesthesia with tracheal intubation.

After premedication, as indicated on clinical grounds (either an oral benzodiazepine or the i.m. opioids morphine, papaveretum or pethidine), anaesthesia was induced with fentanyl 1.5–2.0 μg kg^{-1}, followed 1 min later by thiopentone 3–5 mg kg^{-1}. Vecuronium 0.1 mg kg^{-1} was given 3 min after the induction dose of thiopentone and the trachea intubated 2 min later. Anaesthesia was maintained throughout with 66% nitrous oxide in oxygen supplemented with enflurane ($\leqslant 1\%$ inspired concentration).

Arterial pressure (systolic (SAP), diastolic (DAP), mean (MAP)) was measured at 1-min intervals before and during induction of anaesthesia by the Critikon Dinamap (XT 1846); heart rate (HR), stroke volume (SV) and cardiac output (CO) were similarly recorded continuously using a TEB method (BoMed $NCCOM_3$, BoMed Medical Manufacturing Ltd, Irvine, CA, USA). Data from the BoMed $NCCOM_3$ were collected as the average values obtained over 16 cardiac cycles and recorded on a Thinkjet printer (Hewlett Packard, Watford, UK). The mean value of three successive determinations was calculated so as to coincide with the cuff deflation cycle of the Dinamap.

Those patients presenting on concurrent therapy (ACE inhibitors, β adrenoceptor blocking drugs, calcium channel blockers or diuretics) received their daily medication at the time of premedication.

STATISTICAL METHODS

Data were analysed in the following manner. Preinduction (baseline) haemodynamic values were determined as the mean of data collected at 1 and 5 min before induction of anaesthesia.

The responses of the different patient groups to induction, laryngoscopy and intubation were measured as: number of patients with SAP < 90 mm Hg after induction; number of patients exhibiting HR < 50 beat min^{-1} during the induction–intubation sequence; number of patients in whom SAP after laryngoscopy and intubation exceeded the preinduction (baseline) value by > 20 mm Hg; and the number of patients in whom HR exceeded 100 beat min^{-1} (or exceeded the preinduction value by an increase of $> 20\%$) after either induction or laryngoscopy and intubation.

The overall changes in the five groups in SAP, DAP, HR, CO and systemic vascular resistance (SVR) during the whole induction–intubation sequence were measured as the area under the haemodynamic variable–time curve [11].

The baseline values for the five treatment groups were compared using analysis of variance (SPSS for MS Windows, release 5.0) and the Student's unpaired t test, while within-group analysis was made using the Wilcoxon matched-pairs signed rank test or paired Student's t test with Bonferroni correction for multiple comparisons. Comparison of the changes with time in the five groups was determined using analysis of serial measurements based on calculation of the area under the variable–time curve for each patient and then use of ANOVA to compare the five groups.

Results

One hundred and three patients (43 male) were recruited. Groups were similar in height, weight and preoperative arterial pressure, although patients in group D were older than the other groups (table 1). The induction doses of thiopentone, doses of fentanyl and opioid premedication regimens were comparable for all five groups.

There were no significant differences between groups in the baseline values of SAP and DAP; however, as expected, preinduction HR was slower in group B (table 2). Baseline HR values in excess of 100 beat min^{-1} were seen in 12 patients (group A = 4; group C = 3, group D = 3 and group U = 2). There was no difficulty in airway management during the induction–intubation sequence in any patient.

PATIENTS RECEIVING CHRONIC MONOTHERAPY (GROUPS A, B, C AND D)

Induction of anaesthesia was associated with a decrease in SAP, DAP and CO in all four groups ($P < 0.01$, $P < 0.01$ and $P < 0.05$, respectively), while HR decreased in groups A and D ($P < 0.01$). SVR decreased in groups A and B ($P < 0.05$).

Laryngoscopy and induction was associated with an increase in SAP and HR in all four groups ($P < 0.01$). SVR increased in all groups ($P < 0.05$), except in those receiving calcium channel antagonists. As a result of the increase in SVR, SV decreased significantly in all groups ($P < 0.05$). There were no significant changes in CO in any of the four groups after laryngoscopy and intubation (figs 1–4).

Table 1 Characteristics of the 103 hypertensive patients receiving one of the four monotherapies (groups A–D) or presenting with mild–moderate untreated hypertension (group U) (mean (SD) or range) and numbers of patients receiving opioid premedication, and doses of fentanyl and thiopentone. ** $P < 0.01$ compared with the other four groups

Group	Sex (M/F)	Weight (kg)	Height (cm)	Age (yr)	Opioid premed.	Fentanyl ($\mu g\ kg^{-1}$)	Thiopentone ($mg\ kg^{-1}$)
A ($n = 16$)	8/8	73 (12)	169 (7)	61 (38–84)	8/16	1.6 (0.6)	4.5 (1.1)
B ($n = 24$)	9/15	76 (12)	168 (8)	58 (32–83)	16/24	1 6 (1.0)	4.7 (0.8)
C ($n = 18$)	11/7	70 (11)	167 (8)	60 (25–76)	9/18	1.7 (0.6)	4.5 (1.4)
D ($n = 21$)	6/15	64 (12)	164 (8)	73 (58–74)**	12/21	1 8 (0.8)	4.7 (0.8)
U ($n = 24$)	9/15	67 (11)	164 (6)	58 (30–78)	15/24	1.9 (1 1)	4.7 (1.1)

Table 2 Mean (SD) baseline haemodynamic variables of the 103 hypertensive patients receiving one of the four monotherapies (groups A–D) or presenting with mild–moderate untreated hypertension (group U). ** $P < 0.01$ compared with all other groups

Group	SAP (mm Hg)	DAP (mm Hg)	HR ($beat\ min^{-1}$)	CO ($litre\ min^{-1}$)	SVR ($mm\ Hg\ min\ litre^{-1}$)
A	155 (25)	88 (21)	81 (20)	5.4 (1.6)	21.79 (6.14)
B	156 (20)	84 (13)	62 (9)**	5.0 (1.0)	22.50 (5.09)
C	156 (33)	83 (12)	79 (17)	5.0 (1.2)	22.12 (4.88)
D	166 (18)	83 (16)	77 (16)	4.9 (1 6)	25.39 (9.15)
U	160 (12)	86 (10)	78 (18)	5.5 (1.3)	21.69 (6.35)

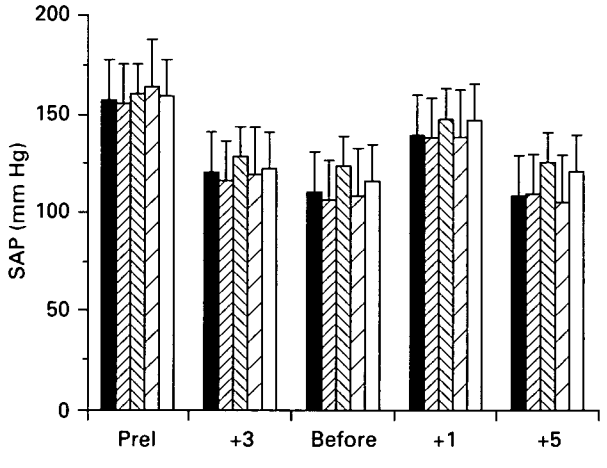

Figure 1 Systolic arterial pressure (SAP) values (mean, SD) in group A (ACE inhibitor, ■), group B (β-blockers, ▨), group C (calcium channel blockers, ▧), group D (diuretics ▨) and group U (untreated, □). Data show preinduction (Prel) values and values 3 min after induction (+3), before laryngoscopy (Before), and 1 and 5 min (+1, +5) after laryngoscopy and intubation.

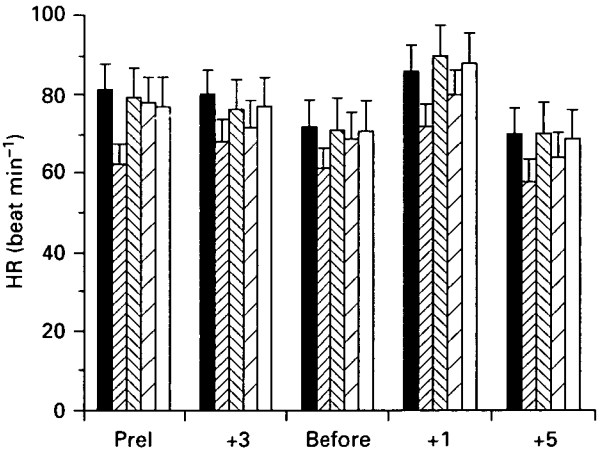

Figure 2 Mean (SD) heart rate (HR) values in the five groups. Explanations as in figure 1.

UNTREATED MILD–MODERATE HYPERTENSIVE PATIENTS (GROUP U)

In these patients, there were significant decreases in SAP and DAP ($P < 0.01$) after induction of anaesthesia, while HR was unchanged. CO decreased ($P < 0.01$) because of a reduction in SV ($P < 0.05$). SVR remained unaltered.

With laryngoscopy and tracheal induction, there were significant increases in SAP, DAP and HR ($P < 0.01$), coupled with a decrease in SV ($P < 0.05$). The increases in arterial pressures were secondary to increased SVR ($P < 0.01$). CO was unchanged.

There were no differences between the five groups in the number of patients in whom SAP decreased to $\leqslant 90$ mm Hg after induction of anaesthesia or in the number of patients in whom HR exceeded 100 $beat\ min^{-1}$ (chi-square = 5.041; 4 df). Comparison of the haemodynamic effects of laryngoscopy and intubation showed no differences in the magnitude of the increases in SAP and DAP, but there was a significant difference between the groups in the number of patients exhibiting HR values $\geqslant 100$ $beat\ min^{-1}$ after laryngoscopy and intubation (chi-square = 15.90; 4 df; $P < 0.01$). This was the result of the high percentage of subjects in group U exhibiting large increases in HR.

The mean maximum value for SAP after laryngoscopy and intubation was not significantly greater than the preinduction value in all groups. However, in 10 of the 103 patients studied, individual values of SAP exceeded the preinduction value by 20 mm Hg or more (group A = 1, group B = 3, group C = 2, group D = 2 and group U = 2; ns). Similarly, HR values exceeded 100 $beat\ min^{-1}$ (or were increased by $\geqslant 20\%$ from the preinduction value) in 41 patients

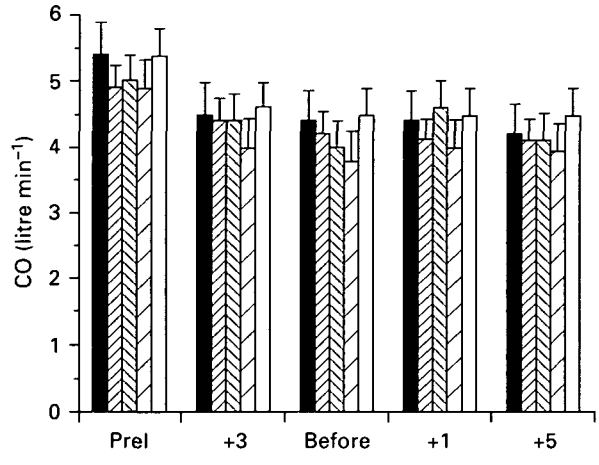

Figure 3 Mean (SD) cardiac output (CO) in the five groups. Explanations as in figure 1.

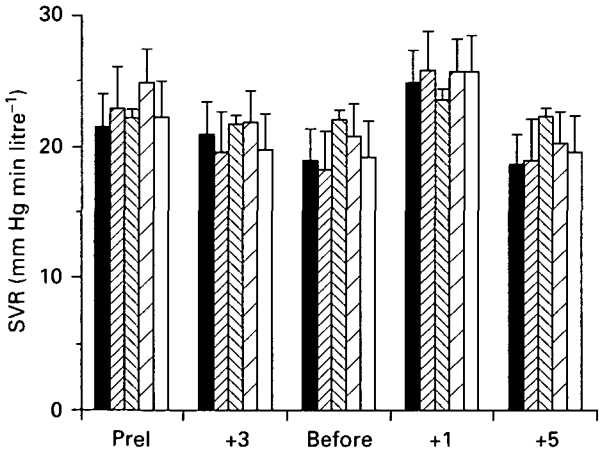

Figure 4 Mean (SD) systemic vascular resistance (SVR) values in the five groups. Explanations as in figure 1.

during the induction–intubation sequence (chi-square = 3.57; 4 df; $P \geq 0.5$). This analysis excluded nine patients whose baseline HR values were > 100 beat min^{-1} (group A = 3, group C = 3, group D = 1 and group U = 2).

Twelve patients had HR values ≤ 50 beat min^{-1} (group A = 2, group B = 6, groups C and D 1 each and group U = 2). None of these patients required active treatment for any associated hypotension.

Comparison of the changes with time for all five groups was made by the technique of analysis of serial measurements using ANOVA on the area under the curve for variable against time. There were no differences between the five groups in SAP, DAP, MAP, CO and SVR (F values: 0.451, 0.764, 0.374, 1.064 and 0.739, respectively). However, there was a significant difference for HR ($F = 4.829$; $P < 0.01$). The respective values for the areas under the HR–time curves for groups A, B, C, D and U were mean 1199.1 (SD 269.5), 970 (122.7), 1178.6 (215.4), 1115.7 (191.8) and 1174.1 (200.9) beat min^{-1}. Using the Student's unpaired t test with a significance level of $P < 0.01$, the area under the HR–time curve was less in group B than in the other four groups (t = 3.187, 3.685, 2.987 and 4.248, respectively). However, the maximum increases in HR after laryngoscopy and intubation were similar in all five treatment groups: 14.3 (13.6), 12.7 (8.3), 19.9 (19.1), 13.0 (13.0) and 17.0 (15.0) beat min^{-1}, respectively, for groups A, B, C, D and U.

Discussion

Myocardial ischaemia occurs frequently during anaesthesia [12–14] and is more frequent in hypertensive patients who are either untreated or poorly controlled [15–18]. In these latter groups of patients, the application of a noxious stimulus (e.g. laryngoscopy and intubation) can result in significant increases in both HR and arterial pressure [15, 16]. Many pharmacological approaches have been adopted to attenuate these circulatory changes (e.g. topical anaesthesia, i.v. lignocaine, vasodilators, β adrenoceptor block, narcotic supplementation). The studies of Stone and colleagues showed that in mild untreated hypertensive patients (diastolic pressures < 100 mm Hg), the administration of an oral dose of a β adrenoceptor blocking drug at the same time as premedication reduced the incidence of ECG-detected myocardial ischaemia [3, 4]. Ischaemia was associated with episodes of tachycardia [3].

We have arbitrarily chosen three end-points to assess the efficacy of the various treatment regimens: SAP after induction of anaesthesia of ≤ 90 mm Hg; SAP after laryngoscopy and intubation exceeding the baseline preinduction value by 20 mm Hg or more; and HR after laryngoscopy and intubation greater than baseline by 20 % or more, or HR > 100 beat min^{-1}. Other authors have chosen other end-points as potential indices of myocardial ischaemia (HR > 100 or 110 beat min^{-1}, rate–pressure product > 20000 or pressure–rate ratio > 1) [19–22]. There are no comparative data to show that any of these indices are better than others. Knight and colleagues [19] found that the majority of perioperative ischaemic ECG changes occurred *without* associated acute haemodynamic changes before the onset of ischaemia, but Slogoff and Keats [20] demonstrated that tachycardia (HR > 110 beat min^{-1}) was the only haemodynamic abnormality related to intraoperative ischaemia. Both of these studies were in patients undergoing coronary artery bypass surgery and may not be readily comparable with our present hypertensive population. Other suggested indices of ischaemia include the rate–pressure product [21], but this has been found to be wanting. Similarly, a pressure–rate ratio of > 1 may be in error [22]. High pressure and fast rate yield a normal ratio, yet the fast rate may be a major contributor to ischaemia. A low pressure and slow rate may also be disastrous.

Because of the need for invasive monitoring, many previous studies on the effects of antihypertensive medication on the pressor and chronotropic responses to laryngoscopy and intubation have been conducted in small numbers of patients, especially those receiving β adrenoceptor blocking drugs. These drugs (administered either chronically or as a single premedicant dose) act to reduce tachycardia, but do not blunt the pressor responses to laryngoscopy and intubation [23]. On the other hand, those calcium entry blockers used in the treatment of

hypertension (the dihydropyridine drugs) act mainly by reduction in afterload and may therefore be expected to influence the hypertensive response rather than the tachycardia after laryngoscopy and intubation [5–7, 24].

Our previous studies and those of Prys Roberts and colleagues [4, 15, 16] have indicated that treatment of hypertension with diuretic therapy alone may cause significant hypotension after induction of anaesthesia, with no attenuation of the pressor responses to laryngoscopy and intubation, or surgical incision.

More recent interest has turned to the possible protective effects of ACE inhibitors when used as monotherapy for the treatment of hypertension, especially in elderly patients. Miller and colleagues have proposed that angiotensin II may be responsible for haemodynamic regulation during anaesthesia [25, 26] and hence it is not surprising that there have been reports of profound hypotension and bradycardia during anaesthesia in patients treated with ACE inhibitors [27]. However, other data do not support this view [28–30]. In a more recent paper, Colson and colleagues have examined the haemodynamic effects of anaesthesia in hypertensive patients receiving ACE inhibitors [31]. Induction of anaesthesia with fentanyl and flunitrazepam caused a greater reduction in arterial pressure in the ACE inhibitor group, with accompanying reductions in pulmonary capillary wedge pressure and cardiac index, necessitating treatment with fluids and phenylephrine.

Thus it was surprising to find in our groups of mild–moderate hypertensive patients maintained with one of four monotherapies that global analysis revealed only minor differences between treatment regimens with respect to haemodynamic responses to induction of anaesthesia, laryngoscopy and intubation. Our previous studies using the TEB method for measurement of CO have shown that, although there are differences in output estimates compared with thermal dilution (because of differences in measurement principles), the two methods are comparable in their ability to accurately follow trends [32]. The lack of exaggerated responses to induction of anaesthesia, laryngoscopy and intubation in the untreated group is at variance with other data published previously [15, 16]; however the preinduction pressures were significantly greater in the patients studied by Prys Roberts and colleagues. Thus our present data would support the view that there are no important advantages of one treatment over another, or over non-treatment in mild–moderate hypertensive patients subjected to anaesthesia and surgery.

We can conclude, therefore, that the pressor responses to laryngoscopy and intubation appear to be unaffected by choice of medication in those mild–moderate hypertensive patients with preoperative diastolic pressures $\leqslant$ 110 mm Hg.

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