Low-dose fentanyl: haemodynamic response during induction and intubation in geriatric patients

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Twenty-eight surgical patients aged 65–84 were randomly assigned to either a control group (12) induced with thiopentone alone, or a treatment group (16), induced with 3 $\mu g \cdot kg^{-1}$ fentanyl followed by thiopentone, to determine whether the use of fentanyl during induction would attenuate the cardiovascular response to laryngoscopy and intubation.

Patients in the fentanyl group required 47 per cent less thiopentone for induction. Increases in systolic (SBP) and diastolic (DBP) blood pressure were significantly smaller in the group receiving fentanyl at one minute post intubation. SBP rose by 56 mmHg in the control group, compared to 15 mmHg in the fentanyl group; DBP increased 42 mmHg compared to 20 mmHg, respectively. Increases in rate-pressure product were twice as great in the control group compared to the fentanyl group (72.2 vs 36.0 per cent, respectively).

Thus, fentanyl, as an adjunct to barbiturate induction, effectively lowered the thiopentone requirement and attenuated the pressor response to laryngoscopy and intubation.

Key words

ANALGESICS: fentanyl; INTUBATION, ENDOTRACHEAL: cardiovascular responses; AGE FACTORS.

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Laryngoscopy and intubation in the lightly anaesthetized patient are accompanied by considerable increases in heart rate and arterial blood pressure. These changes are of short duration, and well tolerated by patients in the absence of cardiovascular disease. However, sudden death has occurred immediately after intubation. Myocardial ischaemia, ventricular arrhythmias, left ventricular failure, and cerebral haemorrhage have all been reported with the post-intubation pressor responses.

Geriatric patients may be at particular risk. Hypertension and ischaemic heart disease are common in the elderly. In addition, decreased autoregulation and sympathetic tone, and increased peripheral vascular resistance result in a decreased adaptability of the circulatory system to stress.

The objective of the present study was to determine whether the use of 3 $\mu g \cdot kg^{-1}$ fentanyl would attenuate the change in blood pressure and pulse in geriatric patients during laryngoscopy and intubation, and following intubation.

Methods

The study protocol was approved by the Human Experimentation Committee. Twenty-eight surgical patients of either sex, 65–84 years of age, ASA physical status II or III, gave informed consent to enter the study.

No premedication was given. While breathing 100 per cent oxygen, each patient rested quietly for five minutes, after which time tubocurarine, 5 $\mu g \cdot kg^{-1}$, was administered intravenously. Patients were randomly assigned to one of two groups, induced as follows:

Control: Thiopentone bolus at 50 $mg \cdot min^{-1}$ until loss of consciousness.

TABLE Demographic and intraoperative data

	Treatment group	
	Control (n = 12)	*Fentanyl n = 16)*
Sex	7 M; 5 F	4 M; 12 F
Weight	71.8 ± 3.8	73.2 ± 5.2
ASA class	I II III	I II III
	1 10 1	– 11 5
Duration of anaesthesia (min)	104 ± 37.4	133 ± 76.5
Induction		
Total fentanyl (μg)	0	187.5 ± 36.3
(μg·kg^{-1})		3.0 ± 0.14
Total thiopentone (mg)	216.7 ± 74.9	115.6 ± 35.2*
Maintenance fentanyl (μg)	204.5 ± 75.7	96.9 ± 83.9*
Total fentanyl (μg)	204.5 ± 75.7	235.9 ± 81.0

*Significant between-group difference. Values presented as mean ± SEM.

Fentanyl: Fentanyl, 3 μg·kg^{-1} intravenously at 1 μg·kg^{-1}·min^{-1}, followed immediately by thiopentone bolus at 50 mg·min^{-1} until loss of consciousness.

Loss of consciousness was defined as loss of response to voice command and loss of lid reflex, and was assessed every 15 seconds by two anaesthetists during the induction. Succinylcholine (2 mg·kg^{-1}) was then administered, followed by controlled ventilation with oxygen. One minute later, laryngoscopy and intubation were performed, and controlled ventilation with 70 per cent nitrous oxide/30 per cent oxygen was initiated.

Heart rate, systolic blood pressure, and diastolic blood pressure were monitored via a radial artery catheter, and were recorded at:

1 Baseline (following a rest period of five minutes, breathing 100 per cent oxygen)
2 Pre-induction (after tubocurarine and fentanyl)
3 Pre-intubation (unconscious before intubation)
4 Intubation (laryngoscopy and intubation)
5 At each minute, for five minutes following intubation.

Following this observation period, maintenance of anaesthesia was by additional fentanyl, tubocurarine, 0.25–1.0 per cent enflurane, and nitrous oxide/oxygen. However, if blood pressure exceeded 200/110, active measures, such as deepening the level of anaesthesia with volatile agents, were employed. Cardiac rhythm was monitored by electrocardiogram with a modified V_5 lead.

Naloxone was administered postoperatively if respiratory rate fell below 10/min. On the day following surgery, patients were questioned regarding intraoperative awareness and anaesthetic complications.

Statistical evaluation

Within-group differences from baseline for systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) and rate–pressure product (RPP) were determined using two-way analysis of variance with Tukey's multiple range test. Between-group differences, using the change from baseline value for each variable studied, were determined by Student's t test for unpaired data. Between group differences in non-parametric data were assessed using Chi-square. Differences were considered significant when $p < 0.05$.

Results

Patient Population (Table)

Twenty-eight patients completed the study. Sixteen patients were randomised to the fentanyl induction group, and 12 did not receive fentanyl during induction (control group). There were no significant differences between the two groups in sex distribution, age, weight or ASA physical status.

Both groups were comparable in mean duration of surgery and duration of anaesthesia. Patients in the fentanyl group required 47 per cent less thiopentone on induction. All but one patient in the control

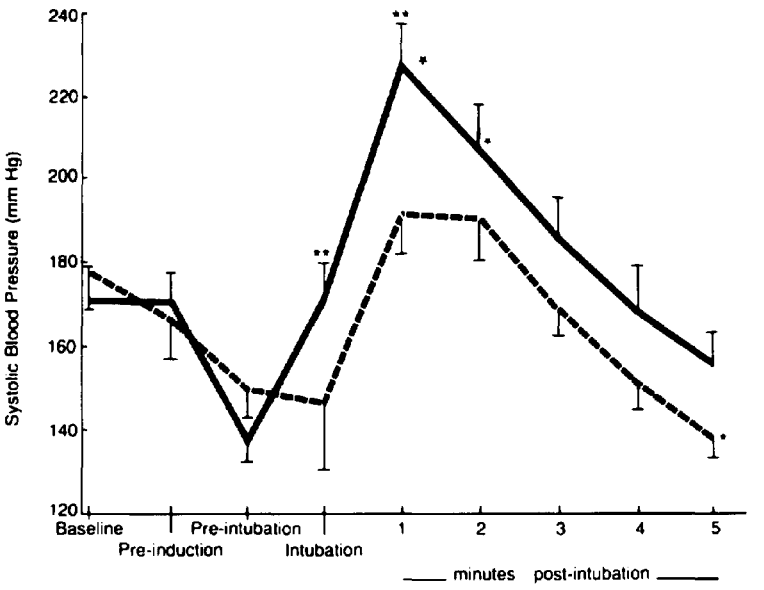

FIGURE 1 Effect of induction, laryngoscopy and intubation on systolic blood pressure in the control (solid line) and fentanyl (dashed line) groups.
*Significant within-group difference from baseline value.
**Significant between-group difference, based on mean change from baseline value in each group.

group, and eight patients in the fentanyl group, required fentanyl during the maintenance phase. The total dose of fentanyl administered (induction plus maintenance in the fentanyl group; maintenance only in the control group) did not differ between the groups.

Cardiovascular stress response (Figures 1 to 4)
Baseline values for SBP, DBP, HR and RPP were similar in both groups. In the control group, SBP, DBP, HR and RPP all rose significantly above the baseline value at one and two minutes post-intubation. In the fentanyl group no variable increased significantly above baseline at any time, although at five minutes post-intubation SBP was lower than the baseline value, possibly due to the absence of surgical manipulation, which was allowed only after the five minute post-intubation observation period. SBP fell below 115 mmHg in two patients (99 mmHg; 93 mmHg).

Between-group comparison, using the difference from baseline value at subsequent time intervals, showed that the increases in SBP, DBP and RPP were significantly smaller in the fentanyl group at one minute post-intubation. Increases were two to four times greater in the control group. For instance, SBP rose by 56 mmHg in the control group, compared to an increase of 15 mmHg in the fentanyl group; DBP increased by 42 mmHg compared to 20 mmHg, respectively. RPP increased 72.2 per cent compared to 36.0 per cent respectively. Fentanyl also had a favourable effect on SBP and DBP at intubation. Changes in HR did not differ significantly between groups at any time.

During the induction/intubation period, blood pressure exceeded 200/110 in seven patients (58 per cent) in the control group and in four patients (25 per cent) in the fentanyl group. Nine patients (75 per cent) in the control group, and seven patients (44 per cent) in the fentanyl group required additional anaesthetic agents (enflurane) during this period ($x = 3.19$, NS).

Four patients in each treatment group were known hypertensives, and all were receiving anti-

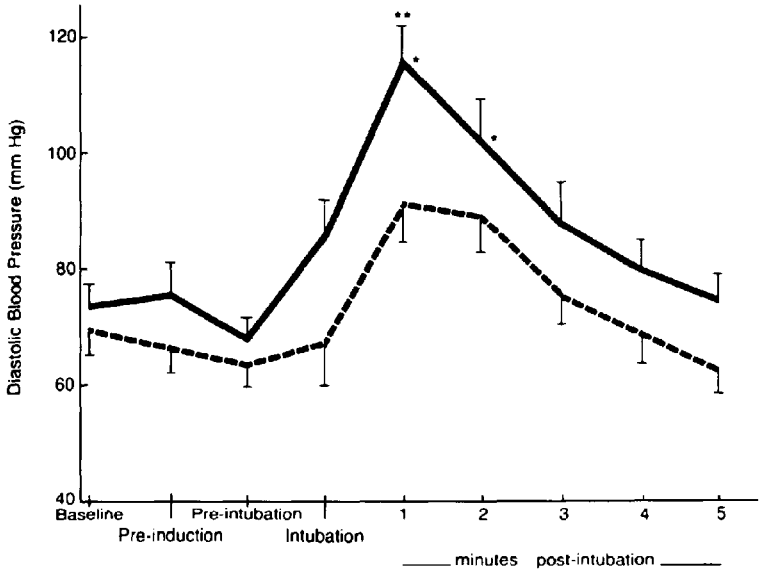

FIGURE 2 Effect on induction, laryngoscopy and intubation on diastolic blood pressure in the control (solid line) and fentanyl (dashed line) groups.
*Significant within-group difference from baseline value.
**Significant between-group difference, based on mean change from baseline value in each group.

hypertensive medication. Baseline blood pressure in these patients was not remarkable. No significant difference was noted in the response of hypertensive patients compared to those without diagnosed hypertension.

Complicatons

No serious bradycardia or other rhythm disturbances, truncal rigidity, or recall of the laryngoscopy and intubation were noted in any patients. Three patients in the fentanyl group required a small dose of naloxone (0.08–0.1 mg) for reversal of respiratory depression.

Discussion

The pressor response to laryngoscopy and intubation is well recognized. Various methods have been suggested to attenuate the increases in arterial pressure and heart rate, including the use of deeper inhalation anaesthesia, sympathetic blockade, hypotensive agents, and local anaesthesia. However, these methods have not been found to be uniformly successful.

Several studies have reported a beneficial effect of fentanyl as an adjunct to barbiturate induction. Dahlgren and Messeter administered fentanyl, 5 $\mu g \cdot kg^{-1}$, prior to induction with thiopentone and succinylcholine, to eight neurosurgical patients, and found a significant blunting of the cardiovascular stress response to intubation, compared to seven patients who did not receive fentanyl. All patients were without a history of hypertension, and the mean age was approximately 50 years. In a double-blind, saline-controlled study, Kautto evaluated two doses of fentanyl (2 and 6 $\mu g \cdot kg^{-1}$) as an adjunct to thiopentone induction in 45 normotensive ASA physical status class I patients, less than 55 years of age. The higher dose of fentanyl completely prevented the pulse rate and arterial pressure increases, while significant pressure increases still occurred in the lower dosage group. Martin *et al.* used 8 $\mu g \cdot kg^{-1}$ fentanyl as an adjunct to thiopentone induction in 18 patients and com-

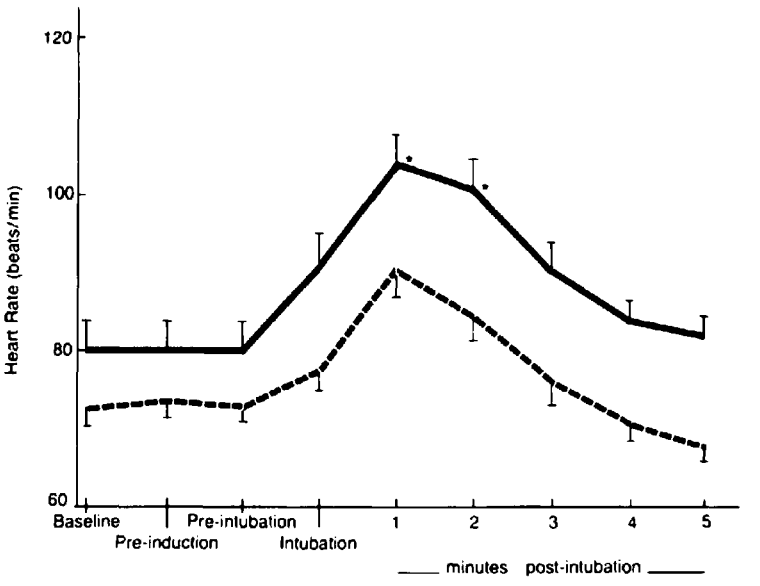

FIGURE 3 Effect on induction, laryngoscopy and intubation on heart rate in the control (solid line) and fentanyl (dashed line) groups.
*Significant within-group difference from baseline value.

pared the circulatory changes to 18 patients induced by thiopentone alone. All patients underwent major vascular surgery; more than half the patients in each group had a history of hypertension, and the patients were older (mean age 68 years in the fentanyl group) than in previous studies. Fentanyl abolished both the pulse and pressure elevation associated with intubation.

Although Martin *et al.* did not observe respiratory depression or other complications at the relatively high dose used, it may have been masked by the prolonged surgery which their patients underwent, allowing more time for fentanyl elimination before extubation. It seems prudent to employ as little fentanyl as is necessary to reduce the intubation stress response to an acceptable level with minimal risk of other untoward effects. This may be especially important in elderly patients, since fentanyl pharmacokinetics change with age. Elimination half-life in patients over 60 years of age is prolonged, as a result of diminished systemic clearance, to approximately 3.5 times that in younger (<50 years) patients. Following a given dose, serum drug concentrations are higher in the elderly. Thus, the results of studies of fentanyl in younger patients cannot be extrapolated to the geriatric population. In addition, blood pressure changes are more labile in the elderly. Thiopentone induction in such patients commonly results in a "roller coaster" effect: the pressor response to laryngoscopy and intubation followed by hypotension secondary to cardiovascular depression, a few minutes later. Therefore, measures that reduce the sleep dose of thiopentone may contribute to a more stable blood pressure during the induction–intubation period. Slow titration of barbiturate to loss of consciousness, as in this study, is not practical on a routine basis, but this allowed us to establish that 1.5–2.0 $mg \cdot kg^{-1}$ thiopentone is an adequate sleep dose when fentanyl is used as an adjunct to induction.

The present study has demonstrated that, in elderly patients, the use of 3 $\mu g \cdot kg^{-1}$ fentanyl as an adjunct to thiopentone induction provided a two-fold beneficial effect: a 47 per cent reduction in the induction dose of thiopentone, and a significant

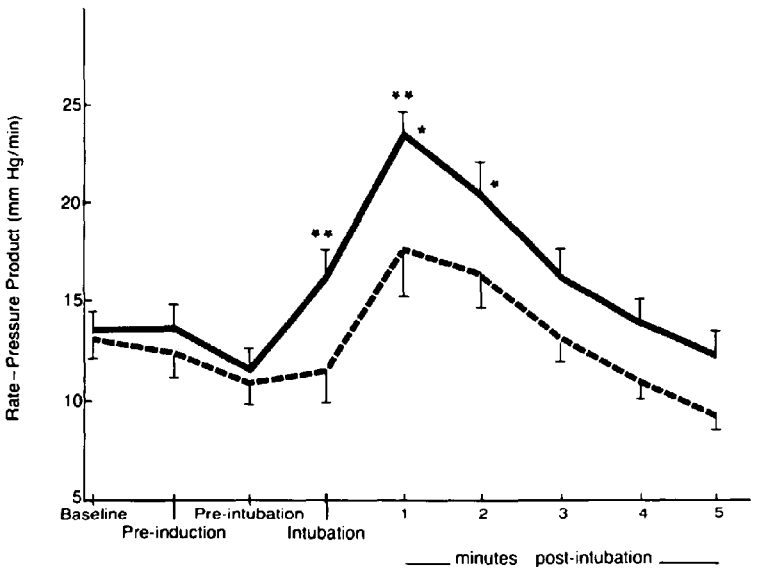

FIGURE 4 Effect on induction, laryngoscopy and intubation on rate-pressure product in the control (solid line) and fentanyl (dashed line) groups.
*Significant within-group difference from baseline value.
**Significant between-group difference, based on mean change from baseline value in each group.

attenuation of the cardiovascular stress response to intubation. Post-intubation increases in SBP, DBP and RPP were one-half to one-quarter of those in the control group. Although the present study was not "blinded" as to treatment group, measurement of variables of interest was such as to minimise observer bias. Blood pressure and heart rate were monitored by radial artery catheter and electrocardiograph, and recorded by a respiratory technologist. Thiopentone was administered as a constant infusion until loss of consciousness as determined by two variables assessed independently by two anaesthetists. Thus, the present findings should not be jeopardised by lack of "blinding."

Since respiratory depression, albeit easily reversed with naloxone, occurred in three patients in the fentanyl group, the use of higher doses of fentanyl during induction, as advocated in earlier studies, may be inadvisable in geriatric patients, especially if surgery is of short duration. Patients in the control group required an amount of fentanyl during maintenance of anaesthesia equivalent to that administered to patients in the fentanyl group during induction and maintenance. It seems prudent, therefore, to use fentanyl as an adjunct to induction, thereby taking advantage of its beneficial effects on thiopentone requirements and the stress response following laryngoscopy and intubation, rather than administering fentanyl simply during the maintenance phase and not deriving these potential benefits.

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Résumé

Vingt-huit patients âgés de 65 à 84 ans et subissant une intervention chirurgicale ont été répartis au hasard entre un groupe témoin (12 patients) recevant du thiopentone seul, et un groupe actif (16 patients) recevant 3 $\mu g \cdot kg^{-1}$ de fentanyl suivis de thiopentone. Le but de l'étude est de déterminer si l'utilisation du fentanyl pendant la période d'induction diminue la réponse cardiovasculaire observée durant la laryngoscopie et l'intubation.

Les patients du groupe recevant le fentanyl ont reçu 47 pour cent de thiopentone en moins lors de l'induction. Dans le groupe recevant le fentanyl les augmentations de la pression artérielle systolique (PAS) et diastolique (PAD) ont été significativement moins importantes une minute après l'intubation. La PAS a augmenté de 56 mmHg dans le groupe temoin et seulement de 15 mmHg dans le groupe traité au fentanyl. La PAD a augmenté de 42 mmHg et de 20 mmHg dans les deux groupes. Les augmentations du produit de la fréquence cardiaque par la pression artérielle ont été deux fois plus importantes dans le group témoin que dans le group recevant le fentanyl (72,2 et 36,0 pourcent respectivement).

L'utilisation du fentanyl comme adjuvant lors de l'induction par les barbirutiques a dimunué les besoins en thiopentone et a atténué la réponse vasopressive observée lors de la laryngoscopie et de l'intubation.