

Haemodynamic Changes during Induction; Comparison of Propofol with Mixture of Propofol-Ketamine

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ABSTRACT

The objective of this study was to compare haemodynamic changes during induction of general anaesthesia with propofol and mixture of propofol-ketamine. That was Quasi experimental study. One hundred patients undergoing surgical procedure were included and divided into two equal groups A and B by using random number table. Each group comprised of fifty patients. In group A propofol was used as an inducing agent, dose 2.5mg / kg intravenously within 30 seconds. In group B propofol 2.5 mg/kg and ketamine 2 mg / kg intravenously within 30 seconds. No other drug like muscle relaxants and analgesics were given to patients. Only 100% O₂ given to patient with face mask. Heart rate, systolic and diastolic blood pressure were recorded for three minutes at the interval of 30 seconds. Students "t" test was used and analysis with SPSS version 10. Significant decrease in systolic, diastolic blood pressure and heart rate was recorded with propofol and minimal haemodynamic changes were recorded with propofol-ketamine mixture.

Conclusion: Propofol-ketamine mixture is a better inducing agent as compared to propofol alone.

Keywords: Ketamine, Propofol, Propofol-ketamine mixture, haemodynamic changes.

INTRODUCTION

Cardiovascular effects principally hypotension and bradycardia are the most important physiological changes at the time of induction of general anaesthesia. Cardiovascular complications are the most common caused of postoperative morbidity and mortality in patients who undergo surgery¹. Propofol (2,6 di-iso-propyl phenol) is 1% aqueous solution². It is an oil-in-water emulsion containing soybean oil, glycerol and egg lecithin. Induction dose of propofol is 1.5-2.5mg/kg. The initial distribution half-life is 2 to 8 minutes and mainly excreted in urine.

Ketamine, an anaesthetic agent with sedative and analgesic properties³. Ketamine down-regulates stimulus induced expression of adhesion molecules and inhibits neutrophil activation and associated superoxide anion generation⁴. Ketamine is a dissociative anaesthetic⁵. The mixture of propofol and ketamine is also called "ketofol". The use of propofol and ketamine as single agents for procedural sedation and analgesic in the emergency department has grown in popularity. The reasonable premise behind ketofol is that the two agents ketamine and propofol are theoretically synergistic⁶. Ketofol appears to be safe and efficacious for use in emergency department⁷ and sedation depth appeared to be more consistent with ketofol⁸. Ketofol is associated with improved haemodynamic stability⁹.

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The ketamine-propofol combination provides adequate sedation and analgesia for painful procedures and appears to be safe and useful technique in the emergency department¹⁰.

MATERIAL AND METHODS

After the approval of study from the hospital ethics committee hundred patients undergoing short gynaecological procedure were included and divided into two equal groups A and B by using a random number table.

Each group was comprise 50 patients. Group A patients were induced with propofol and group B patients with mixture of propofol and ketamine.

That was Quasi experimental study and was conducted in the department of Anaesthesiology services hospital. On the preoperative visit informed consents were taken and signed. Intravenous lines were maintained with 18G cannulas and advised nothing by mouth (NPO) after midnight.

Baseline monitoring was carried with help of pulseoximeter, ECG and noninvasive blood pressure monitor.

During study period all patients received 100% O₂ four liter perminute with face-mask through circle system. No other drugs like muscle-relaxant, analgesics were given and no surgical stimulus was permitted. Blood pressure and heart rate were recorded at interval of 30 seconds for three minutes continuously on specially designed proforma. In group A propofol 2.5mg/kg intravenously in 30

seconds. In group B propofol 2.5mg/kg along with ketamine 2mg/kg given intravenously within 30 seconds Student's "t" test was used along SPSS version 10 for data analysis.

were selected. Mean age in group A was 33.02±9.529 and in group B was 31.62± 8.189. Mean weight in group A was 55.480±10.122 and in group B was 54.620±11.245.

Significant value of P at 2 minutes for heart rate and diastolic pressure and for all three parameters at 2:30 minutes and upto 3 minutes.

RESULTS

During this study 100 female patients of ASA class 1 and Class 2 undergoing short surgical procedure

Table 1: Distribution of patients according to age and study groups

Age of patients	Group "A" Propofol Group		Group "B" Propofol-Ketamine Group		Total	
	Freq	%	Freq	%	Freq	%
< 20 years	3	6.0%	2	4.0%	5	5.0%
20-30 years	22	44.0%	23	46.0%	45	45.0%
> 30 years	25	50.0%	25	50.0%	50	50.0%
Total	50	100.0%	50	100.0%	100	100.0%

Table 2: Mean age of patients in the study groups

Study groups	(n)	Mean	Std. Deviation	Student t test
Group "A" Propofol group	50	33.02	9.529	t-value = 0.79 p-value = 0.43
Group "B" Propofol-ketamine Group	50	31.62	8.189	

Table 3: Distribution of patients according to weight and study groups

Patient Weight	Group "A" Propofol Group		Group "B" Propofol-Ketamine Group		Total	
	Freq	%	Freq	%	Freq	%
< 50 kg	12	24.0%	18	36.0%	30	30.0%
50-60 kgs	26	52.0%	23	46.0%	49	49.0%
> 60 kgs	12	24.0%	9	18.0%	21	21.0%

Table 4: Mean weight of patients in the study groups

Study groups	(n)	Mean	Std. Deviation	Student t test
Group "A" Propofol group	50	55.480	10.122	t-value = 0.402 p-value = 0.69
Group "B" Propofol-ketamine Group	50	54.620	11.245	

Table 5: Comparison of only Systolic Blood pressure at different time intervals in the study groups

Study groups	(n)	Mean	Std. Deviation	Student t test
At 0 Second				
Group "A" Propofol group	50	131.34	10.871	t-value = 1.171 p-value = 0.24
Group "B" Propofol-ketamine Group	50	129.06	8.445	
At 30 Second				
Group "A" Propofol group	50	125.20	10.971	t-value = 1.185 p-value = 0.24
Group "B" Propofol-ketamine Group	50	122.80	9.212	
At 1 minute				
Group "A" Propofol group	50	118.34	10.905	t-value = 1.213 p-value = 0.23
Group "B" Propofol-ketamine Group	50	115.62	11.510	
At 1 minute 30 seconds				
Group "A" Propofol group	50	111.70	11.589	t-value = 0.017 p-value = 0.99
Group "B" Propofol-ketamine Group	50	111.66	11.651	
At 2 minutes				
Group "A" Propofol group	50	105.38	10.751	t-value = 2.323 p-value = 0.02
Group "B" Propofol-ketamine Group	50	112.40	18.468	
At 2 minutes 30 seconds				
Group "A" Propofol group	50	99.90	9.609	t-value = 9.645 p-value = 0.01
Group "B" Propofol-ketamine Group	50	121.00	12.122	
At 3 minutes				
Group "A" Propofol group	50	97.34	9.052	t-value = 12.078 p-value = 0.01
Group "B" Propofol-ketamine Group	50	125.60	13.947	

Table 6: Comparison of only Diastolic Blood pressure at different time intervals in the study groups

Study groups	(n)	Mean	Std. Deviation	Student t test
At 0 Second				
Group "A" Propofol group	50	80.60	8.512	t-value = 1.409 p-value = 0.16
Group "B" Propofol-ketamine Group	50	78.40	7.031	
At 30 Second				
Group "A" Propofol group	50	75.80	8.711	t-value = 1.046 p-value = 0.30
Group "B" Propofol-ketamine Group	50	74.20	6.414	
At 1 minute				
Group "A" Propofol group	50	70.46	8.242	t-value = 0.970 p-value = 0.34
Group "B" Propofol-ketamine Group	50	68.90	7.843	
At 1 minute 30 seconds				
Group "A" Propofol group	50	65.98	8.424	t-value = 0.070 p-value = 0.94
Group "B" Propofol-ketamine Group	50	65.86	8.609	
At 2 minutes				
Group "A" Propofol group	50	61.84	7.896	t-value = 3.829 p-value < 0.01
Group "B" Propofol-ketamine Group	50	68.10	8.445	
At 2 minutes 30 seconds				
Group "A" Propofol group	50	57.90	7.360	t-value = 10.851 p-value < 0.01
Group "B" Propofol-ketamine Group	50	73.90	7.385	
At 3 minutes				
Group "A" Propofol group	50	56.26	8.055	t-value = 13.006 p-value < 0.01
Group "B" Propofol-ketamine Group	50	76.84	7.765	

Table 7: Comparison of only Heart Rate at different time intervals in the study groups

Study groups	(n)	Mean	Std.Deviation	Student t test
At 0 Second				
Group "A" Propofol group	50	88.44	10.645	t-value = 484 p-value = 0.63
Group "B" Propofol-ketamine Group	50	87.80	6.041	
At 30 Second				
Group "A" Propofol group	50	83.44	8.867	t-value = 1.222 p-value = 0.23
Group "B" Propofol-ketamine Group	50	81.78	6.052	
At 1 minute				
Group "A" Propofol group	50	78.18	8.236	t-value = 1.331 p-value = 0.19
Group "B" Propofol-ketamine Group	50	76.16	6.879	
At 1 minute 30 seconds				
Group "A" Propofol group	50	73.22	7.694	t-value = 0.221 p-value = 0.83
Group "B" Propofol-ketamine Group	50	73.56	7.656	
At 2 minutes				
Group "A" Propofol group	50	68.74	7.491	t-value = 3.967 p-value < 0.01
Group "B" Propofol-ketamine Group	50	74.82	7.832	
At 2 minutes 30 seconds				
Group "A" Propofol group	50	62.70	10.735	t-value = 9.243 p-value < 0.01
Group "B" Propofol-ketamine Group	50	78.40	5.387	
At 3 minutes				
Group "A" Propofol group	50	61.56	7.799	t-value = 14.926 p-value < 0.01
Group "B" Propofol-ketamine Group	50	81.70	5.497	

DISCUSSION

This study shows that the use of mixture of propofol-ketamine provides more stability in haemodynamics of patients at the time of induction of general anaesthesia as compare to propofol alone. We know that ketamine alone is causing increase in systemic vascular resistance, cardiac output and mean arterial pressure and raises blood pressure upto 25% and heart rate about 20% and its effect start within 30 to 60 seconds after Intravenous dose and remain for 10

to 15 minutes. On the other hand mechanism of propofol is totally different and its effect start within 20 to 40 seconds and remain for 2 to 8 minutes and cause decrease in Blood pressure upto 40% and has cardiac depressant action and decrease mean arterial pressure, cardiac output and systemic vascular resistance. Ketamine is also effective in the treatment of CRPS pain symptoms¹¹ and it has been shown to induce a consistently antidepressant effects within a short period of time¹² and Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist¹³. Similarly

intrathecal ketamine has been reported to have evident analgesic effects on neuropathic pain induced by nerve injury¹⁴ and neuropathic pain is an intractable clinical problem¹⁵. In one study they found that spinally administered ketamine (preservative free) improve the duration or quality of analgesia in children¹⁶. Propofol also has anti-inflammatory properties and can suppress cytokines and chemokines production¹⁷.

Propofol and etomidate depress the neurons in the cortex, thalamus and reticular formation and produce unconsciousness¹⁸. Painful procedures on children and adolescents often have to be performed with the aid of analgesia and sedation in order to prevent pain and emotional distress¹⁹. Propofol is superior to midazolam in reducing inflammation and oxidative stress and in improving post-operative recovery in children²⁰. Similarly in the study of Yalcin S et al they found mixture of propofol and ketamine are better than alone for electroconvulsive therapy²¹.

Similarly in the study of Khutia SK et al they found combination of ketamine and propofol is more effective and as safe sedoanalgesia regimen than propofol-fentanyl combination in paediatric emergency. Short surgical procedures in term of haemodynamic stability & less incidence of apnoea²².

CONCLUSION

Mixture of propofol-ketamine is a better inducing drug as compared to propofol alone, as it caused less haemodynamic changes at the time of induction of general anaesthesia.

REFERENCES

1. Salahuddin N, Fatimi S, Huda S, Islam M. Predicting a postop cardiopulmonary complications by a test of stair climbing. *J Coll physicians Surg Pak* 2005;15:761-764.
2. Joseph D, Leder M. Procedural Sedation: A review of sedative agents, monitoring and management of complications. *Saudi J Anaesth.* 2011; 5: 395-410.
3. Ward JL, Harting MT, Cox CS. Effects of ketamine on endotoxin and traumatic brain injury. Induced cytokines production in rats. *J Trauma* 2011;70:1471.
4. Lu HW, He GN, Ma H, Wang J. Ketamine reduces inducible superoxide generation in human neutrophils in vitro by modulating the p 38. mitogen activated protein kinase (MAPK) mediated pathway. *Clin Exp Immunol* 2010; 160 (3): 450-456.
5. Lankenau SE, Bloom JJ, Shin C, Longitudinal Trajectories of ketamine use among young injection drug users. *Int J Drug Policy* 2010; 21 (4): 306-314.
6. Sheta SA. Procedural sedation analgesia. *Saudi J Anaesth* 2010; 4 (1): 11-16.
7. Arora S. Combining ketamine and propofol (ketofol) for emergency department procedural sedation and analgesia: A review. *West J Emerg Med* 2008;9(1):20.
8. Andolfatto G, Abu-Laban RB, Zed PJ, Staniforth SM, Ketamine-propofol combination (ketofol) versus

propofol alone for emergency department procedural sedation and analgesia: a randomized double-blind trial. *Ann Emerg Med* 2012; 59 (6): 504-512.

9. Smischney NJ, Beach ML, Loflus RW, Dodds TIM, Koff MD. Ketamine/Propofol admixture (Ketofol) is associated with improved hemodynamics as an induction agent: A randomized, controlled trial. *J Trauma Acute Care Surg* 2012; 73(1): 94-101.
10. Nejati A, Moharari RS, Ashraf H, Labaf A, Golshanik Ketamine / Propofol versus midazolam Fentanyl for procedural sedation and analgesia in the emergency department: a randomized, prospective, double-blind trial. *Acad Emerg Med* 2011; 18 (8): 800-806.
11. Goldberg ME, Tarjman MC. Pharmacodynamic profile of ketamine (R) and (S⁺) with five day in patient infusion for the treatment of complex regional pain syndrome. *Pain Physician* 2010;13(4): 379 -387.
12. Vieira RM, Salvadore G, Granados ND. Ketamine and the next generation of antidepressants with a rapid onset of action. *Pharmacol Ther* 2009; 123(2):143-150.
13. Baumgartner C, Bollerhey M, Ebner J, Schuster T, Erhardt W. Effect of ketamine-xylazine intravenous bolus injection on cardiovascular function in Rabbits. *Can J Vet Res* 2010; 74 (3): 200-208.
14. Mei X, Zhang H, Wang W, Wei YY. Inhibition of spinal astrocytic C-Jun N Terminal Kinase (JNK) activation correlates with analgesic effects of ketamine in neuropathic pain. *J Neuroinflammation* 2011; 8: 6.
15. Mei XP, Wang W, Zhu C, Chen L et al. Combining ketamine with astrocytic inhibitor as a potential analgesic strategy for neuropathic pain. *Ketamine astrocytic inhibitor and pain. Mal Pain* 2010; 6 : 50.
16. Walker SM, Westin BD, Deumens R, Grafe M, Yaksh TL. Effects of intrathecal ketamine in the neonatal rat : Evaluation of apoptosis and long term functional outcome. *Anesthesiology*: 2010; 113 (1): 147-159.
17. Hsing C, Lin M, Choi P, Huang W, et al. Anesthetic propofol reduces endotoxin inflammation by inhibiting reactive oxygen species-regulated AKT/IKKB/NF-KB signaling. *PLOS One* 2011; 6 (3): e 175-98.
18. Andrada J, Livingston P, Lee BJ. Propofol and etomidate depress cortical, thalamic and reticular formation neurons during anaesthetic induced unconsciousness. *Anesth Analg* 2012; 114 (3): 661-9.
19. Neuhauser C, Wagner B, Heckmann M. Analgesia and sedation for painful interventions in children and adolescents. *Dtsch Arztebl Int.* 2010; 107(14):241-247.
20. Xia W, Liu Y, Zhou Q. Comparison of the effects of propofol and midazolam on inflammation and oxidative stress in children with congenital heart disease undergoing cardiac surgery. *Yonsei Med J* 2011;52(2) : 326-332.
21. Yalcin S, Aydogan H, Selek S, Kunch A, Yuce HH, Ketofol in electroconvulsive therapy anesthesia: Two stones for one bird. *J Anesth* 2012; 26 (4): 562-567.
22. Khutia SK, Mandal MC, Das S, Basu SR. Intravenous infusion of ketamine-propofol can be an alternative to intravenous infusion of fentanyl-propofol for deep sedation and analgesia in paediatric patient undergoing emergency short surgical procedures. *Indian J Anaesth* 2012; 56 (2): 145-150.

