ABSTRACT :

Comparison of Alfentanil and Lignocaine in blunting the pressor response during endotracheal intubation.

Laryngoscopy and tracheal intubation produce marked increases in heart rate and blood pressure, which is potentially dangerous in certain patients. Various pharmacological agents have been used before laryngoscopy and tracheal intubation in an attempt to attenuate the adrenergic response, but with varying degree of success.

OBJECTIVE

To compare the efficacy of lignocaine to alfentanil in blunting the pressor response to endotracheal intubation.

DESIGN

An open label comparative study.

POPULATION

Seventy eight ASA I and II adult patients between the ages of 18 and 65 years booked for elective surgery which requires endotracheal intubation.

SETTING

Dr George Mukhari Hospital, a tertiary level training hospital in Gauteng, South Africa.

METHOD

After obtaining ethical clearance the study was conducted on 78 ASA class I & II patients. The patients were randomly allocated to three groups according to their treatment regime. All patients were premedicated with diazepam 10mg 2 hours pre operatively. Anaesthesia was induced with Thiopentone 5mg/kg followed by Vecuronium 0,1mg/kg and maintained with Isoflurane in nitrous oxide and oxygen mixture.

Group A patients received lignocaine 1.5mg/kg iv 3 minutes before intubation. Group B – alfentanil 15ug/kg iv 1 minute before intubation and group C patients did not receive any treatment before intubation. Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were recorded at the following intervals: pre- induction, pre- intubation 1, 2 and 3 minutes post intubation.

STATISTICS

Statistical analysis was done by Chi Square test followed by the normal approximation of the binomial distribution. Increase in blood pressure and heart rate in the three treatment groups were compared by analysis of variance, followed by pairwise comparisons. A p- value <_ 0,05 was considered significant.

MAIN RESULT

The three treatment groups did not differ in relation of Gender ratio, Mean weight and Mean age.

ALFENTANIL GROUP

There was a non significant increase in heart rate 1 minute post intubation (P= 0,7625), and there was no increase 2 and 3 minutes post intubation. A decrease in SBP, DBP and MAP was observed at 1, 2 and 3 minutes post intubation.

LIGNOCAINE GROUP

There was an increase in all parameters 1 minute post intubation which was comparable to the control group. A decrease in all parameters which differed from that of the control group except for heart rate, was observed at 2 and 3 minutes post intubation.

CONTROL GROUP

There was an increase in all parameters 1 minute post intubation. A decrease in all parameters 2 and 3 minutes post intubation remained above the baseline.

CONCLUSION

Alfentanil is superior to lignocaine in blunting the pressor response to endotracheal intubation.

Chapter 1
INTRODUCTION AND LITERATURE REVIEW

Laryngoscopy and tracheal intubation produce marked increases in heart rate and blood pressure. These changes are considered potentially dangerous in patients with cardiovascular disease because they may be associated with post-operative myocardial infarction or cerebral haemorrhage (1,2,3).In pregnant hypertensive patients increases in intracranial pressure with risk of cerebral haemorrhage, cardiac failure and pulmonary oedema result in morbidity and mortality in both the mother and the baby. (4,5)

Stress response is characterized by hormonal and metabolic changes which follow injury or trauma. It is part of the systemic reaction to injury which encompasses a wide of endocrinological, immunological and haemotological effects. The endocrine stress response is characterized by secretion of the pituitary hormones and activation of the sympathetic nervous system. The main hormones involved are catecholamines, glucocorticoids, growth hormone, thyroid hormone and glucagons. The overall metabolic effect of the hormonal changes is increased catabolism which mobilizes substrates to provide energy sources, and a mechanism to retain salt and water and maintain fluid volume and cardiovascular homeostasis.

Hypothalamic activation of the sympathetic autonomic nervous system results in increased secretion of catecholamines from the adrenal medulla and release of noradrinaline from presynaptic nerve terminals. Noradrinaline is primarily a neurotransmitter, but there is some spillover of noradrinaline released from nerve terminals into the circulation. The increased sympathetic activity results in the well recognized cardiovascular effects of tachycardia and hypertension.

Immunological and haematological changes involve cytokine production, acute phase reaction, neutrophil leucocytosis and lymphocyte proliferation. This process is designed to minimize immediate blood loss, limit injury associated infection and optimize the access of response protein to the injured site. All the above are stress response to trauma and surgery.(6)

There are various techniques by which this intubation related stress response can be attenuated. These depend on reduction in input stimuli, blockage of adrenergic response and blockage of catecholamine release. These methods include the use of lignocaine topically or intravenously, use of direct acting vasodilators, use of large doses of opiods e.g alfentanil and fentanyl, and the use of magnesium sulphate which blocks the release of catecholamines from adrenergic nerve terminals. Most of these techniques have disadvantages related to either cardiovascular or respiratory depression. (5,7)

Alfentanil is a synthetic opioid analgesic acting at mu receptors, which is one of the opioid receptors located throughout the central nervous system and other tissues, and are responsible for supraspinal and spinal analgesia. Other opioid receptors are kappa, delta and sigma. (1,8)

In general opioids do not seriously impact cardiovascular function. High doses of alfentanil and related opioids are associated with vagus- mediated bradycardia, venodilation and decreased sympathetic reflexes. They are often used to blunt the hypertensive and heart rate response caused by endotracheal intubation (1,8) . Negative inotropic effect of alfentanil is observed with very large doses in excess of 5mg.

Alfentanil depresses ventilation, particularly respiratory rate and high doses can cause chest wall rigidity severe enough to prevent adequate ventilation. This centrally mediated muscle rigidity is effectively treated with muscle relaxants. Other side effects are nausea and vomiting.

Alfentanil has been shown to have a more rapid onset of effects and shorter duration of action. These pharmacological properties of alfentanil suggest it would be of value in reducing the haemodynamic responses to endotracheal intubation, furthermore because of shorter duration of actions and an early opportunity may be provided to reassess or terminate the anaesthetic. The effects of alfentanil are permanently reversed by naloxone which has a longer duration of action than alfentanil (2,8) .

Lignocaine is an amino amide local anaesthetic metabolized in the liver by microsomal enzymes. It acts by binding to sodium channels in the inactivated state, preventing subsequent channel activation and the large transient sodium-influx associated with membrane depolarization (8).

In general, local anaesthetics depress myocardial automaticity and reduce duration of refractory period. Myocardial contractility and arterial blood pressure are generally unaffected by the usual intravascular doses of lignocaine. The pressor response associated with laryngoscopy and intubation is attenuated by intravenous administration of lignocaine 1,5 mg/kg iv 3 minutes prior to instrumentation. It relaxes bronchial smooth muscles and can be effective in blocking the reflex bronchoconstriction sometimes associated with intubation (9).

Intravenous lignocaine 1,5mg/kg iv decreases cerebral blood flow and attenuates the rise in intracranial pressure that accompanies intubation in patients with decreased intracranial compliance (8).

Lignocaine has been used to supplement general anaesthetic techniques, since it is capable of reducing the minimal alveolar concentration (MAC) of volatile anaesthetic by up to 40 % (8).

Many studies questioned the effectiveness of lignocaine in blunting of pressor response to endotracheal intubation. Most of such studies utilized the

rapid sequence induction and intubation method with succinylcholine rather than the use of non depolarizing muscle relaxants. (5,10,11).

Allen et al indicated that alfentanil and magnesium were significantly better than lignocaine in containing the mean cardiovascular response to intubation in hypertensive proteinuric pregnant patients.(5)

Abou-Madi et al showed that intravenous lignocaine 1,5mg/kg iv 2-3 minutes prior intubation caused borderline protection against hypertension and tachycardia. They concluded that intravenous lignocaine 1,5mg/kg iv appears to be a good alternative if time or circumstances do not permit topical aerosol anaesthesia. (16)

Chapter 2

2.1 Study Design and Patient Selection

This was an open label comparative study undertaken at Dr George Mukhari hospital, a tertiary level training hospital in Pretoria.

Seventy eight patients between ages of 18 & 65 years booked for elective surgery which required general anaesthesia and endotracheal intubation were included.

Excluded from the study were patients with :

- Hypertension
- American Society of Anaesthesiology (ASA) grade III &IV
- Mallampati airway class III & IV
- Current cardiovascular and neurological disease.

2.2 Methods and Material

The study was approved by the Research Ethics and Publication Committee of Dr George Mukhari Hospital / Medunsa Reference number : MP 43/2005 Informed written consent was obtained from all patients.

2.3 Randomisation

The three treatment groups in the study were labeled as follows :

- Group A : Treatment with Lignocaine 1,5mg/kg 3 minutes before intubation.
- Group B : Treatment with Alfentanyl 15ug/kg 1 minute before intubation.
- Group C : Control group, no treatment.

Randomisation plan was used to decide who gets which drug.

The seventy eight patients in the study were randomly assigned in a 1:1:1: ratio to the three treatment groups in the study. A randomisation plan was prepared, which was balance in blocks of six patients. (i.e in each conservative block of six patients, two patients were randomly assigned to lignocaine, two to Alfentanyl and two patients to no treatment. The patient randomisation number assigned was at the same time also the patient's identity number.

All patients received pre-medication with diazepam 10mg- given orally 2 hours pre- operatively.

COMPARISON OF ALFENTANYL AND LIGNOCAINE IN BLUNTING OF PRESSOR RESPONSE DURING ENDOTRACHEAL INTUBATION

DR. S.J. MOUMAKOE

RANDOMISATION PLAN

Legend:

A = Lignocaine (26)
B = Alfentanyl (26)
C = No treatment (26)

Pt number	Treatment	Blocks
1	C	1
2	C	2
3	A	3
4	A	4
5	B	5
6	B	6
7	B	1
8	C	2
9	B	3
10	A	4
11	C	5
12	A	6
13	A	1
14	B	2
15	C	3
16	A	4
17	B	5
18	C	6
19	B	1
20	B	2
21	C	3
22	A	4
23	C	5
24	A	6

25	B	1
26	C	2
27	A	3
28	C	4
29	A	5
30	B	6
31	B	1
32	B	2
33	A	3
34	A	4
35	C	5
36	C	6
37	B	1
38	C	2
39	A	3
40	A	4
41	B	5
42	C	6
43	C	1
44	B	2
45	A	3
46	C	4
47	A	5
48	B	6
49	A	1
50	A	2
51	C	3
52	C	4
53	B	5
54	B	6
55	C	1
56	B	2
57	A	3
58	A	4
59	C	5
60	B	6
61	A	1
62	B	2
63	C	3
64	A	4
65	B	5
66	C	6
67	A	1
68	C	2
69	B	3
70	C	4
71	B	5
72	A	6
73	C	1
74	B	2
75	A	3
76	A	4
77	C	5
78	B	6

2.4 Anaesthesia

Anaesthesia was induced with thiopentone 5mg/kg followed by vecuronium 0,1mg/ kg to achieve muscle relaxation. Alfentanyl or lignocaine administration followed thereafter.

The peripheral nerve stimulation was used to monitor the degree of muscle paralysis.

Endotracheal intubation proceeded 3 minutes after administration of lignocaine and 1 minute after administration of Alfentanyl. Anaesthesia was maintained with isoflurane and 67 % nitrous oxide in oxygen mixture.

A Datex Omeda ventilator was used for control of ventilation . Monitoring consisted of continuous three lead electrocardiography, non invasive blood pressure, pulse oximetry and capnography

2.5 Hemodynamic Data

Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure, were recorded 5 minutes before induction with patients in the supine position on the operating table. The next reading was at pre-intubation and then each minute post intubation for three minutes.

Surgical stimulation or analgesic supplements was avoided during the period of data recording.

Chapter 3
Results

The demographics of the three groups were comparable for age, gender, weight and general conditions.

Separate data collection forms were compiled for heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure.

Measurements were recorded pre-induction, pre-intubation, 1 minute post intubation, 2 minutes post intubation and 3 minutes post intubation.

3.1 Statistical Methods

Seventy eight patients were recruited into the study. (26 in each group). No patients were excluded subsequent to recruitment.

The three treatment groups A,B,C were comparable in terms of demographics.

3.2 Statistical Analysis

Changes in blood pressure, mean arterial pressure and heart rate were compared with each group as well as between groups. Changes were compared between groups before induction of anaesthesia, pre- intubation, 1 minute post intubation, 2 minutes post intubation and 3 minutes post intubation.

The proportion/ percentages of patients in which pressor responses were successfully blunted during endotracheal intubation were compared by the chi square test, followed by pairwise comparison by the normal

approximation of the binominal distribution. A 95% confidence interval was calculated for the proportion/ percentages of patients in which pressor responses were successfully blunted with each treatment.

Increase in blood pressure and heart rate in the three treatments were compared by analysis of variance, followed by pairwise comparisons.

A p value $\leq$ 0,05 was considered as significant.

3.3 Summary of Results

The three treatment groups A:B:C did not differ in relation of gender ratio, mean weight and mean age.

Heart Rate

The results are tabulated in Table 1 below. The values are expressed as means. There was an increase in the heart rate in the three groups at 1 minute post intubation (see Table 2). The increase was significant in both the control and lignocaine group.(26.19 & 24.42 beats/minute respectively ; $p<0,0001$ for both). A non- significant increase of 0,85 beats/minute was observed after alfentanil at 1 minute post intubation. (P= 0,7155)

The changes from baseline in group A and C did not differ significantly at any point. (See Table 9 ; P = 0,6723 ; P = 0,7624 and P = 0,7305 respectively). Both profiles however differ from the profiles of group B. (See Table 9; and Figure 1 & 2).

Table 1: Mean values of Heart Rate (HR) within A, B & C, (beats\min)

	Variable	n	Mean	SD
A	Pre-induction(Baseline)	26	75.88	14.57
	Pre-intubation	26	88.23	13.49
	1 min post-intubation	26	102.08	11.24
	2 min post-intubation	26	97.73	13.39
	3 min post-intubation	26	95.27	14.57
B	Pre-induction(Baseline)	26	82.19	15.00
	Pre-intubation	26	76.46	16.38
	1 min post-intubation	26	83.04	17.06
	2 min post-intubation	26	78.00	17.00
	3 min post-intubation	26	75.54	15.70
C	Pre-induction(Baseline)	26	76.12	13.54
	Pre-intubation	26	81.46	13.57
	1 min post-intubation	26	100.54	11.29
	2 min post-intubation	26	99.35	10.85
	3 min post-intubation	26	93.88	11.85

Fig. 1: Mean values of Heart Rate (HR) within A, B & C, (beats\min)

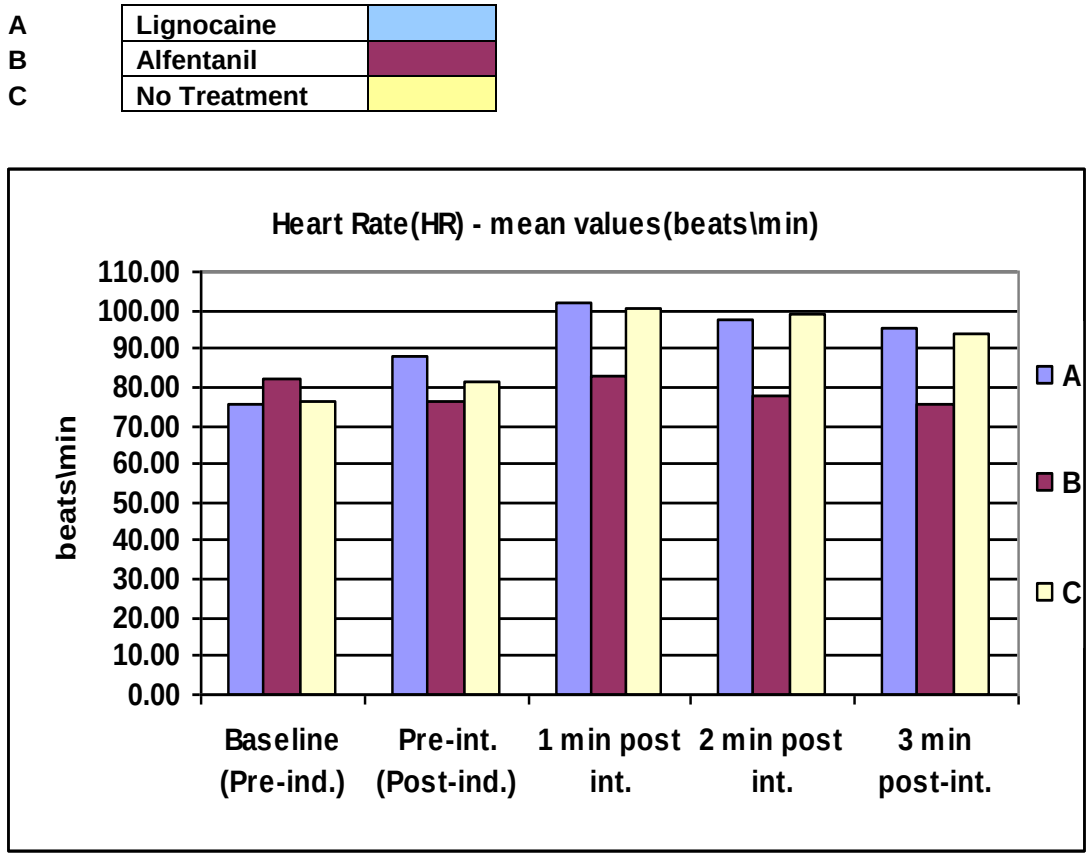
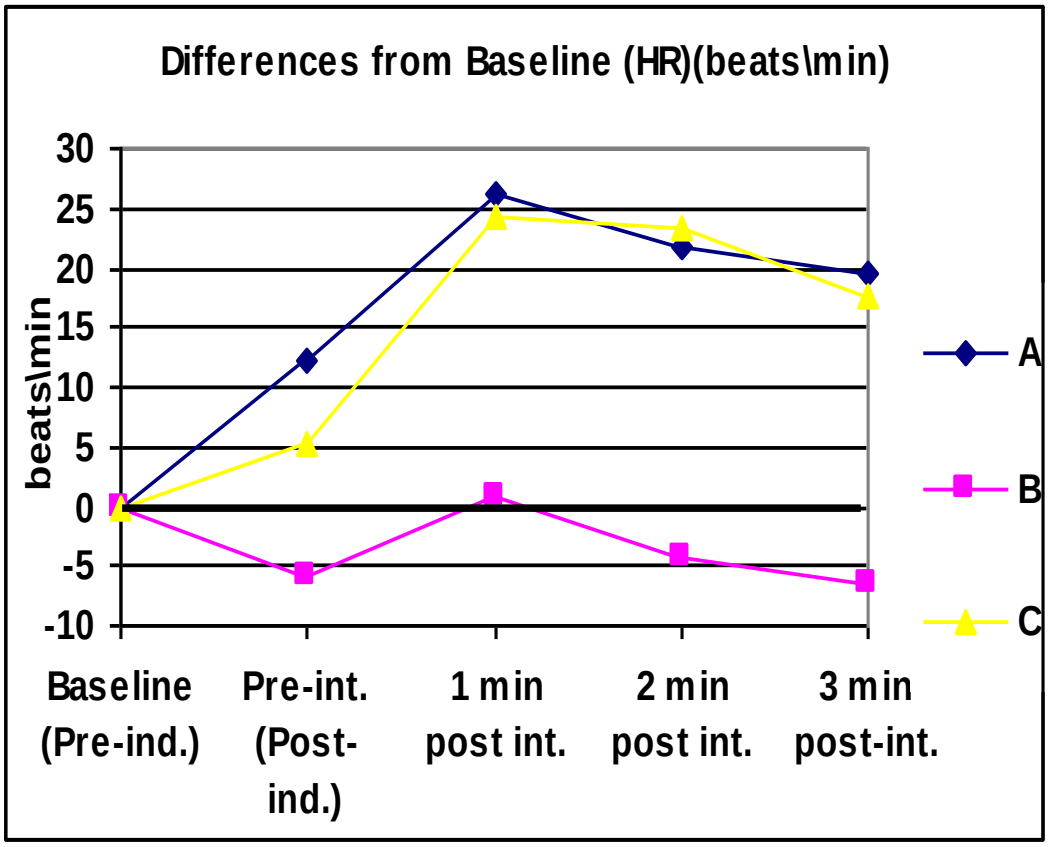


Table 2: Mean differences from Baseline (HR), (beats\min)

	Variable	n	Mean	SD	P value
A	Pre-intubation	26	12.35	17.22	0.0012*
	1 min post-intubation	26	26.19	15.88	<0.0001*
	2 min post-intubation	26	21.85	19.35	<0.0001*
	3 min post-intubation	26	19.38	20.39	<0.0001*
B	Pre-intubation	26	-5.73	10.91	0.0129*
	1 min post-intubation	26	0.85	11.71	0.7155
	2 min post-intubation	26	-4.19	13.21	0.1182
	3 min post-intubation	26	-6.65	13.98	0.0227*
C	Pre-intubation	26	5.35	16.37	0.1084
	1 min post-intubation	26	24.42	17.06	<0.0001*
	2 min post-intubation	26	23.23	16.22	<0.0001*
	3 min post-intubation	26	17.77	15.51	<0.0001*
* statistically significant (p<0.05)					

Fig. 2: Mean differences from Baseline (HR), (beats\min)

A	Lignocaine
B	Alfentanil
C	No Treatment



Systolic Blood Pressure

A decrease in SBP was observed in all three treatment groups after induction of anaesthesia (see Table 3). There was a significant increase in the Lignocaine and control groups at 1 minute post intubation. (10,23 mmHg with $p = 0,005$ and 18,88 mmHg with $p < 0,001$ respectively ; see Table 4). A decrease in systolic blood pressure was observed with the Alfentanyl group and continued to drop 3 minutes post intubation (See Table 3). The changes from baseline with A, B & C differ from one another at each time point (see table 9) . The profiles of A; B; & C are shown in Figures 3 & 4.

Table 3: Mean values of Systolic Blood Pressure (SBP) within A, B & C, (MmHg)

	Variable	n	Mean	SD
A	Pre-induction(Baseline)	26	125.77	13.26
	Pre-intubation	26	106.00	13.73
	1 min post-intubation	26	136.00	19.92
	2 min post-intubation	26	119.62	19.01
	3 min post-intubation	26	112.50	16.17
B	Pre-induction(Baseline)	26	123.27	14.72
	Pre-intubation	26	102.96	15.55
	1 min post-intubation	26	105.92	16.09
	2 min post-intubation	26	98.15	12.89
	3 min post-intubation	26	95.19	12.36
C	Pre-induction(Baseline)	26	121.15	11.76
	Pre-intubation	26	111.58	10.42
	1 min post-intubation	26	140.04	15.88
	2 min post-intubation	26	132.85	12.76
	3 min post-intubation	26	123.69	9.24

Fig. 3: Mean values of Systolic Blood Pressure (SBP) within A, B & C, (MmHg)

A	Lignocaine	
B	Alfentanil	
C	No Treatment	

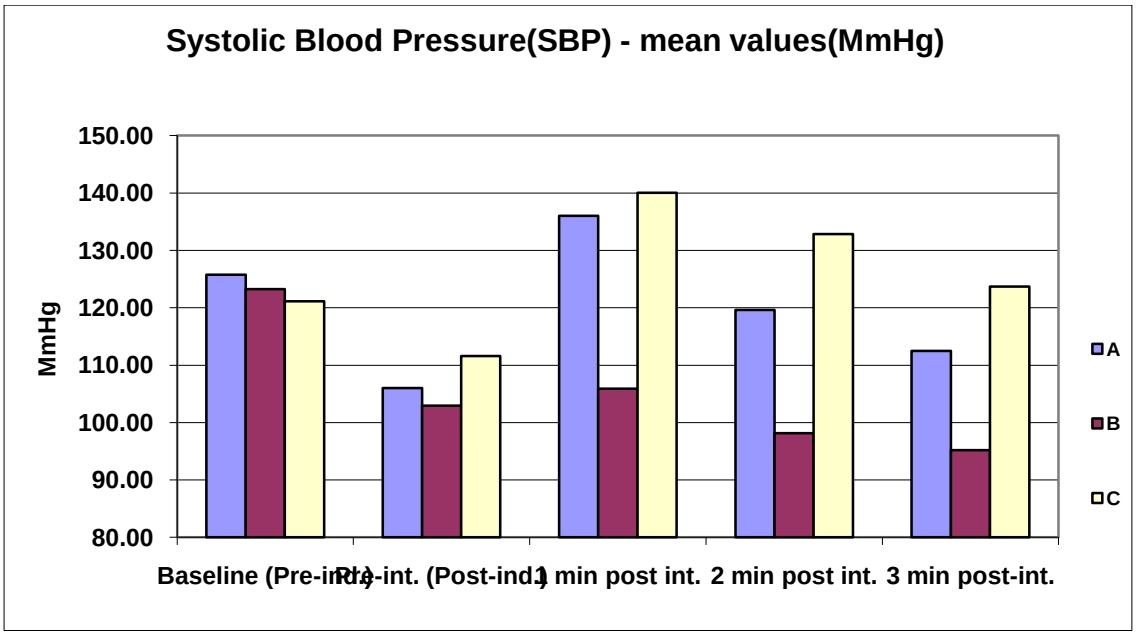
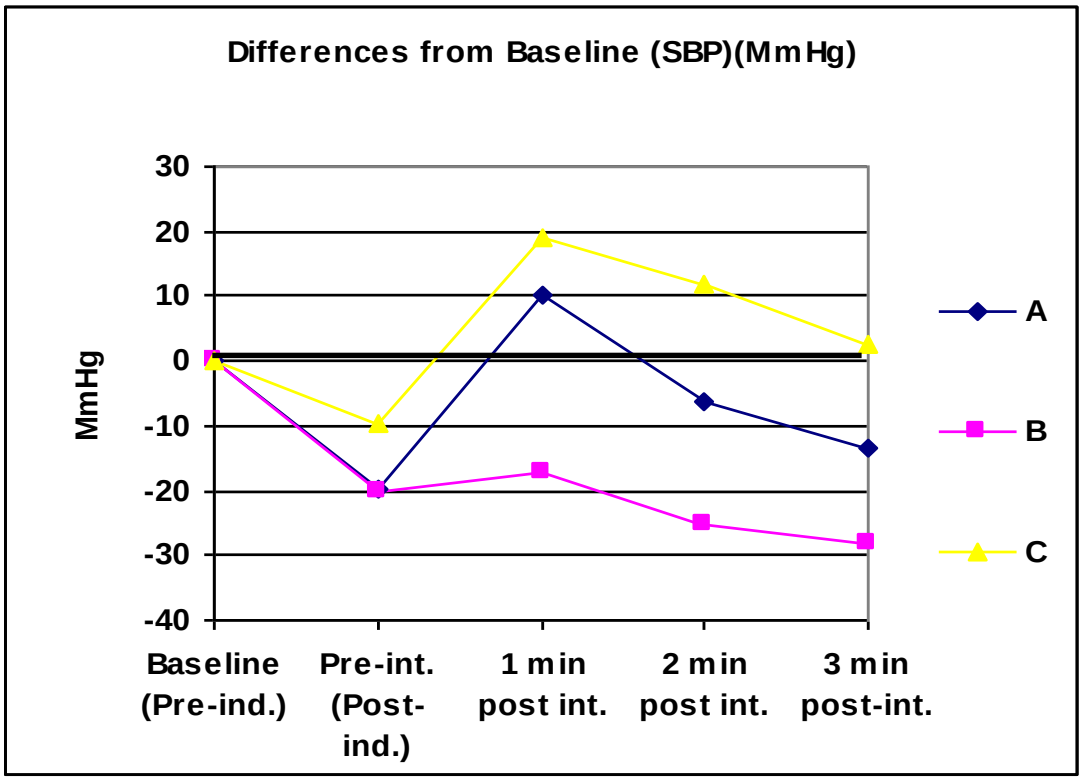


Table 4: Mean differences from Baseline (SBP) , (MmHg)

	Variable	n	Mean	SD	P value
A	Pre-intubation	26	-19.77	9.44	<0.0001*
	1 min post-intubation	26	10.23	14.59	0.0015*
	2 min post-intubation	26	-6.15	13.26	0.0255*
	3 min post-intubation	26	-13.27	10.81	<0.0001*
B	Pre-intubation	26	-20.35	14.66	<0.0001*
	1 min post-intubation	26	-17.35	14.89	<0.0001*
	2 min post-intubation	26	-25.12	14.59	<0.0001*
	3 min post-intubation	26	-28.08	15.60	<0.0001*
C	Pre-intubation	26	-9.58	8.48	<0.0001*
	1 min post-intubation	26	18.88	14.23	<0.0001*
	2 min post-intubation	26	11.69	13.68	0.0002*
	3 min post-intubation	26	2.54	13.09	0.3322
* statistically significant (p<0.05)					

Fig. 4: Mean differences from Baseline (SBP), (MmHg)

A	Lignocaine	
B	Alfentanil	
C	No Treatment	



Diastolic Blood Pressure

A decrease in DBP was observed in all three groups after induction of anaesthesia. (See Table 5). There was an increase in DBP at 1 minute post intubation in the lignocaine and control groups (10,15 mmHg with $p < 0,0001$ and 13,08 mmHg with $p < 0.0001$ respectively; see Table 6). The changes from baseline with A; B; & C differed from one another at each time point, except at 1 minute post intubation where A and C did not differ. ($P = 0,4030$, see Table 9). The points of A; B & C are reflected in Figures 5 & 6).

Table 5: Mean values of Diastolic Blood Pressure (DBP) within A, B&C, (MmHg)

	Variable	n	Mean	SD
A	Pre-induction(Baseline)	26	80.23	9.38
	Pre-intubation	26	68.73	10.50
	1 min post-intubation	26	90.38	13.98
	2 min post-intubation	26	77.73	14.87
	3 min post-intubation	26	72.46	13.88
B	Pre-induction(Baseline)	26	78.54	11.08
	Pre-intubation	26	60.81	13.21
	1 min post-intubation	26	64.50	14.95
	2 min post-intubation	26	56.88	10.95
	3 min post-intubation	26	53.26	10.52
C	Pre-induction(Baseline)	26	74.85	11.14
	Pre-intubation	26	67.88	10.92
	1 min post-intubation	26	87.92	11.36
	2 min post-intubation	26	82.08	10.99
	3 min post-intubation	26	78.31	11.15

Fig. 5: Mean values of Diastolic Blood Pressure (DBP) within A, B&C, (MmHg)

A	Lignocaine
B	Alfentanil
C	No Treatment

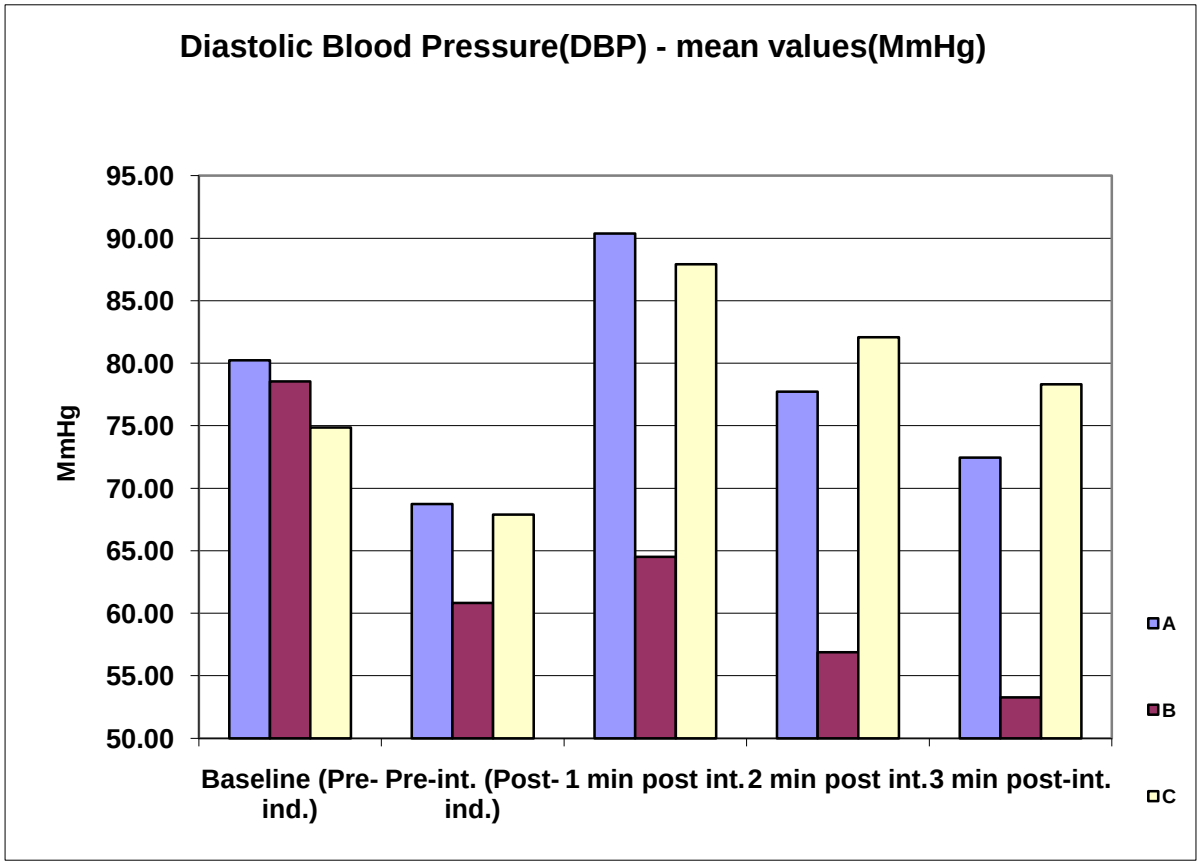
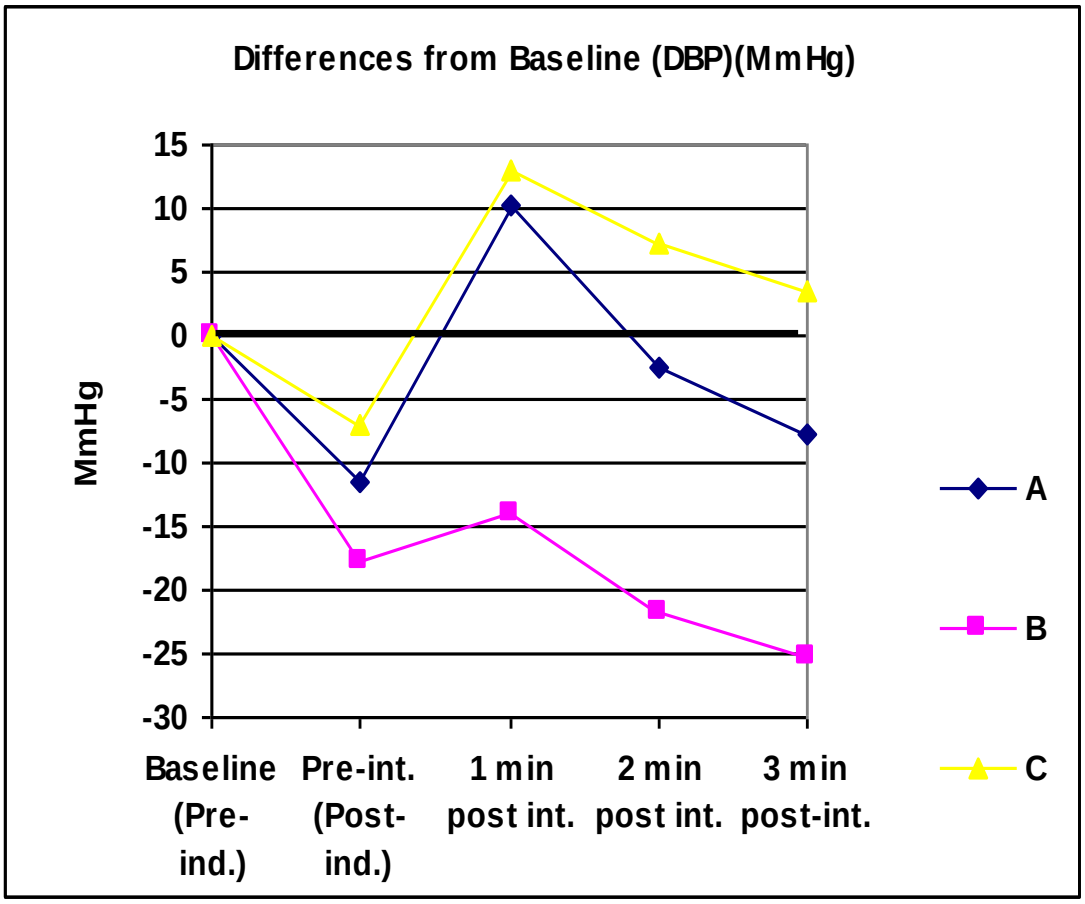


Table 6: Mean differences from Baseline (DBP), (MmHg)

	Variable	n	Mean	SD	P value
A	Pre-intubation	26	-11.50	8.03	<0.0001*
	1 min post-intubation	26	10.15	10.01	<0.0001*
	2 min post-intubation	26	-2.50	12.30	0.3101
	3 min post-intubation	26	-7.77	12.80	0.0048*
B	Pre-intubation	26	-17.73	14.46	<0.0001*
	1 min post-intubation	26	-14.04	15.15	<0.0001*
	2 min post-intubation	26	-21.65	12.81	<0.0001*
	3 min post-intubation	26	-25.27	12.21	<0.0001*
C	Pre-intubation	26	-6.96	11.89	0.0062*
	1 min post-intubation	26	13.08	11.89	<0.0001*
	2 min post-intubation	26	7.23	12.14	0.0055*
	3 min post-intubation	26	3.46	12.01	0.1543
* statistically significant (p<0.05)					

Fig. 6: Mean differences from Baseline (DBP), (MmHg)

A	Lignocaine
B	Alfentanil
C	No Treatment



Mean Arterial Pressure(MAP)

There was an increase in MAP in the lignocaine and control group at 1 minute post intubation. (See table 7). A decrease in MAP was observed in the alfentanil group 1 minute post intubation and continued to decrease at 3 minutes post intubation. (See Table 8).

The changes from baseline in group A; B; & C differed from one another at each time point, except at 1 minute post intubation where A & C did not differ. (P = 0,1230 see Table 9). The profiles of A; B; &C are reflected in Figures 7 & 8).

Table 7: Mean Arterial Pressure (MAP) within A, B & C, (MmHg)

	Variable	n	Mean	SD
A	Pre-induction(Baseline)	26	95.46	9.46
	Pre-intubation	26	81.15	10.89
	1 min post-intubation	26	105.46	15.54
	2 min post-intubation	26	91.73	15.58
	3 min post-intubation	26	85.77	13.92
B	Pre-induction(Baseline)	26	93.46	11.03
	Pre-intubation	26	74.88	13.14
	1 min post-intubation	26	78.26	14.06
	2 min post-intubation	26	70.69	10.61
	3 min post-intubation	26	67.23	10.20
C	Pre-induction(Baseline)	26	90.27	10.59
	Pre-intubation	26	82.50	9.29
	1 min post-intubation	26	105.31	11.47
	2 min post-intubation	26	99.04	10.21
	3 min post-intubation	26	93.35	9.75

Fig. 7: Mean Arterial Pressure (MAP) within A, B & C, (MmHg)

A	Lignocaine
B	Alfentanil
C	No Treatment

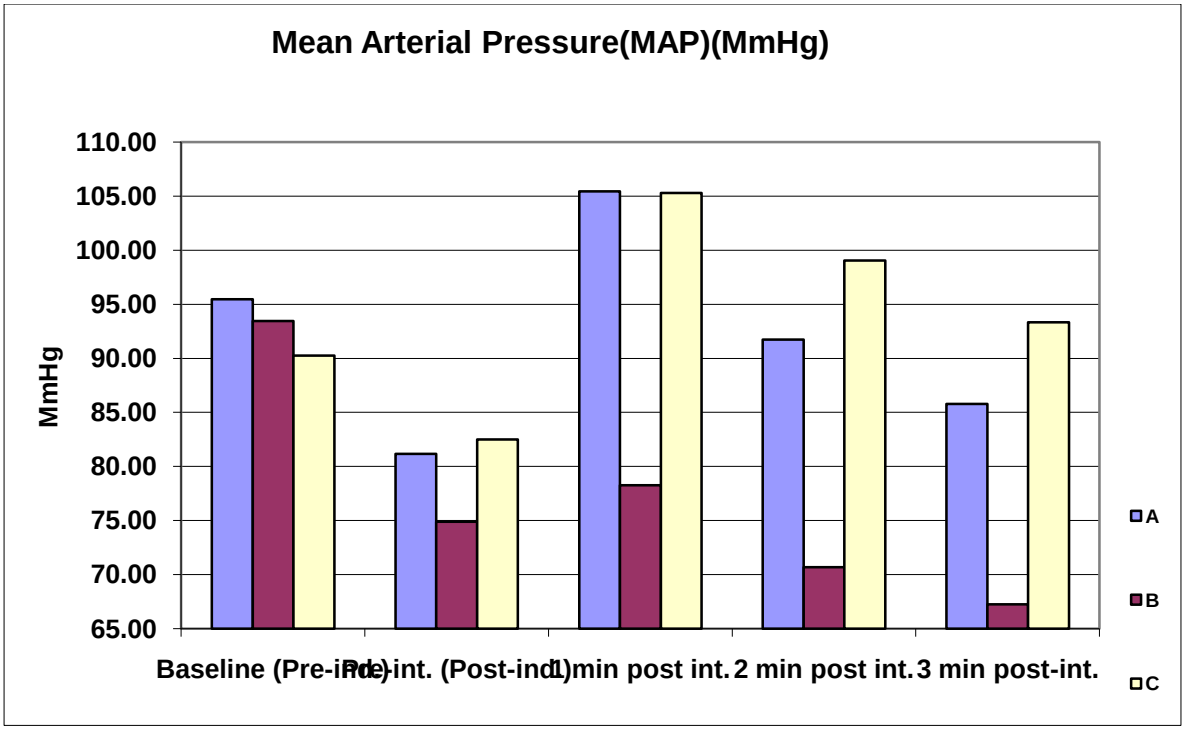


Table 8: Mean differences from Baseline (MAP), (MmHg)

	Variable	n	Mean	SD	P value
A	Pre-intubation	26	-14.31	6.96	<0.0001*
	1 min post-intubation	26	10.00	9.80	<0.0001*
	2 min post-intubation	26	-3.73	11.45	0.1092
	3 min post-intubation	26	-9.69	10.36	<0.0001*
B	Pre-intubation	26	-18.58	12.90	<0.0001*
	1 min post-intubation	26	-15.19	13.46	<0.0001*
	2 min post-intubation	26	-22.77	11.81	<0.0001*
	3 min post-intubation	26	-26.23	11.73	<0.0001*
C	Pre-intubation	26	-7.77	9.42	0.0003*
	1 min post-intubation	26	15.04	11.38	<0.0001*
	2 min post-intubation	26	8.77	11.53	0.0007*
	3 min post-intubation	26	3.08	11.71	0.1923
* statistically significant (p<0.05)					

Fig. 8: Mean differences from Baseline (MAP), (MmHg)

A	Lignocaine	
B	Alfentanil	
C	No Treatment	

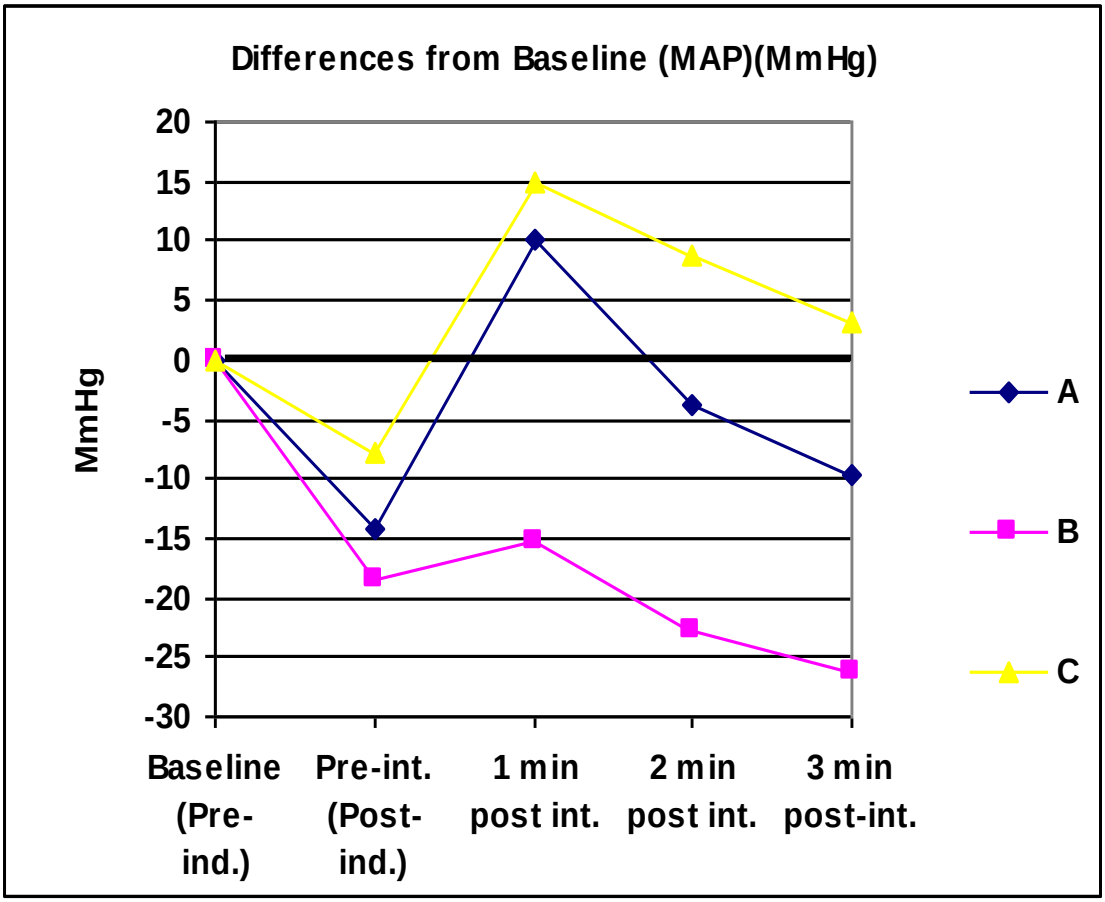


Table 9: p values for Comparison of A, B & C

	Change from baseline (HR)			
	Pre-intubation	1min	2 min	3 min
A vs B	<0.0001*	<0.0001*	<0.0001*	<0.0001*
A vs C	0.0987	0.6723	0.7624	0.7305
B vs C	0.0099*	<0.0001*	<0.0001*	<0.0001*
	Change from baseline (SBP)			
	Pre-intubation			
A vs B	0.8530	<0.0001*	<0.0001*	<0.0001*
A vs C	0.0016*	0.0355*	<0.0001*	<0.0001*
B vs C	0.0009*	<0.0001*	<0.0001*	<0.0001*
	Change from baseline (DBP)			
	Pre-intubation			
A vs B	0.0599	<0.0001*	<0.0001*	<0.0001*
A vs C	0.1682	0.4030	0.0061*	0.0061*
B vs C	0.0015	<0.0001*	<0.0001*	<0.0001*
	Change from baseline (MAP)			
	Pre-intubation			
A vs B	0.1304	<0.0001*	<0.0001*	<0.0001*
A vs C	0.0218*	0.1230	0.0002*	0.0001*
B vs C	0.0002*	<0.0001*	<0.0001*	<0.0001*
* statistically significant (p<0.05)				

Chapter 4
Discussion

Cardiovascular stimulation as demonstrated by increase in arterial pressure and heart rate accompanies direct laryngoscopy and tracheal intubation. Direct laryngoscopy and tracheal intubation is associated with a rise in noradrenaline concentration which suggests increased sympathetic nervous activity(14).

In most patients these changes are well tolerated. In certain groups of patients, such as those who are at risk of developing arterial hypertension or myocardial ischaemia, such changes may be detrimental. Several methods of attenuating the rise in blood pressure and heart rate have been described. These depend on reduction in input stimuli, blockage of adrenergic response and blockage of catecholamine release (15,16).

This study compared the effect of lignocaine and alfentanil in blunting the pressor response to endotracheal intubation. The results obtained in this study for blunting of pressor response in the control group compared with those of other previous studies which showed a significant increase in HR, SBP & DBP post endotracheal intubation. (1, 3).

Alfentanil is an opioid analgesic which has been shown to be less potent, but have a more rapid onset of effects and shorter duration of action. A non significant increase in heart rate (P= 0.7625), was observed in the Alfentanyl group 1 minute post intubation. This is in contrast with other studies which showed that Alfentanyl 15ug/kg did not blunt heart rate response to endotracheal intubation(16;12). Such studies utilized suxamethonium and rapid sequence induction and intubation, rather than intubation following a non depolarizing muscle relaxant used in this study.

There was a significant decrease in SBP, DBP & MAP 1 minute post intubation in the Alfentanyl group. The decrease persisted 3 minutes post intubation. This may be undesirable in patients with cardiovascular instability and the elderly, because hypotension and bradycardia can lead to decrease in cardiac output with risk of myocardia ischaemia, stroke, cardiac arrhythmias and sudden death (13).

Lignocaine is advocated widely and was the standard drug for attenuation of the pressor response to endotracheal intubation. Davidson and Gillespie demonstrated that the use of intravenous lignocaine to supplement propofol-alfentanil anaesthesia improved intubating conditions. The improvement in intubating conditions was largely caused by a reduction in the incidence and severity of cough after insertion of the tracheal tube, although an improvement in the case of laryngoscopy was also apparent (7).

Lignocaine has been used as lignocaine gargle for oropharyngal anaesthetic, as lignocaine aerosol for intratracheal anaesthesia, or as an intravenous bolus for general anaesthesia. Intravenous lignocaine in particular has been found to suppress the cough reflex (10), to prevent increase in intracranial pressure, to attenuate hemodynamic responses and to possess antiarrhythmic properties. (17)

The mechanism by which intravenous lignocaine attenuates the circulatory responses is still unclear, but proposed mechanism consists of a direct myocardial depressant and vasodilating effect, a central stimulant effect and an effect on sympathetic transmission (18)

Tam et al indicated that intravenous lignocaine at 1,5mg/kg attenuates increase in heart rate and arterial blood pressure only when given 3 minutes before intubation (17). This was the dose and time used in this study. In contrast to Tam et al, lignocaine did not blunt the pressor response to

endotracheal intubation 1 minute post intubation and its profile did not differ from that of control group. There was however, a decrease below baseline in all parameters in the lignocaine group except for heart rate 2 and 3 minutes post intubation which indicated blunting of only blood pressure response 2 and 3 minutes post intubation. Allen et al indicated that alfentanil and magnesium were significantly better than lignocaine in containing the mean cardiovascular responses to intubation in proteinuric pregnant patients. (5)

In their study, Okuda et al concluded that intravenous lignocaine can attenuate the circulatory response due to laryngoscopy and endotracheal intubation, and that lignocaine should be administered at least 1 minute before laryngoscopy and endotracheal intubation with fentanyl, nitrous oxide and oxygen anaesthesia (18). Fentanyl was not used in this study. The attenuation of the circulatory response by lignocaine in their study 1 minute post intubation could be due to the addition of fentanyl, because Black et al showed that fentanyl 5ug/kg prevented the increase in blood pressure during laryngoscopy and endotracheal intubation (1).

In conclusion alfentanil is superior to lignocaine in blunting the pressor response to endotracheal intubation. Alfentanil at 15ug/kg can be used as a supplement during induction to prevent the rise in blood pressure and heart rate associated with laryngoscopy and endotracheal intubation.

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APPENDIX A : RAW DATA FOR HEART RATE.

Legend : HR_1 = Ward
HR_2 = Pre-Induction
HR-3 = Pre-Intubation
HR_4 = 1 Minute post intubation
HR_5 = 2 Minutes post intubation
HR_6 = 3 Minutes post intubation

OBS	GROUP	HR_1	HR_2	HR_3	HR_4	HR_5	HR_6
1	A	63	59	100	107	112	110
2	A	84	94	94	105	96	93
3	A	78	63	78	94	87	79
4	A	86	74	91	113	112	105
5	A	76	74	95	110	113	101
6	A	87	63	94	112	110	106
7	A	65	52	75	100	95	94
8	A	78	64	81	93	85	85
9	A	80	66	91	95	97	98
10	A	82	88	78	110	101	101
11	A	80	73	90	98	95	88
12	A	64	84	78	106	91	84
13	A	84	75	111	118	118	123
14	A	72	77	57	81	70	61
15	A	80	91	102	111	110	109
16	A	87	66	98	108	108	107
17	A	68	76	96	97	103	109
18	A	86	77	112	122	116	109
19	A	79	102	91	107	103	101
20	A	68	68	75	99	104	104
21	A	82	58	69	87	80	79
22	A	82	61	87	93	88	88
23	A	92	102	109	121	106	100
24	A	78	70	71	81	73	73
25	A	72	101	81	92	82	70
26	A	88	95	90	94	86	100
27	B	86	90	90	97	95	90
28	B	84	98	99	112	114	112
29	B	61	59	54	71	68	63
30	B	87	102	106	111	109	104
31	B	92	88	80	100	58	58
32	B	80	87	78	99	74	71
33	B	67	98	99	103	97	79
34	B	77	76	61	72	68	72
35	B	76	94	109	101	95	89
36	B	88	56	62	62	62	64
37	B	95	96	92	100	100	101
38	B	84	88	79	79	69	66
39	B	85	76	79	77	77	78
40	B	70	63	53	52	52	51
41	B	86	110	76	82	82	82
42	B	72	85	87	91	89	72
43	B	78	63	66	67	66	72
44	B	71	61	56	64	60	60
45	B	82	97	79	81	83	83
46	B	78	72	67	92	87	89
47	B	72	66	54	57	53	53
48	B	80	84	75	75	73	67
49	B	86	82	54	59	57	58
50	B	69	72	72	79	75	73
51	B	78	76	82	84	88	88
52	B	78	98	79	92	77	69
53	C	78	60	95	113	109	105
54	C	68	69	95	112	110	110
55	C	78	103	95	100	98	93
56	C	84	97	81	98	81	84
57	C	78	90	95	99	98	87
58	C	77	83	63	78	81	76
59	C	86	91	100	110	110	119
60	C	78	69	67	87	89	77
61	C	81	79	80	99	100	101
62	C	68	81	77	99	101	89
63	C	70	90	69	101	105	96
64	C	78	69	61	101	110	96
65	C	87	83	75	103	102	100
66	C	75	67	77	81	90	92
67	C	96	93	98	104	103	99
68	C	78	52	73	92	90	83
69	C	81	76	79	89	91	91
70	C	70	67	65	97	98	88
71	C	67	50	76	100	90	84
72	C	76	77	69	101	100	98
73	C	69	82	101	122	121	108
74	C	86	75	112	129	123	119
75	C	84	59	74	93	82	78
76	C	73	78	75	98	99	92
77	C	62	61	90	112	101	79
78	C	68	78	76	96	101	97

APPENDIX B : RAW DATA FOR SYSTOLIC BLOOD PRESSURE

Legend : SBP_1 = Ward
SBP_2 = Pre-Induction
SBP-3 = Pre-Intubation
SBP_4 = 1 Minute post intubation
SBP_5 = 2 Minutes post intubation
SBP_6 = 3 Minutes post intubation

OBS	GROUP	SBP_1	SBP_2	SBP_3	SBP_4	SBP_5	SBP_6
1	A	120	123	107	120	108	104
2	A	110	137	112	108	117	109
3	A	120	147	122	164	125	113
4	A	130	132	121	153	140	120
5	A	110	108	103	121	132	123
6	A	130	150	135	185	176	159
7	A	130	144	118	139	135	128
8	A	130	133	117	140	128	122
9	A	100	115	106	128	110	110
10	A	120	121	92	144	111	99
11	A	110	127	110	153	142	129
12	A	128	131	102	146	124	113
13	A	120	116	107	123	109	108
14	A	100	109	95	124	102	94
15	A	110	128	105	123	109	105
16	A	120	140	125	154	129	122
17	A	110	137	119	150	134	133
18	A	120	121	107	124	114	107
19	A	110	104	85	109	93	93
20	A	110	131	82	121	115	117
21	A	110	119	99	112	107	102
22	A	110	132	94	142	140	129
23	A	110	97	75	110	90	79
24	A	130	127	109	168	126	107
25	A	110	113	102	127	94	92
26	A	120	128	107	148	100	108
27	B	120	139	124	135	123	128
28	B	110	103	108	103	97	96
29	B	124	130	115	112	118	113
30	B	120	109	95	117	106	97
31	B	130	140	134	130	102	103
32	B	110	112	82	97	83	86
33	B	100	103	108	106	94	96
34	B	110	109	95	92	87	89
35	B	110	130	122	117	101	106
36	B	120	102	84	78	79	78
37	B	100	127	119	134	114	110
38	B	110	152	118	110	94	89
39	B	110	109	99	99	98	96
40	B	130	137	92	94	88	87
41	B	139	130	102	90	84	87
42	B	120	131	123	107	106	92
43	B	130	115	93	87	82	79
44	B	130	132	78	100	89	82
45	B	120	118	88	82	86	83
46	B	110	120	84	121	113	108
47	B	110	112	92	86	83	83
48	B	130	140	126	123	121	114
49	B	120	125	96	101	96	90
50	B	110	144	105	115	105	103
51	B	120	101	92	94	93	94
52	B	130	135	102	124	110	86
53	C	130	102	99	130	112	102
54	C	110	113	119	120	129	124
55	C	130	138	108	126	117	108
56	C	130	134	127	153	155	135
57	C	140	110	101	132	127	117
58	C	100	110	92	137	132	128
59	C	120	128	121	168	138	120
60	C	100	102	106	131	128	127
61	C	120	128	122	144	130	135
62	C	130	121	112	140	147	125
63	C	140	134	127	160	146	131
64	C	100	106	102	131	152	128
65	C	130	128	124	152	140	146
66	C	120	124	109	105	128	127
67	C	120	129	114	160	140	129
68	C	110	107	109	138	124	113
69	C	120	124	110	131	128	127
70	C	130	128	118	144	135	127
71	C	130	131	116	167	145	120
72	C	100	106	94	130	129	128
73	C	130	128	114	161	130	117
74	C	120	101	100	125	115	115
75	C	120	126	97	121	107	117
76	C	120	127	114	135	128	131
77	C	110	134	127	155	158	115
78	C	120	131	119	145	134	124

APPENDIX C : RAW DATA FOR DIASTOLIC BLOOD PRESSURE

Legend : DBP_1 = Ward
DBP_2 = Pre-Induction
DBP-3 = Pre-Intubation
DBP_4 = 1 Minute post intubation
DBP_5 = 2 Minutes post intubation
DBP_6 = 3 Minutes post intubation

OBS	GROUP	DBP_1	DBP_2	DBP_3	DBP_4	DBP_5	DBP_6
1	A	70	87	77	83	82	77
2	A	70	56	66	78	80	81
3	A	90	93	78	106	91	83
4	A	90	84	78	98	86	76
5	A	70	71	73	78	84	87
6	A	90	90	89	120	114	102
7	A	90	90	69	93	83	79
8	A	90	86	78	97	84	81
9	A	70	78	69	85	69	60
10	A	70	83	69	101	78	71
11	A	70	71	60	83	76	63
12	A	80	93	77	106	90	70
13	A	90	89	80	92	79	73
14	A	60	77	51	76	64	50
15	A	70	76	59	76	65	56
16	A	80	90	78	95	78	74
17	A	70	93	75	108	98	94
18	A	80	74	68	86	71	70
19	A	60	67	47	69	57	53
20	A	70	81	60	89	85	85
21	A	60	76	61	72	68	60
22	A	70	78	72	99	96	86
23	A	70	67	45	67	55	41
24	A	90	82	71	111	78	67
25	A	70	80	68	80	68	71
26	A	70	74	69	102	42	74
27	B	80	81	82	70	61	60
28	B	70	73	71	71	57	54
29	B	81	80	50	46	51	51
30	B	70	56	42	51	46	42
31	B	90	90	61	90	56	57
32	B	70	76	50	69	48	49
33	B	60	73	71	69	59	55
34	B	70	77	51	48	49	46
35	B	70	90	63	59	54	51
36	B	90	52	36	31	29	28
37	B	60	84	80	87	82	80
38	B	70	92	79	67	59	53
39	B	70	81	64	62	55	55
40	B	90	71	57	53	49	50
41	B	90	90	65	54	51	48
42	B	80	70	85	70	67	47
43	B	80	73	67	58	55	52
44	B	90	98	44	64	54	49
45	B	80	93	48	49	48	46
46	B	60	70	47	84	77	74
47	B	70	73	56	53	55	42
48	B	80	90	73	68	73	68
49	B	90	82	50	88	55	53
50	B	70	82	67	79	72	68
51	B	80	66	55	53	53	53
52	B	90	79	67	84	64	54
53	C	90	65	58	89	71	62
54	C	70	74	79	87	59	81
55	C	90	95	74	87	80	74
56	C	90	89	60	93	82	74
57	C	90	60	54	84	71	59
58	C	70	70	57	71	84	85
59	C	80	87	53	95	73	73
60	C	70	64	67	71	87	79
61	C	80	84	81	90	89	83
62	C	90	78	51	86	93	91
63	C	90	87	84	100	106	93
64	C	60	67	77	71	92	87
65	C	90	80	76	92	90	104
66	C	70	76	77	68	87	79
67	C	70	74	75	100	80	80
68	C	60	54	69	97	82	71
69	C	80	76	60	83	87	79
70	C	90	79	68	90	83	79
71	C	80	70	63	106	86	80
72	C	60	64	50	81	87	87
73	C	90	54	55	72	54	49
74	C	80	65	71	81	75	77
75	C	80	76	63	89	70	74
76	C	80	84	82	88	87	71
77	C	70	82	81	109	92	75
78	C	80	92	80	106	87	90

APPENDIX D : RAW DATA FOR MEAN ARTERIAL PRESSURE

Legend : MAP_1 = Ward
MAP_2 = Pre-Induction
MAP-3 = Pre-Intubation
MAP_4 = 1 Minute post intubation
MAP_5 = 2 Minutes post intubation
MAP_6 = 3 Minutes post intubation

OBS	GROUP	MAP_1	MAP_2	MAP_3	MAP_4	MAP_5	MAP_6
1	A	87	99	87	95	91	86
2	A	83	83	81	88	92	90
3	A	100	111	93	125	102	93
4	A	103	100	92	116	104	91
5	A	83	83	83	92	100	99
6	A	103	110	104	142	135	121
7	A	103	108	85	108	100	95
8	A	103	102	91	111	99	95
9	A	80	90	81	99	83	77
10	A	87	96	77	115	89	80
11	A	83	90	77	106	98	85
12	A	96	106	85	119	101	84
13	A	100	98	89	102	89	85
14	A	73	88	66	92	77	65
15	A	83	93	74	92	80	72
16	A	93	107	94	115	95	90
17	A	83	108	90	122	110	107
18	A	93	90	81	99	85	82
19	A	77	79	60	82	69	66
20	A	83	98	67	100	95	96
21	A	77	90	74	85	81	74
22	A	83	96	79	113	111	100
23	A	83	77	55	81	67	54
24	A	103	97	84	130	94	80
25	A	83	91	79	96	77	78
26	A	87	92	82	117	61	85
27	B	93	100	96	92	82	83
28	B	83	83	83	82	70	68
29	B	95	97	72	68	73	72
30	B	87	74	60	73	66	60
31	B	103	107	85	103	71	72
32	B	83	88	61	78	60	61
33	B	73	83	83	81	71	69
34	B	83	88	66	63	62	60
35	B	83	103	83	78	70	69
36	B	100	69	52	47	46	45
37	B	73	98	93	103	93	90
38	B	83	112	92	81	71	65
39	B	83	90	76	74	69	69
40	B	103	93	69	67	62	62
41	B	106	103	77	66	62	61
42	B	93	90	98	82	80	62
43	B	97	87	76	68	64	61
44	B	103	109	55	76	66	60
45	B	93	101	61	60	61	58
46	B	77	87	59	96	89	85
47	B	83	86	68	64	64	56
48	B	97	107	91	86	89	83
49	B	100	96	65	92	69	65
50	B	83	103	80	91	83	80
51	B	93	78	67	67	66	67
52	B	103	98	79	97	79	65
53	C	103	77	72	103	85	75
54	C	83	87	92	98	82	95
55	C	103	109	85	100	92	85
56	C	103	104	82	113	106	94
57	C	107	77	70	100	90	78
58	C	80	83	69	93	100	99
59	C	93	101	76	119	95	89
60	C	80	77	80	91	101	95
61	C	93	99	95	108	103	100
62	C	103	92	71	104	111	102
63	C	107	103	98	120	119	106
64	C	73	80	85	91	112	101
65	C	103	96	92	112	107	118
66	C	87	92	88	80	101	95
67	C	87	92	88	120	100	96
68	C	77	72	82	111	96	85
69	C	93	92	77	99	101	95
70	C	103	95	85	108	100	95
71	C	97	90	81	126	106	93
72	C	73	78	65	97	101	101
73	C	103	79	75	102	79	72
74	C	93	77	81	96	88	90
75	C	93	93	74	100	82	88
76	C	93	98	93	104	101	91
77	C	83	99	96	124	114	88
78	C	93	105	93	119	103	101