VARIABLE RATE IV INFUSION OF MORPHINE AND HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND TRACHEAL INTUBATION

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ABSTRACT

Haemodynamic response to laryngoscopy and tracheal intubation was studied in two groups of 45 patients each. Group I patients received variable rate infusion of morphine for 30 minutes followed by intravenous (IV) bolus dose of diazepam. Group II patients received intramuscular morphine as preanaesthetic premedication and preinduction IV bolus dose of diazepam. The method of induction of GA was same in both the groups. Systolic and diastolic blood pressure (SBP and DBP) mean arterial pressure and pulse-rate were recorded at intubation and at different time intervals upto 10 minutes after intubation. In group I patients, there was no statistically significant increase in pulse-rate and SBP following intubation but transient significant increase in DBP. In group II patients, there was statistically significant increase in pulse-rate, SBP and DBP upto 3 minutes post-intubation. Thus IV infusion of morphine in combination with IV bolus dose of diazepam proved more effective in attenuating haemodynamic response to tracheal intubation.

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KEY WORDS : Laryngoscopy; Tracheal intubation; Haemodynamic response; Morphine.

Introduction

Laryngoscopy and tracheal intubation is very often associated with undesirable haemodynamic response like systolic/diastolic hypertension and tachycardia of a variable degree [1-3]. This adverse effect may be of little or no consequence in healthy patients but in patients with pre-existing cardio-vascular disease, it may precipitate myocardial infarction, cerebrovascular accident, acute left ventricular failure and pulmonary oedema [4]. Various pharmacological methods have been used to attenuate this reflex cardiovascular response to laryngoscopy and intubation with variable results [5-10].

We evaluated the efficacy of preinduction variable rate infusion of morphine followed by a bolus dose of diazepam in attenuating the reflex haemodynamic response to laryngoscopy and intubation.

Material and Methods

Ninety individuals (ASA grade I) of either sex, aged between 21 and 60 years were randomly divided into two groups. The patients likely to pose intubation problem due to any cause were excluded from the study. Informed consent was obtained from all the patients.

Group I (45 patients) : In pre-operative room, these patients were premedicated with injection glycopyrrolate 0.2 mg intramuscularly (IM). They were then shifted to anaesthesia room and IV line was set up with 5% dextrose 500 ml using microdrip set to which morphine sulphate 15 mg was already added (final concentration 30 µg/ml). A loading dose of 60 µg/kg body weight of morphine was infused rapidly in 5 minutes followed by 2 µg/kg body weight in next 25 minutes. This dose was calculated based on the equation given in Table-1 [11]. After 30 minutes IV

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infusion of morphine, this drip was discontinued and replaced by Ringer's lactate drip. Injection diazepam 0.1 mg/kg body wt was then given IV. After this, anaesthesia was induced.

Group II (45 patients) - Control group : In pre-operative room, these patients were pre-medicated with morphine 0.15 mg/kg body wt and glycopyrrolate 0.2 mg IM 45 minutes prior to induction of GA. Then they were shifted to anaesthesia room and IV infusion was set up with Ringer's lactate. Diazepam 0.1 mg/kg body wt was then administered IV.

In all the patients of both groups, pulse oximeter (Ohmeda Biex 3706) and non-invasive BP monitor were attached and preinduction values of pulse rate, systolic and diastolic BP (SBP and DBP) mean arterial pressure (MAP) were recorded. Anaesthesia was induced with thiopentone 4 mg/kg body wt followed by pancuronium 0.1 mg/kg body wt IV to facilitate tracheal intubation and the patient was ventilated with nitrous oxide, oxygen (70 : 30). Patient's pulse rate, systolic, diastolic and mean arterial pressure were recorded at laryngoscopy and at intubation and at 1,2,3,5,7 and 10 minute intervals after intubation. The patients requiring repeated attempts at intubation or prolonged intubation time (> 30 sec) were excluded from the study. Subsequently anaesthesia was maintained throughout operation with N₂O, O₂, pancuronium, controlled ventilation and small doses of morphine.

Results were statistically analysed using Student's paired 't' test. The intergroup comparison was also made using Student's unpaired 't' test.

Results

The sex distribution and mean ($\pm$ SD) values of age, body weight and pre-operative pulse rate, SBP, DBP and MAP in both the groups are shown in Table 2.

In group I, there was no significant increase in pulse rate, SBP and MAP following tracheal intubation but there was transient significant rise in DBP at laryngoscopy and in-

TABLE 1

Dose for IV infusion of morphine

Loading dose	= $C_{pss} \times V_{dss}$
Maintenance dose	= $C_{pss} \times C_1$
C_{pss}	= desired plasma concentration of the drug per ml (2 μ g/ml for morphine)
V_{dss}	= Volume of distribution of the drug at steady state (3 lit/kg for morphine)
C_1	= Clearance of the drug (15 ml/kg/min for morphine).

TABLE 2

Preoperative data (mean $\pm$ SD)

Value of	Group I (n = 45)	Group II (n = 45)
Age (year)	35.8 $\pm$ 8.6	37.6 $\pm$ 3.7
Weight (kg)	53.0 $\pm$ 5.1	48.7 $\pm$ 3.3
Pulse rate (per min)	92.6 $\pm$ 10.4	92.2 $\pm$ 11.1
Systolic BP (mm Hg)	116.8 $\pm$ 11.3	120.6 $\pm$ 11.9
Diastolic BP (mm Hg)	76.4 $\pm$ 8.6	78.6 $\pm$ 9.1
MAP (mm Hg)	89.8 $\pm$ 6.5	93.6 $\pm$ 7.4

tubation ($p < 0.05$) as compared to pre-induction values that persisted for one minute only (Table 3).

In group II (Table 4), there was increase in pulse rate at intubation and at 1 and 3 minute interval following intubation as compared to preinduction values. This increase in pulse rate was statistically highly significant ($p < 0.001$) at intubation and 1 minute and significant at 3 minute ($p < 0.05$) after intubation. Similarly rise in SBP, DBP and MAP was statistically significant/highly significant during and immediately following tracheal intubation.

Intergroup comparison showed that there was significant increase in pulse rate and BP following laryngoscopy and intubation in group II patients.

The mean preinduction dose of morphine administered by IV infusion was 5 mg (SD $\pm$ 1.2 mg).

There was no respiratory depression, allergic manifestations or sickness in any of these patients prior to induction of anaesthesia.

TABLE 3

Showing pulse rate and arterial BP in group I (mean $\pm$ SD)

Time interval	Pulse rate (per min)	Systolic	Arterial BP (mm Hg) Diastolic	MAP
Preinduction	92.6 $\pm$ 10.4	116.8 $\pm$ 10.3	76.4 $\pm$ 8.6	89.8 $\pm$ 6.5
Post intubation				
At intubation	97.0 $\pm$ 8.2	124.4 $\pm$ 16.2	*86.6 $\pm$ 12.4	99.2 $\pm$ 14.6
1 minute	100.2 $\pm$ 9.4	122.6 $\pm$ 12.4	84.0 $\pm$ 13.6	96.9 $\pm$ 13.4
3 minute	99.1 $\pm$ 7.2	116.4 $\pm$ 14.2	81.2 $\pm$ 12.4	92.9 $\pm$ 15.2
5 minute	97.4 $\pm$ 9.7	114.2 $\pm$ 16.4	80.0 $\pm$ 13.2	91.4 $\pm$ 12.6
7 minute	93.1 $\pm$ 11.8	114.2 $\pm$ 15.6	80.0 $\pm$ 8.2	91.4 $\pm$ 9.1
10 minute	92.0 $\pm$ 7.4	110.0 $\pm$ 15.1	78.2 $\pm$ 9.4	88.8 $\pm$ 8.9

* Significant $p < 0.05$

TABLE 4

Showing pulse rate and arterial BP at different time intervals in Group II (mean $\pm$ SD)

Time interval	Pulse rate (per min)	Systolic	Arterial BP (mm Hg) Diastolic	MAP
Pre-induction	92.2 $\pm$ 11.1	120.6 $\pm$ 11.9	78.6 $\pm$ 9.1	92.6 $\pm$ 7.4
Post intubation				
At intubation	**104.4 $\pm$ 8.0	*135.8 $\pm$ 18.4	*90.2 $\pm$ 10.0	**105.4 $\pm$ 11.8
1 minute	**108.6 $\pm$ 11.8	*134.2 $\pm$ 13.0	**90.1 $\pm$ 11.8	104.8 $\pm$ 13.6
3 minutes	*101.8 $\pm$ 8.4	*132.0 $\pm$ 16.6	*87.2 $\pm$ 13.6	**102.1 $\pm$ 10.2
5 minutes	101.0 $\pm$ 8.0	130.0 $\pm$ 18.6	84.0 $\pm$ 14.9	99.3 $\pm$ 13.8
7 minutes	99.0 $\pm$ 10.9	121.6 $\pm$ 16.4	82.2 $\pm$ 8.7	95.3 $\pm$ 9.2
10 minutes	96.4 $\pm$ 8.6	120.4 $\pm$ 13.9	80.0 $\pm$ 8.0	93.4 $\pm$ 7.9

*Significant $p < 0.05$ ** Highly significant $p < 0.001$

Discussion

The present study found that variable rate IV infusion of morphine with IV bolus dose of diazepam was effective in attenuating circulatory response to laryngoscopy and intubation. The principle underlying IV infusion of opiates is that if a single bolus dose of an opioid is given, its plasma concentration falls in a very short time due to distribution of the drug [11-13]. Therefore to maintain a therapeutic effect, the falling concentration of the drug needs to be augmented. For this a loading infusion or a variable rate infusion is required as a fixed rate infusion would take about three elimination half lives to fill the volume of distribution. The loading dose can be determined from the steady state distribution volume (Vdss) of the drug and desired

steady state plasma concentration (Cpss) as given by the formula in Table 1 [11]. By giving a loading dose one achieves plasma concentration higher than desired for a finite period of time. As the loading dose distributes into the tissues, the desired steady state plasma concentration is approached. Subsequently to maintain this constant drug plasma concentration, maintenance dose can be determined by the formula as given in Table 1.

Morphine is a very important drug in the armament of anaesthesiologist. It is cheap and easily available in Armed Forces. It is effective in reducing the stress response. So it is useful in controlling cardiovascular responses and arrhythmias. It does not cause depression of myocardium. So cardiac output and BP are well maintained. It also produce

mild bradycardia due to its parasympathomimetic action. Thus it provides stable haemodynamic conditions during induction of GA and intubation. Morphine also effectively suppresses cough reflex and thereby prevents rise in pulse rate and BP due to this cause during intubation.

Diazepam was administered to all the patients under study by a bolus IV injection. It is a good tranquilliser with amnesic and anxiolytic properties. Thus it suppresses stimulation of sympathetic nervous system due to extreme anxiety which otherwise invariably occurs in a surgical patient in immediate pre-induction period. Diazepam has negligible action on cardiovascular system. It reduces peripheral vascular resistance if it is already high. It also enhances the action of morphine when used in combination [14,15].

It has been observed that in patients of coronary artery disease pretreated with intravenous morphine prior to induction of GA, there is decrease in myocardial oxygen consumption, left ventricular end diastolic pressure and cardiac work [13]. This pharmacological property of morphine is beneficial for intubation in these poor risk patients. Administration of morphine by intramuscular route is associated with variable rate of absorption and a variable time for achieving peak plasma levels and therefore its effect is unpredictable.

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