International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 01-01-2021; Accepted: 20-01-2021; Published: 13-02-2021
www.medicalsciencejournal.com
Volume 7; Issue 2; 2021; Page No. 24-27

Impact of ketamine (low dose) on intracranial pressure among subjects with space occupying lesion of the brain

Rajesh Kumar[1*], Rohit Kumar[1], Sanjay Kumar[2]
[1] SR Anaesthesia, Aiims, Patna, Bihar, India
[2] SR Anesthesia, IGIMS, Patna, Bihar, India

Abstract
Aim: To study the effects of low doses of ketamine on intracranial pressure in patients having space occupying lesion of the brain.
Material and Methods: The present hospital based, observational, experimental study was conducted in the department of neurosurgery operating theatre, Aiims, Patna. 45 patients were patients were divided into 3 groups i.e. Group A, Group B and Group C. Group A was induced with standard induction agents 1-2 µg/ kg of fentanyl, 0.1 mg / Kg vecuronium, 2-3 mg/kg of propofol and 5 ml of normal saline (placebo) through intravenous (IV) route. Group B was induced with 1-2 µg/ kg of fentanyl, 0.1 mg / Kg vecuronium 2-3 mg/kg of propofol and 0.25 mg/kg of ketamine diluted with normal saline in 5ml volume. Group C was induced with 1-2 µg/ kg of fentanyl, 0.1 mg / Kg vecuronium 2-3 mg/kg of propofol and 0.5 mg/kg of ketamine diluted with normal saline in 5ml volume.
Results: OSND values varies from 4 to 5.8 mm among all the groups at baseline, with mean of 5.4mm, 5.4mm and 5.3mm among group A, B and C respectively. According to the criteria used in the present study, ICP values decreases approximately similar in group B and C, while it decreased at 2 min in group A and increased again to previous values after 5min.
Conclusion: The authors concluded that combined with a benzodiazepine and barbiturates ketamine may be the preferred sedative/anesthetic agent for patients with space occupying lesion, and it can probably be used safely in surgical situations.

Keywords: space occupying lesion, ketamine, ICP

Introduction

The brain and spinal cord are enclosed by bone. ICP is defined as the pressure within the cranium which comprises a fixed volume of neural tissue, blood and cerebrospinal fluid (CSF). Normal ICP varies according to age and ranges between 5 mmHg and 15 mmHg in adults [1]. Expansion of intracranial contents by a space-occupying lesion (SOL) leads to compression and distortion of the tissues of the CNS. Slowly enlarging SOLs can be accommodated by atrophy of adjacent brain or spinal tissue [2]. In patients with intracranial space-occupying lesions, control of mean arterial (MAP) and intracranial (ICP) pressure during anaesthetic induction and tracheal intubation is essential to prevent an untoward increase or decrease in cerebral perfusion pressure [3].

In patients with various intracranial pathologies and reduced intracranial compliance, adequate sedation and analgesia is the basic important measure to control ICP along with controlled ventilation. Deepening sedation is one of the routine first steps when ICP rises. The commonly available sedative and hypnotic agents- benzodiazepines, propofol, and barbiturates- decrease blood pressure and may potentially decrease CPP [4].

Ketamine is unique among the anesthetic agents in that it maintains protective airway reflexes and spontaneous respiration. Although ketamine has a cardiodepressive effect, this is usually overwhelmed by its indirect central sympathetic action and it does not decrease blood pressure [5, 6]. It is widely stated that ketamine increases ICP, its routine use is practically precluded in patients with TBI and with increased ICP. But there is ample of research available now on the effects of ketamine on ICP which suggests that ketamine does not increase ICP in adult non traumatic neurological illness when the patients are adequately sedated and Pco2 is maintained in normal limits. Albanese *et al* conducted a prospective controlled study to determine the effect of IV bolus doses of ketamine on ICP and cerebral perfusion pressures in patients with severe traumatic brain injury, using patients baseline as controls, at the end of the study he concluded that there was a small but statistically significant decrease in ICP [7].

Due to conflicting literature, the present case control observational study was conducted to investigate the effects of low doses of ketamine on intracranial pressure in patients having space occupying lesion of the brain.

Material and method

The present hospital based, observational, experimental study was conducted in the department of neurosurgery operating theatre, Aiims, Patna. This study includes all patients undergoing neurosurgery for space occupying lesion of the brain during the study period (January 2019 to January 2020). The study was performed after obtaining ethical committee approval and written informed consent

from all participants before enrolment into the study. The patients were selected according to the following inclusion and exclusion criteria:

Inclusion criteria

a. Patient with ASA CLASS I/ II
b. Adult Patient aged 18-55years with weight 50 to 70 kg
c. Patients scheduled for elective supratentorial surgeries for brain tumour more than 2.5 cm symptomatic and radiologicaly evidence of raised ICP under general anesthesia

Exclusion criteria

a. Patient with ASA CLASS III, IV & V
b. Patients having predicted difficult airway, mouth opening less than 2.5 cm, intra oral pathology.
c. Non-consenting patients.

After applying the inclusion and exclusion criteria, 45 patients were selected for the present study. In operation theatre routine monitoring including NIBP, Spo2, ECG was done for all the patients and all the patients were pre-oxygenated with 100% O_2 for 3 mins. Selected patients were divided into 3 groups i.e. Group A, Group B and Group C.

Group A

Was induced with standard induction Agents 1-2 µg/ kg of fentanyl, 0.1 mg / Kg vecuronium, 2 -3 mg/kg of propofol and 5 ml of normal saline (placebo) through intravenous (IV) route.

Group B

Was induced with 1-2 µg/ kg of fentanyl, 0.1 mg / Kg vecuronium 2-3 mg/kg of propofol and 0.25 mg/kg of ketamine diluted with normal saline in 5ml volume.

Group C

Was induced with 1-2 µg/ kg of fentanyl, 0.1 mg / Kg vecuronium 2-3 mg/kg of propofol and 0.5 mg/kg of ketamine diluted with normal saline in 5ml volume.

Selection of the drug under study was done by the person who was not involved in the anaesthesiologist's team for that particular patient. That person withdraws a chit from the box and then will prepare drug accordingly in 5 ml volume. After given of IV drugs all 3 group patients were intubated with appropriate size endotracheal tube, 1% propofol infusion @ 50-200 mcg/kg/hr was stared just after intubation and patients were ventilated with 50% O_2, 50% air for next 5 mins. Ocular USs were performed on a Sonosite Micromaxx machine with a 10–5 MHz linear probe using a standard technique i.e. 3mm behind the eye globe using B-mode. Briefly, subjects were examined in the supine position. Conductive US gel was placed over a closed eyelid. A linear probe was used to obtain axial cross-sectional images of the optic nerve, and the ONSD was measured 3 mm posterior to the orbit. Readings were taken at 3 different intervals i.e. before start of IV boluses of drugs, at 2 mins of bag and mask ventilation and at 5 mins of post endotracheal intubation. At the end of surgery patients were reversed using a combination of injection neostigmine 0.05 mg/kg iv and injection glycopyrrolate 0.008 mg/kg Iv and extubated after achieving adequate respiratory efforts. After extubation patients were shifted to Post Anaesthesia Care Unit for Postoperative monitoring.

ICP

There is lot of disparity in available literature for the upper cut-off value of ONSD but many has identified it near about 5 mm, above which patients exhibit either clinical or radiologic signs of elevated ICP [8]. Hence in the present study, same standard was used. ONSD cut-off values of 4.7 mm was used (as mentioned in the literature the cut-off 4.6 mm for females and 4.8 mm for males were used for the diagnosis of elevated ICP) [9, 11].

Statistical analysis

Data so collected was tabulated in an excel sheet, under the guidance of statistician. Data was analyzed using IBM SPSS. Statistics Windows, Version 24.0. (Armonk, NY: IBM Corp) for the generation of descriptive and inferential statistics. The statistical significant difference among groups was determined by the anova test.

Results

In the present study, males were slightly more as compared to females in all the three groups, but statistically insignificant. The mean age of the study subjects was 43.2±7.19, 41.3±6.79 and 44.68±8.12 years in group A, B and C respectively (table 1). Table 2 shows the mean arterial pressure (MAP) and heart rate (HR) before induction of anaesthesia and tracheal intubation. Statistically no significant difference was found among the three groups in relation to the mentioned parameters at baseline. There was little increase in HR (bpm) among the three groups after post-tracheal intubation at two and five minutes (table 2). In the present study, OSND values varies from 4 to 5.8 mm among all the groups at baseline, with mean of 5.4mm, 5.4mm and 5.3mm among group A, B and C respectively. In group A, B and C, post intubation at 2 minutes, mean OSND values were 4.8mm, 4.8mm, 4.9mm and at 5 minutes there were 4.94mm, 5.1mm, 5mm respectively. Therefore according to the criteria used in the present study, ICP values decreases approximately similar in group B and C, while it decreased at 2 min in group A and increased again to previous values after 5min.

Table 1: Demographic characteristics of the study population

Variables	Group A, (N=20)	Group B, (N=20)	Group C, (N=20)
Male, N (%)	11 (55)	12 (60)	11 (55)
Female, N (%)	9 (45)	8 (40)	9 (45)
Age (Mean ±SD)	43.2±7.19	41.3±6.79	44.68±8.12

Table 2: Mean arterial pressure (MAP), heart rate (HR), OSND before and after induction of anaesthesia and tracheal intubation

Baseline	Group A, (N=20)		Group B, (N=20)		Group C, (N=20)		p value
	Mean	SD	Mean	SD	Mean	SD	
MAP (mmHg)	92	4	93	4	93	4	0.81
HR (bpm)	86	6	86	7	85	6	0.92
OSND (mm)	5.4	1.67	5.4	1.56	5.3	1.76	0.81
Post 2 Min of Induction							
MAP (mmHg)	91	3	90	3	89	4	0.71
HR (bpm)	89	5	93	7	92	4	0.24
OSND (mm)	4.8	1.4	4.8	1.03	4.9	0.98	0.83
Post 5 Min of Induction							
MAP (mmHg)	93	4	91	3	94	6	0.58
HR (bpm)	89	5	93	7	92	4	0.24
OSND (mm)	4.94	1.1	5.1	0.82	5.0	0.93	0.42

Discussion

Ketamine is a short-acting, fast-onset dissociative drug that induces effective sedation, and analgesia with a high safety margin. In its effective therapeutic range, it does not depress spontaneous ventilation and does not lower blood pressure. As such, ketamine would be an optimal drug for short interventions in emergency situations and in unstable patients. In the present experimental study, we studies the effects of ketamine on ICP in patients with space occupying lesion of the brain, in light of the long-standing, deeply entrenched opinion that ketamine increases ICP [12, 13]. Based on preliminary observations, we hypothesized that ketamine will not only, not increase ICP but that it may effectively reduce it and prevent potentially detrimental ICP elevations during distressing interventions in susceptible patients. Our results clearly show that in well sedated, mechanically ventilated patients having space occupying lesion, our basic hypothesis is true, namely that ketamine decreases rather than increases the ICP. Similar results were reported by Gad Bar-Joseph *et al* in their study. They found that in well sedated pediatric patients with intracranial hypertension (mostly due to TBI), ketamine decreases, rather than increases the ICP [4].

The notion that ketamine increases ICP stems from several case reports [14, 15] and case series [16, 17] published mostly between 1970 and 1972, shortly after ketamine was introduced as an anesthetic agent in the mid-1960s. Increases in ICP were observed following administration of ≥ 2-mg/kg doses of ketamine for short diagnostic or surgical procedures in awake children and adults. Elevations in ICP were observed in patients who were breathing spontaneously, although most of the reports stress that the patients continued to breath effectively and that their arterial or end-tidal PCO2 did not increase. The ICP increased only in patients who had received ketamine as a sole anesthetic agent or who were only lightly anesthetized with nitrous oxide [18]. The ICP did not increase when thiopental was administered before ketamine, and when thiopental was administered following ketamine-induced ICP elevation, ICP decreased promptly [19].

In patients with severe TBI who were sedated with propofol, Albanèse *et al* found that ICP decreased following ketamine administration [7]. In adult patients with severe TBI, Bourgoin *et al* found no significant differences in the mean daily values of ICP and CPP or in the number of ICP elevations between patients in whom sedation was achieved with a continuous infusion of ketamine/midazolam or with sufentanil/midazolam [20]. Similarly, Kolenda *et al* compared ketamine/midazolam sedation with fentanyl/midazolam sedation in patients with moderate to severe TBI and found a lower requirement for catecholamines, higher CPP and only non-significant 2 mm Hg higher ICP values in the ketamine/midazolam group [21].

From the results of the present study, it can be said that although our findings were observed in sedated, mechanically ventilated patients, we believe that they may be applicable to other patient populations and clinical scenarios.

Conclusion

In patients with space occupying lesion undergoing mechanical ventilation, ketamine effectively decreased ICP and prevented untoward ICP elevations during potentially distressing interventions, without lowering blood pressure. These results refute the notion that ketamine increases ICP. Combined with a benzodiazepine and barbiturates ketamine may be the preferred sedative/anesthetic agent for patients with space occupying lesion, and it can probably be used safely in surgical situations.

References

1. Campbell WW. DeJong's the neurologic examination. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2005, 600.
2. Betmouni S, Love S. Pathology of space-occupying lesions of the CNS. Surgery (Oxford). 2004; 22(3):1-6.
3. Stullken Eli Jr, Milde JH, Michenfelder JD, Tinker JH. The nonlinear responses of cerebral metabolism to low concentrations of halothane, enflurane, isoflurane, and thiopental. Anesthesiology. 1977; 46:28-34.
4. Bar-Joseph G, Guilburd Y, Tamir A, Guilburd JN. Effectiveness of ketamine in decreasing intracranial pressure in children with intracranial hypertension. Journal of Neurosurgery: Pediatrics. 2009; 4(1):40-6.
5. Evers AS, Crowder CM, Balser JR. General anesthetics, in Brunton LL, Lazo JS, Parker KL (eds): Goodman and Gilman's The Pharmacological Basis of Therapeutics, ed 11. New York: McGraw-Hill, 2006, 341-368.
6. Sehdev RS, Symmons DA, Kindl K. Ketamine for rapid sequence induction in patients with head injury in the emergency department. Emerg Med Australas 2006; 18:37-44.
7. Albanese J, Arnaud S, Rey M, Thomachot L, Alliez B, Martin C *et al*. Ketamine decreases intracranial pressure and electroencephalographic activity in traumatic brain injury patients during propofol sedation. Anesthesiology: The Journal of the American Society of Anesthesiologists. 1997; 87(6):1328-34.
8. Kimberly HH, Shah S, Marill K, Noble V. Correlation

of optic nerve sheath diameter with direct measurement of intracranial pressure. Academic Emergency Medicine. 2008; 15(2):201-4.
9. Dubourg J, Javouhey E, Geeraerts T, Messerer M, Kassai B. Ultrasonography of optic nerve sheath diameter for detection of raised intracranial pressure: A systematic review and meta-analysis. Intensive Care Med. 2011; 37:1059-68.
10. Dubost C, Le Gouez A, Jouffroy V, Roger-Christoph S, Benhamou D, Mercier FJ *et al*. Optic nerve sheath diameter used as ultrasonographic assessment of the incidence of raised intracranial pressure in preeclampsia: A pilot study. Anesthesiology. 2012; 116:1066-71.
11. Rajajee V, Vanaman M, Fletcher JJ, Jacobs TL. Optic nerve ultrasound for the detection of raised intracranial pressure. Neurocrit Care. 2011; 15:506-15.
12. Ralston CS: Introduction to pediatric neurosurgery: physiologic and anesthetic considerations, in Choux M, Di Rocco C, Hockley AD, *et al* (eds): Pediatric Neurosurgery. London: Churchill Livingstone, 1999, 1-29.
13. Reves JG, Glass PSA, Lubarsky DA, McEvoy MD. Intravenous nonopioid anesthetics, in Miller RD (ed): Miller's Anesthesia, ed 6. Philadelphia: Elsevier Churchill Livingstone, 2005, 317-378.
14. Evans J, Rosen M, Weeks RD, Wise C. Ketamine in neurosurgical procedures. Lancet. 1971; 1:40-41.
15. Gardner AE, Dannemiller FJ, Dean D. Intracranial cerebrospinal fluid pressure in man during ketamine anesthesia. Anesth Analg. 1972; 51:741-745.
16. Schulte am Esch J, Pfeifer G, Thiemig I, Entzian W. The influence of intravenous anaesthetic agents on primarily increased intracranial pressure. Acta Neurochir (Wien). 1978; 45:15-25.
17. Sehdev RS, Symmons DA. Kindl K. Ketamine for rapid sequence induction in patients with head injury in the emergency department. Emerg Med Australas. 2006; 18:37-44.
18. Gibbs JM. The effect of intravenous ketamine on cerebrospinal fluid pressure. Br J Anaesth. 1972; 44:1298-1301.
19. Wyte SR, Shapiro HM, Turner P. Ketamine-induced intracranial hypertension. Anesthesiology. 1972; 36:174-176.
20. Bourgoin A, Albanèse J, Wereszczynski N, Charbit M, Vialet R, Martin C *et al*. Safety of sedation with ketamine in severe head injury patients: comparison with sufentanil. Crit Care Med. 2003; 31:711-717.
21. Kolenda H, Gremmelt A, Rading S, Braun U, Markakis E. Ketamine for analgosedative therapy in intensive care treatment of head-injured patients. Acta Neurochir (Wien). 1996; 138:1193-1199.