DISCUSSION
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Cardiovascular instability following laryngoscopy and tracheal intubation mainly in the form of tachycardia and hypertension has been investigated extensively since 1951 when King and his colleagues reported this first. This was recognised as a potential cause of a number of complications especially in patients with hypertension, coronary artery disease or cerebrovascular disease. Hence it is widely accepted that these reflex responses which are mediated by an increased sympathetic nervous activity should be prevented or minimized.

Aim of this study was to determine the efficacy of various drug combinations in attenuating or abolishing these reflex responses. Patients under ASA grade I or II who were scheduled for elective surgical procedures requiring general anaesthesia and intubation were selected for the study. Very few studies are reported in which such combinations of drugs were used for this purpose.

Numerous techniques and agents have been employed for this purpose, but none was found to be 100 percent successful. Deep anaesthesia with cyclopropane or ether (King et al, 1951) was found to suppress the
cardiovascular responses. But a significant incidence of (33%) ventricular dysrhythmia was detected (Colondre-Yordan et al, 1953) during intubation under deep cyclopropane-ether anaesthesia. Neuroleptanalgesia (Prys-Roberts et al, 1971) was found to be unsatisfactory in this respect, even though the percentage increase in arterial pressure following neuroleptanalgesia induction was less than with other agents. Beta-blockers were also studied very extensively. Prys-Roberts et al (1969) reported that propranolol was effective in suppressing the cardiovascular response to tracheal and nasopharyngeal suction of secretions in tetanus patients. Practolol (Prys-Roberts, 1973) given i.v. or orally was shown to be effective in suppressing the pressor responses to laryngoscopy and intubation. The incidence of dysrhythmia and e.c.g. evidence of myocardial ischemia were also significantly lower. Metoprolol, a cardio-selective beta-blocker was shown to be reducing arterial pressure during intubation and after extubation (Magnusson et al, 1986).

Sodium nitroprusside (Stoelting, 1979), intranasal nitroglycerine (Fassoulaki and Kaniaris, 1983; Kotak et al, 1986), isosorbide dinitrate (Hatano et al, 1989), trimetaphan (Saitoh et al, 1991) were all found to be reducing the magnitude of the rise in blood pressure following laryngoscopy and intubation, but the associated tachycardia was not prevented. Halothane in various
concentrations were also reported to be effective in reducing the pressor response (Bedford and Marshall, 1984; Turner et al, 1986).

Of the calcium channel blocking agents nifedipine was found to be very effective in reducing the pressor response (Khan et al, 1987, 1989; Puri and Batra, 1988; Bhola and Abraham, 1990). Verapamil was not as effective as nifedipine and also a significant prolongation of P-R interval was observed in some patients (Kolli et al, 1987; Rashid Khan et al, 1989). Diltiazem was reported to be unsuccessful in this respect (Chandrulekha et al, 1990).

Alfentanil in low doses (10-15 μg/kg) modified the haemodynamic changes and in higher doses (above 30 μg/kg) abolished the pressor response to laryngoscopy and intubation (Black et al, 1984; Crawford et al, 1987; Sweeney et al, 1989; Scheinin et al, 1989; Allen et al, 1991). Fentanyl (Bedford and Marshall, 1984; Sweeney et al, 1989) and buprenorphine (Khan and Kamal, 1989) were also found to be effective in reducing the haemodynamic responses to laryngoscopy and intubation. All were either ineffective or partially effective.

In the present study, lignocaine laryngotracheal topical spray, intravenous buprenorphine and sublingual nifedipine were used alone and in three different combinations of two drugs each to attenuate this response.
Use of any of the drugs or drug combinations failed to produce any significant reduction in tachycardia following laryngoscopy and tracheal intubation. This may be due to premedication with intravenous atropine given 5 minutes before induction. It has been shown that atropine administered either i.v. or i.m. does not affect the hypertensive response to laryngoscopy and tracheal intubation but increases the heart rate and the frequency of cardiac arrhythmias resulting from laryngoscopy and tracheal intubation (Fassoulaki and Kaniaris, 1982).

Crawford et al (1987) showed that alfentanil in doses of 10 µg/kg or 40 µg/kg prevented any increase in heart rate and arterial pressure after tracheal intubation. But the drug in the dose of 40 µg/kg produced profound hypotension and bradycardia.

Khan and Kamal (1989) demonstrated that buprenorphine in the dose of 2.5 µg/kg prevented the rise in heart rate following laryngoscopy and intubation to some extent. In their study, heart rate increased by 8% in the control group compared to 1% increase in the buprenorphine group on laryngoscopy and intubation. Anticholinergic premedication was not used in their study. Attenuation of the rise in heart rate with buprenorphine was not seen in the present study.
$B_i =$ Before induction  
$A_i =$ After induction  
$I_0 =$ Immediately after intubation  
$I_1 =$ 1 min. after intubation  
$I_3 =$ 3 min. after intubation  
$I_5 =$ 5 min. after intubation.

Fig. No. 5

Changes in heart rate in groups I, II, III and V.
$B_1 =$ Before induction  
$A_1 =$ After induction  
$I_0 =$ Immediately after intubation  
$I_1 =$ 1 min. after intubation  
$I_3 =$ 3 min. after intubation  
$I_5 =$ 5 min. after intubation.

Fig. No. 6

Changes in heart rate in groups I, II, IV and VI.
Fig. No. 7

Changes in heart rate in groups I, III, IV and VII.

$B_1$ = Before induction
$A_1$ = After induction
$I_0$ = Immediately after intubation
$I_1$ = 1 min. after intubation
$I_3$ = 3 min. after intubation
$I_5$ = 5 min. after intubation.
Application of topical analgesia with lignocaine to the upper airway immediately before intubation of the trachea did not modify the subsequent pressor responses. The findings appear to be at variance with the reports of Denlinger, Ellison, and Ominsky (1974) and that of Stoelting (1977) and in accordance with the findings of Derbyshire, Smith and Achola (1987). However, there are important differences between the design of these studies and the present ones.

In the study of Denlinger, Ellison and Ominsky (1974), the design of the investigation was as follows: in patient undergoing cardiac surgery, anaesthetized with morphine 1 mg/kg and nitrous oxide in oxygen, tubocurarine and suxamethonium, an initial laryngoscopy and tracheal spray with lignocaine was accompanied by a smaller increase in arterial pressure than occurred in a second group of patients in whom saline was used in place of lignocaine. Five minutes later, laryngoscopy and intubation were performed and in the saline-treated group the increase in pressure was greatly exaggerated.

Stoelting (1977) investigated this in patients premedicated with morphine and hyoscine and anaesthetized with thiopental. It was shown that oropharyngeal gurgling with lignocaine 500 mg 10 min. before the induction of anaesthesia was almost equally as effective as lignocaine 1.5 mg/kg given i.v. 90 seconds before laryngoscopy.
The anaesthetic sequence used in the present study was one which might be used in everyday clinical practice. Here laryngotracheal topical spray with lignocaine was done 60 seconds before laryngoscopy, the reason being that nearly maximal topical anaesthesia occurs within approximately 60 seconds of the topical spray: In contrast, studies which have shown laryngotracheal lignocaine to be effective in preventing hypertension and tachycardia after intubation have used a 5 minute interval between instillation of lignocaine and tracheal intubation. Viegas and Stoelting (1975) have shown that blood lignocaine levels are low one minute after laryngotracheal lignocaine spray, but that they gradually rose to a peak value of 1-2.7 μg/ml between 4 and 15 minutes thereafter. It has also been shown that i.v. lignocaine reduces the pressor response to intubation (Stoelting, 1977; Hamill et al, 1981). It is thought that this amelioration occurs as a result of direct myocardial depression (Thomas, 1975; Ritchie and Green, 1980) or deepening of the anaesthesia. Lignocaine blood levels of 3-6 μg/ml are known to potentiate the effects of nitrous oxide anaesthesia in human and a 10-28% reduction in halothane MAC has been observed in dogs with blood lignocaine levels between 3 and 10 μg/ml. Further complicating this picture, Miller and Warren (1990) reported that intravenous lignocaine was not effective
in attenuating these reflex cardiovascular responses. An attenuating effect with lignocaine could not be detected in the present study. Mean arterial pressure and heart rate were closely similar to the control values immediately, and 1, 3 and 5 minutes after intubation.

Intravenous narcotics have been used to ameliorate these responses with variable degrees of success. Alfentanil (Crawford et al, 1987), sufentanil (Kay et al, 1985) have all been used. Fentanyl 5 μg/ml and alfentanil 40 μg/kg have both been successful in obtunding the reflex completely, but both have also been associated with profound hypotension and bradycardia which were resistant to volume replacement and atropine, and an increased degree of respiratory depression. In the present study, buprenorphine was selected for its well known effects on cardiovascular system and cardio-stability. The dose, route and time of administration of the drug with respect to laryngoscopy were chosen on the basis of a study conducted by Khan and Kamal (1989). As mentioned before, the drug failed to show any significant reduction in tachycardia following laryngoscopy and tracheal intubation, but attenuated the rise in mean arterial pressure significantly (P \leq 0.05). Rate pressure product also showed an attenuated response after buprenorphine. The difference from the control was significant (P \leq 0.05) (Table 7).
Fig. No. 8

Changes in mean arterial pressure in groups I, II, III & V

\[ B_i = \text{Before induction} \]
\[ A_i = \text{After induction} \]
\[ T_0 = \text{Immediately after intubation} \]
\[ T_1 = 1 \text{ min. after intubation} \]
\[ T_3 = 3 \text{ min. after intubation} \]
\[ T_5 = 5 \text{ min. after intubation} \]
**Fig. No. 9**

Changes in mean arterial pressure in groups I, II, IV & VI.

- **B₁** = Before induction
- **A₁** = After induction
- **I₀** = Immediately after intubation
- **I₁** = 1 min. after intubation
- **I₃** = 3 min. after intubation
- **I₅** = 5 min. after intubation.
\[ B_1 = \text{Before induction} \]
\[ A_1 = \text{After induction} \]
\[ I_0 = \text{Immediately after intubation} \]
\[ I_1 = 1 \text{ min. after intubation} \]
\[ I_3 = 3 \text{ min. after intubation} \]
\[ I_5 = 5 \text{ min. after intubation} \]

**Fig. No. 10**

Changes in mean arterial pressure in groups I, III, IV & VII.
Nifedipine is an antagonist of calcium influx through slow channel of the cell membrane. Its hypotensive action is mainly due to dilatation of the arterial resistance vessels. Dose and route of administration of the drug used in this study were same as that used by Puri and Batra (1988) and Khan et al (1987). Nifedipine prevented the rise in mean arterial pressure significantly following laryngoscopy and intubation. The rise in mean arterial pressure from the basal to the maximum recorded value in the control group was 43.3% of the basal and in the nifedipine group 21.74%. Compared with buprenorphine, nifedipine produced a significantly higher reduction in maximum rise in mean arterial pressure ($P \leq 0.05$). Three minutes after intubation the mean arterial pressure was significantly lower than that of control, lignocaine or buprenorphine groups ($P \leq 0.05$). The increase in rate pressure product in the nifedipine group was also lesser than in the buprenorphine one, but the difference was insignificant.

The three drug combinations used were lignocaine + buprenorphine, lignocaine + nifedipine and buprenorphine + nifedipine. A combined effect of each of the individual drugs were expected with this technique. But, in fact the study failed to demonstrate any such additive effects (Figures 8, 9 & 10). There was no significant difference
in the mean heart rate values. The degree of reduction in maximum rise in mean arterial pressure with the drug combinations stood close to the effect of that particular individual drug of the combination which showed a better effect than the other when used alone. This is shown in figures (8, 9, 10).

Very few studies are seen in literature in which drug combinations were used to prevent the pressor response to laryngoscopy and intubation. Bedford and Marshall (1984) compared four different anaesthetic techniques, one of which was a combination of fentanyl 5 µg/kg, and droperidol 250 µg/kg, and they found it to be better than 0.4% halothane in attenuating the reflex response to laryngoscopy and intubation. But this combination of drugs also failed to obliterate the reflex response completely.

Manimala Kao et al (1989) compared i.v. lignocaine with i.v. and laryngotracheal topical lignocaine in obtunding the haemodynamic response to laryngoscopy and tracheal intubation. They found both methods to be effective but no special benefit was detected with the combination technique. In fact the results with i.v. lignocaine alone were better.

When lignocaine plus buprenorphine was used the effect on maximum rise in mean arterial pressure was
similar to that of buprenorphine alone. The difference was quite negligible (Figure 8). As discussed before lignocaine alone was found to be ineffective in ameliorating the reflex rise in blood pressure. The mean rate pressure product after intubation was higher in the combination group, than the buprenorphine one but the difference was not significant (P > 0.05).

Maximum rise in mean arterial pressure after intubation in the lignocaine + nifedipine group was slightly higher than when nifedipine alone was used. The difference was not clinically or statistically significant (P > 0.05) (Fig. 9). As in nifedipine group, here also the mean arterial pressure was significantly lower than the control values at 3 minutes after intubation. The increase in rate pressure product was also lesser when nifedipine alone was used.

When buprenorphine plus nifedipine was used the effect was found to be close to that of nifedipine alone (Fig. 10). The maximum recorded mean arterial pressure following intubation was as follows:
buprenorphine alone 122.2 ± 7.66, nifedipine alone 113.1 ± 7.06, and buprenorphine + nifedipine 114.5 ± 7.41. The difference from the nifedipine group was clinically and statistically insignificant. In this group also the mean arterial pressure at 3 minutes after intubation
was lower than that of control value but the difference was not statistically significant \((p \geq 0.05)\). This shows that when nifedipine is used alone or in combination, the mean arterial pressure after rising to a maximum starts falling more rapidly than the control and other groups. The increase in rate pressure product was also more in the combination group than that detected when nifedipine alone was used, even though the difference was insignificant.

Atropine premedication has been found to increase the incidence of arrhythmias following intubation (Fassoulaki and Kaniaris, 1982). In the present study, one patient from the control group, a forty six year old female and another patient from the lignocaine group, a twenty nine year old male developed ventricular extrasystoles. In both cases, the arrhythmia was very transient and disappeared within a few seconds without any drug therapy. In patients in whom buprenorphine and/or nifedipine were used no arrhythmias were detected. It is difficult to say from this study whether this was merely a coincidental finding or the beneficial effect of the drugs administered.

No complications like hypotension or bradycardia were noted in any of the patients during the subsequent period of anaesthesia. This is especially important
with the view that volatile anaesthetic agents can potentiate the effect of calcium channel blockers.

This study shows that both buprenorphine and nifedipine are effective in attenuating the pressor response to laryngoscopy and tracheal intubation and nifedipine provides a statistically better response than buprenorphine. Lignocaine laryngotracheal topical application done immediately before laryngoscopy is not effective in preventing these cardiovascular responses inspite of its widespread clinical use. Also when these drugs were used in different combinations of two each, no added advantage or a better effect could be demonstrated. A safe agent or technique that can prevent the occurrence of these unwanted cardiovascular responses to laryngoscopy and tracheal intubation is yet to be found out and more researches have to be carried out in this regard.

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