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COMPARATIVE EVALUATION OF PROPOFOL WITH KETAMINE, BUTORPHANOL AND PENTAZOCINE IN SHORT SURGICAL PROCEDURE

Dr. Inder Dev Ashahiya[1*], Dr. Rajkumari Bansal[2], Dr. Neeraj Narang[3], Dr. Bhanu Choudhary[4], Dr. Sheetal Panwar[5]

[1]Assistant Professor, Department of Anesthesiology, N.S.C.B. Medical College, Jabalpur (Madhya Pradesh)
[2]P.G. student, Department of Pharmacology, N.S.C.B. Medical College, Jabalpur (Madhya Pradesh)
[3]Assistant Professor, Department of Anesthesiology, N.S.C.B. Medical College, Jabalpur (Madhya Pradesh)
[4]Prof. and HOD Department of Anesthesiology, G R Medical College, Gwalior (Madhya Pradesh)
[5]P.G. student, Department of Anesthesiology, N.S.C.B. Medical College, Jabalpur (Madhya Pradesh)

***Author for Correspondence: Dr. Inder Dev Ashahiya**
Assistant Professor, Department of Anesthesiology, N.S.C.B. Medical College, Jabalpur (Madhya Pradesh)

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ABSTRACT

Background and Aims: The term 'day-care surgery' and 'ambulatory surgery' are used interchangeably for short surgical procedures which indicate that the patient is discharged on the day of surgery without overnight hospital stay. The aim of this study is to assess efficacy of Propofol in combination with either of Ketamine, Butorphanol or Pentazocine for short surgical procedures. **Methods**: Our study included 90 patients of both sex, aged between 18-50 years of ASA Grade I and II, scheduled for short surgical procedures. Group A patients were induced with Propofol (2.0-2.5 mg/kg) and Ketamine (0.5 mg/kg). Group B patients were induced with Propofol (2.0-2.5 mg/kg) and Pentazocine (0.5 mg/kg). Group C patients were induced with Propofol (2.0-2.5 mg/kg) and Butorphanol (0.03-0.05 mg/kg). Various parameters were recorded. Immediate recovery and Home readiness was assessed by Steward Scoring and Street fitness Criteria respectively. **Results:** Group A had best intraoperative cardiovascular stability and group C had best post operative cardiovascular stability. Immediate recovery and Home readiness was best observed in group B with maximum post operative analgesia requirement. Overall side effects were highest in group C. **Conclusion:** It could be concluded that combination of Propofol- Ketamine provides excellent haemodynamic stability, superior analgesia, less respiratory depression but associated with post operative complication viz; PONV.

KEYWORD: Propofol, Ketamine, Butorphanol, Pentazocine, Postoperative Analgesia.

INTRODUCTION

The advantages of Day Care Surgery for Short Surgical Procedures are reduced hospital stay, early resumption of day to day activity, cost effective, reduces anxiety of surgery, recovery in familiar surroundings, reduced hospital acquired infection, faster postoperative recovery, less need for postoperative starvation, reduce the patients overload in the hospital, reduces wait list for surgery. The Day Surgery Operational guide, issued by the Darzi A et al[1] Department of Health, U.K., has described Day Surgery as; the admission of selected patients to hospital for a planned surgical procedure, returning home on the same day. The American author of the book 'Major Ambulatory Surgery', by James E Davis[2], describes day care surgeries as Minor Ambulatory surgery or outpatient surgery, as the care provided to non-hospitalized patients with immediate discharge of the patient. Top priorities for successful outpatient surgery are the four 'A's: alertness, ambulation, analgesia and alimentation. Multiple factors have contributed to this transition, including improved anaesthetic, better preoperative planning, and an enhanced ability to delivery adequate analgesia in the outpatient setting. One of the key components of successful day care surgery is better post operative analgesia. Based on current trends, it is fair to predict an increased use of local or regional anaesthesia alone, in combination with sedative anesthesia or as part of a multimodal technique with general anaesthesia. Several drugs have significant advantages in terms of rapid onset, excellent analgesia and amnesia, good surgical conditions and early recovery. These drugs include sedative-hypnotics such as propofol, analgesics such as remifentanil, alfentanil, fentanyl, butorphanol, pentazocine, and ketorolac, muscle relaxants such as mivacurium, rocuronium and inhalational agents such as desflurane and sevoflurane. These inhalation agents provide rapid and smooth induction, quick adjustments during maintenance and rapid recovery with few side-effects. The purpose of this study is to assess efficacy of Propofol in combination with Ketamine, Butorphanol or

Pentazocine for short surgical procedures. The study also assessed the cardio-vascular and respiratory stability and side effects of these combinations.

MATERIAL AND METHODS

The present study entitled "Comparative evaluation of Propofol with Ketamine, Butorphanol and Pentazocine in short surgical procedure" were carried out in the Department of Anesthesiology, G.R. Medical College and J.A. Group of Hospitals, Gwalior. The study was done in 90 patients of both sex, aged between 18-50 years of ASA Grade I and II, scheduled for short surgical procedure like MTP, MTP with LTT, diagnostic laparoscopy, dilatation and curettage, suction and evacuation, and close reduction in orthopedics, with no overnight hospitalization, after the approval from ethical committee of the college. Well informed written consent was taken. Demographic data, baseline hemodynamic variables were recorded. Patients suffering from any psychiatric illness and epilepsy were excluded from the study. All patients were recommended to undergo minimum investigation as required in individual cases viz. CBC, blood sugar, blood urea, urine for routine and microscopic examination, ECG, X-ray chest. All patients received uniform premedication of Inj. Glycopyrrolate 0.2 mg I/M ½ hour before start of anaesthesia. 90 patients were divided in three groups 30 each. Group A patients were induced with Propofol (2.0-2.5 mg/kg) and Ketamine (0.5 mg/kg). Group B patients were induced with Propofol (2.0-2.5 mg/kg) and Pentazocine (0.5 mg/kg). Group C patients were induced with Propofol (2.0-2.5 mg/kg) and Butorphanol (0.03-0.05 mg/kg). The patients of all groups were placed in supine position and an IV line was established. Necessary monitor was connected to the patient's viz. SpO2, NIBP and ECG. Continuous monitoring of Pulse rate, Systolic and Diastolic B.P., Respiratory rate, Arterial Oxygen Saturation was done throughout peri-operative period and values were recorded. Patients of group A, B and C were given Ketamine (0.5 mg/kg), Pentazocine (0.5 mg/kg), Butorphanol (0.03-0.05 mg/kg) respectively 5 minutes before surgery and thereafter all patients were induced with Propofol (2.0-2.5 mg/kg) over a period of 15 second till the end point of induction was reached, (i.e. loss of consciousness and loss of eyelash reflex). Anesthesia was maintained with intermittent doses of propofol (10 mg/IV) when the depth of anesthesia wear off viz. signs like sweating, lacrimation and limb movements. Airway was maintained with sniff position in the spontaneously breathing patient on air. If oxygen saturation fell below 95% then 100% oxygen was given by mask while breathing spontaneously.

Recovery pattern of the patients were assessed by the following parameters.

1. Immediate recovery- Measured at 1st, 5th, 10th minutes of recovery.

- Pulse rate
- Blood pressure (Systolic and Diastolic)
- Respiratory rate and arterial oxygen saturation
- Eye opening
- Steward Scoring.

Steward Score

(A)	Consciousness:	
(i)	Awake	2
(ii)	Responding to painful stimuli	1
(iii)	No response	0
(B)	Airway	
(i)	Coughing/crying	2
(ii)	Maintenance of good airway	1
(iii)	Supportive airway maintenance	0
(C)	Movements	
(i)	Moving limb purposely	2
(ii)	Not purposeful	1
(iii)	No movement	0
	Max score	6

2. Home readiness

The patients were discharged from the recovery room when they were fulfilling "Street fitness Criteria", which was measured at 2 hr, 4 hr and 6 hr postoperatively

The criteria for 'street fitness' are following

(i) Presence of adult escort
(ii) Vital signs stable for 1 hour
(iii) Absence of respiratory depression
(iv) Ability to perform motor tasks independent
(v) Maintain balance & co-ordination (negative Romberg sign)

Postoperative side effects like nausea-vomiting and headache were recorded. Postoperative analgesic requirement was also recorded.

RESULT

Table I: Demographic data

Parameters	Group A (n=30)	Group B (n=30)	Group C (n=30)
Age (yrs)	34.43±12.22	31.46±13.09	34.80±15.5
Sex ratio (M:F)	1:9	1:14	1:6.5
Weight (kg)	50.45±10.85	52.53±11.49	49.30±13.51
ASA GRADING(1:2)	7:23	22:8	13:17

Table II: Distribution of patients according to nature of surgery

	Group A (n=30)		Group B (n=30)		Group C (n=30)	
	No.	%	No.	%	No.	%
MTP	4	13.33	5	16.66	3	10.00
MTP with LTT	7	23.33	6	20.00	8	26.66
MTP with CuT	6	20.00	5	16.66	6	20.00
Plain LTT	4	13.33	5	16.66	5	16.66
Diagnostic Laparoscopy	3	10.00	4	13.33	2	6.66
Dilatation & Curettage	1	3.33	2	6.66	1	3.33
Suction & Evacuation	2	6.66	1	3.33	1	3.33
Close Fracture reduction	3	10.00	2	6.60	4	13.33
Total	30	100	30	100	30	100

Maximum number of cases had undergone the procedure MTP with LTT in all the three groups. The relative numbers of cases in all three groups are comparable.

Table III: Changes in pulse rate

Pulse Rate (per min)		Group A (n=30)	Group B (n=30)	Group C (n=30)
Pre induction basal value		79.15±9.66	79.26±9.97	78.53±10.15
Just before Induction/ 5 min after giving analgesia		85.20±9.54*	77.30±9.43	80.86±10.52
Start of Surgery/ after the induction		90.13±8.66*	102.80±10.28**	88.66±10.65*
Immediate recovery	1 min	89.80±8.32	91.30±9.84**	86.8±10.85
	5 min	87.13±8.64	85.60±9.05	84.00±11.15
	10 min	85.26±7.38*	86.00±9.18*	81.93±10.58

*Denote significant change ($p<0.05$)

** Denote highly significant change ($p<0.01$)

The preinduction value is the basal value. Pulse rate is represented as mean ± SD per min. At the start of surgery the pulse rate increased in all the groups and significantly ($p < 0.05$) in group A and C, but was highly significant ($p < 0.01$) in group B.

Table IV: Changes in systolic blood pressure

Systolic blood pressure		Group A (n=30)	Group B (n=30)	Group C (n=30)
Pre induction/ basal value		126.06±12.37	134.13±7.38	128.66±9.03
Just before Induction/ 5 min after giving analgesia		135.46±13.22*	131.20±7.23	132.66±9.27
Start of Surgery/ after the induction		143.86±13.93*	149.33±8.70*	141.33±10.56*
Immediate recovery	1 min	143.60±15.64	146.26±7.82	138.26±8.93
	5 min	134.73±13.97*	141.98±8.24	134.26±9.51
	10 min	133.93±14.63*	138.86±8.33	131.46±9.90

*Denote significant change ($p<0.05$)

**Denote highly significant change ($p<0.01$)

Systolic blood pressure is represented as mean ± SD mmHg. At the start of surgery rise in systolic blood pressure was highly significant in group B ($p<0.01$).

Table V: Changes in diastolic blood pressure

Diastolic blood pressure		Group A (n=30)	Group B (n=30)	Group C (n=30)
Pre induction/ basal value		76.73±6.91	76.63±6.46	74.33±6.52
Just before Induction/ 5 min after giving analgesia		83.06±7.67*	76.40±5.08	76.84±7.23
Start of Surgery/ after the induction		86.20±7.05	87.73±5.42*	84.00±7.28
Immediate recovery	1 min	85.53±6.97	86.40±5.37	81.04±7.36
	5 min	81.13±7.17	83.13±5.75	78.53±7.35
	10 min	79.60±6.50	81.80±5.71	77.33±6.63

*Denote significant change ($p<0.05$)

**Denote highly significant change ($p<0.01$)

Diastolic blood pressure is represented as mean ± SD mmHg. Diastolic blood pressure rose in all the three groups but at the start of surgery it was significant in group B ($p < 0.05$) as compared to group A and C.

Table VI: Changes in respiratory rate

Respiratory Rate (per min)		Group A (n=30)	Group B (n=30)	Group C (n=30)
Pre induction basal value		21.20±2.60	19.33±2.69	21.00±3.46
Just before Induction/ 5 min after giving analgesia		24.20±2.84	19.13±2.08	19.33±2.80
Start of Surgery/ after the induction		29.33±3.36*	25.23±74*	24.06±2.74*
Immediate recovery	1 min	26.66±2.97	24.13±3.52	22.06±2.74
	5 min	23.80±2.69	22.00±3.68	19.53±2.54
	10 min	22.96±2.54	21.13±3.35	19.13±2.32

*Denote significant change ($p<0.05$)
**Denote highly significant change ($p<0.01$)
Respiratory rate was represented as mean ± SD per min. At the start of surgery, there was a significant ($p< 0.05$) rise in respiratory rate from basal value in all three groups.

Table VII: Changes in oxygen saturation

SpO_2 (%)		Group A (n=30)	Group B (n=30)	Group C (n=30)
Pre induction basal value		98.40±1.54	98.06±1.53	99.13±1.13
Just before Induction/ 5 min after giving analgesia		97.40±1.56	97.93±1.33	96.80±0.99*
Start of Surgery/ after the induction		97.73±1.32	95.26±1.53*	98.46±1.43
Immediate recovery	1 min	97.73±1.32	97.93±0.96	97.40±06
	5 min	98.40±1.61	97.53±1.13	96.26±0.69
	10 min	98.32±1.52	97.73±0.88	96.33±0.76*

*Denote significant change ($p< 0.05$)
Oxygen saturation was represented by mean ± SD percentage. At the start of surgery there was a significant decrease ($p < 0.05$) in SpO_2 in group B.

Table VIII: Total dose of propofol required during surgery

	Group A (n=30)	Group B (n=30)	Group C (n=30)
Total dose of Propofol (mg)	156.66±16.25	250.66±22.42	214.33±16.04
Total time of surgery (min)	23.80±5.73	26.00±4.04	23.33±4.13
Dose of Propofol per minute of surgery (mg/min)	6.58	9.64	9.18
Dose of Propofol per Kg body weight (mg/min)	3.10	4.77	4.34

The required dose of Propofol was lowest in group A.

Table IX: Parameters in all three groups during immediate recovery

		Group A (n=30)	Group B (n=30)	Group C (n=30)
Eye opening	1 Min	11	24	20
	5 min	17	6	8
	10 min	2	0	2
Following commands	1 min	5	24	18
	5 min	11	6	8
	10 min	14	0	4
Steward Score (Max. 6)	1 min	5	22	17
	5 min	11	8	9
	10 min	14	0	4

Table IX show three parameters in the three groups during immediate recovery which was measured at 1^{st}, 5^{th} and 10^{th} minutes of recovery.

Table X: Parameters determining home readiness by fulfilling "street fitness criteria" in three groups

Criteria	Time in hrs	Group A (n=30)	Group B (n=30)	Group C (n=30)
Street fitness criteria	2 hr	3	18	12
	4 hr	13	12	15
	6 hr	14	0	3

Table XI: Incidence of side effects and postoperative analgesia requirement

	Group A (n=30)		Group B (n=30)		Group C (n=30)	
	No.	%	No.	%	No.	%
PONV	12	40.00	10	33.33	3	10.00
Headache	1	3.33	2	6.66	5	16.66
Postoperative analgesic requirement	4	13.33	20	66.66	9	30.00

Post Operative Nausea Vomiting (PONV) was highest in group A (40%) and lowest in group C (10%). Incidence of headache was highest in group C (16.66) and lowest in group A (3.33%). Postoperative analgesic requirement was highest in group B (66.66%) than group C (30%) and minimum in group A (13.33%).

DISCUSSION

In the present study, it was observed that after 5 minutes of giving analgesia there was a significant rise ($p< 0.05$) in mean pulse rate from base line value in group A (ketamine) as compared to group C (butorphanol) while in group B (pentazocine) there was a fall in pulse rate. These findings are in agreement with Mayer M. et al[3] whose study showed a reduction in pulse rate in patients induced with propofol pentazocine combination as compared to propofol ketamine combination. This variation may be due to the pharmacological stimulation of sympathoadrenal system by ketamine and butorphanol where as lack of any such stimulation of cardiovascular system by pentazocine.

The rise in pulse rate during the start of surgery was observed in all three groups. In group A and group C there was a significant rise ($p < 0.05$) while in group B the rise was very significant ($p < 0.01$). This may be due to inadequate analgesia and depth of anaesthesia provided by pentazocine at the start of surgery. The above statement was supported by the studies of Potter et al[4] which recorded a rise in pulse rate after parenteral administration of pentazocine with propofol due to inadequate analgesia.

During immediate recovery (1 minute) there was a fall in pulse rate in all the three groups but it was highly significant ($p < 0.01$) in group B which support the study of Schuttler J. et al[5] who carried out separate studies in patients of day care surgery and found better hemodynamic stability in ketamine propofol combination as compared to pentazocine propofol combination. There was no significant change ($p > 0.05$) at 5 minutes and 10 minutes of recovery in all three groups. Similar observations were recorded by Grounds et al[6] where they found an insignificant change of pulse rate after propofol induction.

There was a rise in systolic blood pressure from pre induction values which was significant in group A ($p < 0.05$) after giving analgesia as compared to group C where there is no significant rise from the pre induction values ($p > 0.05$). Tweed et al[7] showed that ketamine produced immediate increase in blood pressure and cardiac output. Popio et al[8] have reported increase in blood pressure after intravenous butorphanol (0.03 mg/kg). In group B there is a slight decrease in blood pressure, this is in agreement with Mayer et al[3] who found a significant decrease in systolic blood pressure in patients induced with propofol pentazocine combination as compared to propofol ketamine combination. Sebel and Lowden[9] also concluded that propofol allow insignificant decrease in blood pressure with pentazocine.

At the start of surgery there was a highly significant rise in systolic blood pressure in group B and group A ($p < 0.01$). Saha et al[10] which showed greater surgical tolerability and less cardiovascular variation in patients of propofol ketamine combination in comparison to propofol pentazocine combination.

After 5 minutes of giving analgesia there was an increase in diastolic blood pressure in group A and C. Diastolic blood pressure increase in group A which may be due to superior analgesic action and better depth of anaesthesia provided by ketamine.[11]

There was a rise in respiratory rate in group A and fall in group B and C through they are not statistically significant ($p > 0.05$). The initial fall in respiratory rate may be explained due to respiratory depressant action of opioids (pentazocine and butorphanol), which is in accordance with the findings of Sternol I.B. et al.[12] These finding are also supported by the studies of Baraka et al.[13] The rise in respiratory rate at the start of surgery in all the three groups may be due to pain caused by surgical stimulus.

There was a significant fall in oxygen saturation only in group C ($p < 0.05$).This may is due to respiratory depression caused by butorphanol.[14, 15]

Total dose of propofol required was maximum in group B. This could be due to the fact that when propofol and ketamine were used in combination, they are additive at hypnotic and anesthetic end points.[16, 17]

The recovery parameters (as shown by eye opening following verbal commands and steward scoring system) were delayed in group A and were met earliest in group B patients. Though at 10 minutes, all the patients were able to open eye spontaneously. Edelist et al[18] found the mean time of eye opening was 4.5 minutes, and Candelaria et al[19] observed it to be at approximately 5 minutes.

At 1 min of recovery, only 5 patients belonging to group A were able to follow verbal commands in comparison to 24 patients in group B and 18 patients in group C. Gill et

al[20] found that time to follow command was observed at 4 to11 minutes.

In the Steward scoring, 5 patients of group A got maximum score. Swadia V.N. et al[21] recorded a maximum score at 10-15 minutes of recovery. The prolonged recovery time in group A is because of longer elimination half life of ketamine as compared to that of pentazocine.[10, 17, 22]

Most of the patients in all the three groups were home ready at 4 hr after the surgery, as determined by fulfilling the "Street fitness criteria". It might be because of longer duration of action of drugs in both groups A and group C with added psychosomatic alterations in group A.

Post operative analgesic requirement was maximum in group B (66.66%). This may be due to inadequate analgesia provided by pentazocine in comparison to ketamine. The findings are in consistent with Mayer M et al[3].

CONCLUSION

Thus it appears that combination of Propofol-Ketamine for short surgical procedure in day care surgeries provides excellent haemodynamic stability, superior analgesia, less respiratory depression but associated with post operative complication viz; PONV are concern with this drug. Combination of Propofol-Pentazocine gives excellent recovery profile although with inferior analgesia, cardiovascular instability, and respiratory depression. Propofol-Butorphanol combination shows good cardiovascular stability, moderate analgesia and fair recovery with mild post operative complications.

REFERENCES

1. Darzi A. Dept of Health. The Day Surgery Operational Guide. Augest., 2002; U. K., 1-28.
2. James E Davis. Major Ambulatory Surgery Today, 1987; USA, 33-57.
3. Mayer M, Ochmann O, Doenicke A, Anster R, Suttman H: the effect of propofol ketamine anaesthesia on haemodynamics and anaelgesia in comparison with propofol pentazocine. Anaesthesist, 1990; 39: 609-616.
4. Potter D.R, Payne J. P. Newer analgesic with special reference to pentazocine. British J. Anaesth., 1970; 42; 186-93.
5. Schuttler J, Schuttler M, Kloos S, Nadstaiwek J, Schwilden H. Total Intravenous Anaesthesia with ketamine and propofol with optimized dosing strategies, Anaesthetist, 1991; 40: 199-204.
6. Grounds RM, Tmigley AJ, Carli F, et al. The haemodynamic effects of intravenous induction. Comparison of the effects of thiopentone and propofol. Anaesthesia., 1985; 40: 735-40.
7. Tweed W.A, Mimick M, Mymin D.; Circulatory responses to Ketamine Anaesthesia. Anaesthesiology., 1972; 37: 6; 613-619.
8. Popio K.A; Jackson D.H; Ross A.M; Schreiner B.F and Yu P.N.; Haemodynamic and respiratory effect of morphine and butorphanol. Clinical Pharmacology and Therapeutics., 1978; 23: 281-287.
9. Sebel P S and Lowdon J D; Propofol: A new intravenous anaesthesitic. Anaesthesiology., 1989; 71: 260-277.
10. Saha K, Saigopal M, Sunder R, Palanippan M, Mathew A C: Comparative evaluation of propofol-Ketamine and Propofol-fentanyl in minor gynaecological surgery. Indian J anaesth., 2001; 45(2): 100-103.
11. Wong D H W, Jenkins L C: The cardiovascular effects of ketamine in hypertensive states. Can Anaesth Soc J., 1975; 22: 339-348.
12. Sternol I B, Sandin RH: recurrent respiratory depression after total intravenous anaesthesia with propofol and alfentanyl. Anaesthesia, 1998; 53(4): 378-81.
13. Baraka A, Dobbous A, Siddik S. and Bijjani A. Action of Propofol on resistance and capacitance vessels during cardiopulmonary bypass. Acta. Anaesth. Scand., 1991; 35: 545-547.
14. Adams A P, Pybus D A: delayed respiratory depression after use of fentanyl during anaesthesia. Br Med Jr. 1978; 1: 278-9.
15. Lippman M, Mok MW, Steen SN. Butorphanol in postoperative pain. Clinical Pharmacology and Therapeutics., 1976; 4: 234.
16. Hui T W, Short T G , Hony W , Suen T , Gin T , Plummer J: Addictive interactions between propofol and ketamine when used for anaesthesia induction in female patients. Anaesthesiology, 1995; 82(3): 641-648.
17. Hamdani GA; Khan FA; Comparison of propofol-fentanyl and Propofol – ketamine anaesthesia in minor gynaecological surgery. JACP., 1999; 15(2): 173-7.
18. Edilist G: A comparison of propofol and Thiopentone as induction agent in outpatient surgery. Can. J Anaesth., 1987; 34(2): 110-6.
19. Candeleria L M, Smith R K: Propofol infusion technique for outpatient general anaesthesia. Dept. Of Oral and Maxillofacial surgery., 1995; 53: 124-128.
20. Gill SS, Wright EM and Reilly CS. Pharmacokinetic interaction of Propofol and Fentanyl: Single Bolus injection study. Br J Aanesth., 1990; 65: 760-765.
21. Swadia VN, Total intravenous anaesthesia for day care surgery. J Anaesth. Clinical Pharmacology., 1997; 13(1): 57-61.
22. Jenstrup M, Nielsen J, Fruergård K, Møller AM, Wiberg-Jørgensen F. Total i.v. anaesthesia with propofol-alfentanil or propofol-fentanyl. *Br J Anaesth.* 1990 Jun; 64(6): 717–722.