ORIGINAL ARTICLE

Incidence of consciousness in pediatric patients during Methotrexate injection with monitored anesthesia care

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ABSTRACT

Background: Procedural sedation and analgesia (PSAA) or monitoring anaesthesia care (MAC) must provide analgesia, amnesia and hypnosis with complete and rapid recovery that suits a particular operative procedure with minimum side effects. For a child undergoing a procedure, a major deciding factor is whether it is painful or not. Deep Sedation is required during the procedures to allay the anxiety, pain, and movement. The appropriate level of sedation depth will prevent consciousness, over-sedation, optimisation of dosage and prevents adverse complications. There are few studies about consciousness in pediatric patients during methotrexate injection with monitored anaesthesia care (MAC). The objective is to find out the incidence of consciousness of paediatric patients during methotrexate injection with Monitored Anaesthesia Care.

Methods: Observational study conducted on 68 patients (1-18 yrs.) with physical status of ASA II during methotrexate injection with MAC at the RSUP dr. Sardjito. The depth of anaesthesia was monitored with Observer's Alertness Assessment Sedation Scale (OAAS) every two minutes. Consciousness was defined as OAAS=5, or if there is volunteer movement of patients. The result was analysed and categorised according to age, sex, physical status, Body Mass Index (BMI) and anaesthesia's medication of patients.

Results: Positive consciousness in paediatric patients based on OASS score at 2-minute and 4-minutes was 26.5% and 3.2% respectively, and was rescued by additional propofol 2mg/kg body weight.

Conclusion: The incidence of paediatric consciousness in patients during methotrexate injection with Monitored Anaesthesia Care (MAC) in the Sardjito General Hospital is 26.5% (2-minute after induction) and 3.2% (4-minute after induction), and this is considerably high thus needing futher prevention.

KEY WORDS:
Consciousness, Methotrexate Injection, Monitored Anesthesia Care(MAC), Pediatrics

INTRODUCTION

Procedural sedation and analgesia (PSAA) or monitored anaesthesia care (MAC) is often performed in paediatric patients with oncologic problem like intrathecal injection of Methotrexate. PSAA is characterised by a suppressed level of consciousness that is adequate to allow painful or unpleasant stimuli in a way so as to minimises patient consciousness, discomfort, and memory, but spontaneous respiration and airway-protective reflexes still being preserved.[1] PSAA or MAC must provide analgesia, amnesia, and hypnosis with complete and rapid recovery that suits a particular operative procedure causing minimum side effects. For a child undergoing a painful procedure, deep sedation is required during the procedures to allay the anxiety, pain, and movement. Coaxing and physical restraint is not an alternative and this may make the procedure not only difficult but also unsafe for the child. Moreover, the psychological trauma may be severe enough to even lead to stress disorder.[2]

In the paediatric population, the incidence of consciousness during general anaesthesia tends to be higher than in adult patients. Blusse van Oud-Albas et al., reported consciousness incidence of 0.6% in children aged 5-18 years.[3] Malviya et al., reported consciousness incidence of 0.8% in children aged 5-15 years who underwent general anesthesia.[4] In PSAA or MAC, Mantadakis et al., found that 50% from 100 procedures in 16 patients showed movements during the procedure.[5] Chun et al., study on 55 paediatric patients showed that 24% patients with Dexmedetomidine and Ketamine still needed rescue analgetics and sedatives during procedural sedation to maintain modified Observer's Assessment of Alertness/Sedation (MOAA/S) score<5.[6]

In paediatric oncology case, lumbar punctures can cause considerable discomfort and anxiety in children with Acute Leukemic Leukaemia (ALL). Ideally, agents that have rapid onset and offset of action, thus, offering quick recovery, and that provide adequate amnesia should be used.7 The precise monitoring of sedation depth facilitates avoidance of under or over-sedation, optimisation of dosage and prevents adverse complications like desaturation, hypotension and bradycardia.[7] For this purpose, conventional subjective sedation scales, such as the Observer's Assessment of Alertness/Sedation (OAA/S) can be employed[8] since there is a limitation to using Bispectral index in paediatric sedation/anaesthesia, because the large inter-individual variability of BIS at different levels of aesthetic depth.[9]

The aims of this study were to find out about the incidence and some factors related to the consciousness of paediatric patients during methotrexate injection with MAC.

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Table I: Observer's Alertness Assessment sedation scale (OAAS)

Responsiveness	Speech	Expression	Eyes	Scale
Responds readily to name spoken in normal tone	Normal	Normal	Clear, No ptosis	5
Lethargic response to name spoken in normal tone	Mild slowing or thickening	Mild relaxation	Glazed or mild ptosis (less than half the eye)	4
Responds only after name called loudly and/or repeatedly	Slurring or prominent slowing	Marked relaxation (slack jaw)	Glazed and marked ptosis (half the eye or more)	3
Does not respond to mild prodding or shaking	Delirious	-		2
Does not respond to noxious stimuli	-	-		1

Table II: Demographic data

Variable	Categories	Mean	SD	N	%
Age		6.67	4.74		
Sex	Male			44	64.7%
	Female			24	35.3%
Weight		23.35	15.17		
Height		112.84	26.72		
BMI		16.71	2.82		
BMI by Category	Overweight (>24.9)			1	1.5%
	Non overweight (≤24.9)			67	98.5%
Procedure	Methotrexate Injection			68	100.0%
Physical Status	ASA I			0	0%
	ASAII			68	100.0%
Medication of Anesthesia	Fentanyl+Propofol			34	50.0%
	Midazolam+Ketamine			34	50.0%

Table III: Incidence of Consciousness

Categories		n	%
Consciousness 2-minute	Consciousness	18	26.5%
	No consciousness	50	73.5%
Consciousness 4minute	Consciousness	2	3.2%
	No consciousness	60	96.8%

Table IV: Incidence of consciousness based on some variables

Variable	Categories	Consciousness				P
		Consciousness		Non		
		N	%	n	%	
Age (±SD)		5.8±4.5	6,9±4.8	0.414*		
Medication of Anesthesia	Fentanyl+Propofol	12	35.3%	22	64.7%	0.099**
	Midazolam+Ketamin	6	17.6%	28	82.4%	
Sex	Male	16	36.4%	28	63.6%	0.02**
	Female	2	8.3%	22	91.7%	
BMI	Overweight (>24.9)	1	100.0%	0	0.0%	0.265***
	Non overweight (<24.9)	17	25.4%	50	74.6%	

*Independent t test, **Chi-Square, ***Fisher exact test

Table V: Hemodynamic parameter during MAC

Time (minutes)	Saturation 02 (SpO2) (%) (Mean±SD)		Heart Rate (HR) /minutes (Mean±SD)		Respiration Rate (RR) /minutes (Mean±SD)	
	With consciousness	No consciousness	With consciousness	No consciousness	With consciousness	No consciousness
0	100±1.3*	100±1.3*	103.7±14.5*	103.7±14.5*	22.3±1.9*	22.7±2.2*
2	98.9±1.2*	99±1.1*	112.0±18.2*	107.3±19*	23.7±2.3*	24.1±2.3*
4	98.9±1.1*	99±1.1*	107.5±15.9*	106.3±15.9*	23.7±2.4*	24.4±2.0*

*p>0.05 with independent t test

MATERIALS AND METHODS

The observational study conducted paediatric patients (1-18 yrs.), ASA physical status I and II for methotrexate injection with MAC at the RSUP, Dr. Sardjito. After approval from the Faculty and Hospital Ethical Committees, data collected during the MAC at the RSUP dr. Sardjito in October till December 2016. All patients with meningitis or encephalitis, kidney function disorders, liver function disorders, history of aesthetic drug allergies, developmental delay, acute respiration infection, cardiac abnormalities, Down Syndrome, and patients having contraindications to the drugs used in this study were excluded.

The consciousness was assessed using The Observer's Alertness Assessment Sedation Scale (OAAS) (Table I). The OAAS score consists of four categories: responsiveness, voice/speech, facial expressions, and eyes. OAAS scores are assessed in two ways: the composite score with a range of 1 (sleeping in) to 5 (conscious). The score is the lowest level score that is assessed based on four categories. The number of scores of four components is responsiveness having a possible score of 1, 2, 3, 4, or 5. The vote has a score of 2, 3, 4 or 5; and facial and eye expressions with a score of 3, 4 or 5.[9] The total OAAS score ≤2 indicates the occurrence of loss of consciousness (LOC), consciousness was defined as OASS=5 or if there is patient's volunteer movement.10

Before the study we trained observers to use OAAS, the kappa test then was performed to minimalise inter-observer bias, kappa test >0.6 considered acceptable. Depth of anaesthesia was monitored with OAAS every two minutes measured by two observers that previously have been trained. Rescue of Propofol 0.5mg/kg iv was given if the OAAS>4. The observations were ended when the child was awake and cooperative.

Adverse events like bradypnea (RR <10breaths/min), desaturation (SpO2<90%), bradycardia (Heart Rate<45 bpm), hypotension (drop in systolic blood pressure >20% of baseline or MAP <60mmHg sustained for >10min), hypertension (an increase in systolic blood pressure or MAP >20% of baseline), nausea, vomiting or any other event during the procedure were noted. Bradycardia was treated with IV atropine sulphate 0.01mg/kg, hypotension with fluid administration, if not resolved IV ephedrine sulphate 5mg in incremental doses was administered. In case of bradypnea, patient was woken up and was asked to take deep breaths. Desaturation was treated by increasing O_2 flow up to 5 litters and if needed, using bag mask ventilation with bag and mask.

Data was analysed with SPSS (version 23.0 SPSS inc., Chigago, II, USA). Continuous data are presented as mean ±Standard Deviation (SD) and categorical data as percentage. Independent t test was applied to compare mean between consciousness and non-consciousness group categorised by age. Chi square was applied to compare the percentages of patients with consciousness based on sex, physical status, Body Mass Index (BMI, overweight or non-overweight) and anaesthesia medication used for patients, p<0,05 were considered significant.

RESULTS

Observations were made on 68 patients males (64.7%) and females (35.3%), the mean age was 6.7 (SD4.7) yrs. All patients with ASA physical status II and the proportion of BMI were dominated by non-overweight patients. All patients received methotrexate injections. A total of 34 patients were given injection of fentanyl+propofol and the others 34 were given midazolam+ketamine (Table II).

All procedures were completed in four minutes

The highest incidence of consciousness (26.5%) was found at 2-minute after induction of MAC with a total of 18 patients (Table III). Based on the results of observations (Table IV) there was no significant difference in the mean ages between consciousness group and non-consciousness group. There was also no significant different in consciousness between anaesthesia medication group (fentanyl+propofol and midazolam+ketamine), and BMI (overweight and non-overweight) (p>0.05). The difference was found to be significant in the sex of the patient, where male patients had more consciousness (p<0.05).

During the procedures the hemodynamics of patients was stable, there were no marked desaturation, hypotension and bradycardia (Table V).

DISCUSSION

Procedural sedation or MAC must provide analgesia, amnesia, and hypnosis with complete and rapid recovery that suits a particular operative procedure with minimum side effects.[11] Painful procedures need deep sedation However, any of the agents used for sedation and/or analgesia may result in adverse effects. These most adverse effects occurred during deep PSAA are: obstruction of upper airway patency, ventilatory function or the cardiovascular system. Inadequate sedation on the other hand can also lead to consciousness, anxiety, pain, and movement. Moreover, the psychological trauma may be severe enough to even lead to stress disorder.[12]

In this study, the incidence of consciousness was 26.5% (2-minute after induction) and 3.2% (4-minute after induction), it is considerably high compared to intraoperative consciousness for paediatrics during general anaesthesia (0.6-0.8%)[3,4] but almost similar to other study in PSAA by Chun et al. (24%)[6] and MAC by Sen and Sen et al. (26%).[13] Chun et al., studied 56 patients who were divided to receive dexmedetomidine 1μg/kg in 10 minutes then 0.2-1μg/kg/hour, in the dexmedetomidine and ketamine (DK) group given additional ketamine 0.5mg/kg to maintain MOAAS score 3/4, dexmedetomidine, midazolam, and fentanyl (DMF) group was given midazolam 0.05μg/kg, fentanyl 0.5μg/kg. MOAAS 2 scores were 40% in the DK group and 77.8% in the DMF group.[14] Mantadakis et al., found that 50% from 100 procedures in 16 patients showed movements during the procedure. They received median doses of midazolam 0.19mg/kg (between 0.05-0.42mg/kg) and fentanyl 1μg/kg (between 0-2.75μg/kg) in paediatric invasive procedures.[5] In the study comparing sedation agent using combination of midazolam 0.2mg/kg) + ketamine (2mg/kg) and propofol (2mg/kg), and found that the need to

top up sedation occurred in 17% from midazolam+ketamine and 67% in propofol group.[15]

The difficulties in adjusting the dose of sedative base on the monitoring tool can also lead to inadequate sedation. In a study comparing the effectiveness and safety of ketamine-midazolam and ketamine-propofol combinations for procedural sedation in endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) it was shown that coughing was still present despite of the ramsay sedation score<3.[16] In paediatric patients, the endoscopic procedure have high incidence of consciousness.[4] Procedural sedation by non anaesthesiologist also had high incidence of inadequate sedation.[17]

The most important cause of consciousness during operation is inadequate doses, patient resistance to anaesthesia, younger age, tobacco use, obesity, chronic use of amphetamine, alcohol, and opioids (increase the dose of anaesthesia), engineering problems that result in inadequate delivery of anaesthesia: intravenous blocks, empty gas cylinders, or air trapped in a ventilator and patients with low physiological reserves and low anaesthesia needs.[18] Ghoenim et al., compared the data of 271 cases of consciousness in 19,504 patients who did not suffer it. Consciousness were more likely to occur in females, younger and to those undergoing cardiac and obstetrics operations, while recovery room consciousness episode occurred in 35% patients. They received fewer anaesthetic drugs, and were more likely to exhibit episodes of tachycardia and hypertension during surgery.[19]

From this study we found that being male is the only factor that corelate with the higher incidence of consciousness. Age, BMI, medication (fentanyl+propofol and midazolam+ketamine) were not determinant of consciousness in this study. Our result is different from previous studies that show risk factors for consciousness such as young age, females and total intravenous anaesthesia (TIVA).

CONCLUSION

The incidence of consciousness occurring in paediatric patients during methotrexate injection with Monitored Anaesthesia Care (MAC) was 26,5%. The factors that are associated with consciousness is being male. Following studies using more variable are needed to evaluate the risk factors, causes, and prevention of consciousness during MAC.

REFERENCES

1. Australian and New Zealand College of Anaesthetists. Guidelines on sedation and/or analgesia for diagnostic and interventional medical, dental or surgical procedures. [accessed on 2020 January 3]. Available from : http://www.anzca.edu.au/documents/ps09-2014-guidelines-on-sedation-and-or-analgesia.
2. Das S, Ghosh S. Monitored anesthesia care: An overview. J Anaesthesiol Clin Pharmacol 2015; 31(1): 27-9.
3. Blussé van Oud-Alblas HJ, van Dijk M, Liu C, Tibboel D, Klein J, Weber F. Intraoperative awareness during paediatric anaesthesia. Br J Anaesth 2009; 102(1): 104-10.
4. Malviya S, Galinkin JL, Bannister CF, Burke C, Zuk J, Popenhagen M, et al. The incidence of intraoperative awareness in children: childhood awareness and recall evaluation: Anesth Analg 2009; 109(5): 1421-7.
5. Mantadakis E, Katzilakis N, Foundoulaki E, Kalmanti M. Moderate Intravenous sedation with fentanyl and midazolam for invasive procedures in children with acute lymphoblastic leukemia. J Pediatr Oncol Nurs 2009; 26(4): 217-22.
6. Chun EH, Han MJ, Baik HJ, Park HS, Chung RK, Han JI, et al. Dexmedetomidine-ketamine versus Dexmedetomidine-midazolam-fentanyl for monitored anesthesia care during chemoport insertion: a Prospective Randomized Study. BMC Anesthesiol 2016; 16: 49.
7. Coté CJ, Notterman DA, Karl HW, Weinberg JA, McCloskey C. Adverse sedation events in pediatrics: a critical incident analysis of contributing factors. Pediatrics 2000; 105(4): 805-14.
8. Sheahan CG, Mathews DM. Monitoring and delivery of sedation. Br J Anaesth 2014;113 : ii37-47.
9. Ibrahim AE, Taraday JK, Kharasch ED,. Bispectral index monitoring during sedation with sevoflurane, midazolam, and propofol. Anesthesiology 2001; 95(5): 1151-9.
10. Bauerle K, Greim CA., Schroth M, Geisselbrecht M, Köbler A, Roewer N. Prediction of depth of sedation and anaesthesia by the Narcotrend TM EEG monitor. Br J Anaesth 2004; 92(6): 841-5.
11. Cote CJ, Wilson S, American Academy of Pediatrics, American Academy of Pediatric dentistry. Guidelines for Monitoring and Management of Pediatric Patients Before, During, and After Sedation for Diagnostic and Therapeutic Procedures: Update 2016. Pediatrics 2016; 138(1): e20161212.
12. Tobias JD, Leder M. Procedural sedation: A review of sedative agents, monitoring, and management of complications. Saudi J Anaesth 2011; 5(4): 395-410.
13. Sen J, Sen B. A comparative study on monitored anesthesia care. Anesth Essays Res 2014; 8: 313-8.
14. Chung HS. Awareness and recall during general anesthesia. Korean J Anesthesiol 2014; 66(5): 339-45.
15. Chayapathi V, Kalra M, Bakshi AS, Mahajan A. A comparison of ketamine + midazolam to propofol for procedural sedation for lumbar puncture in pediatric oncology by nonanesthesiologists-a randomized comparative trial. Pediatr Blood Cancer 2018; 65(8): e27108.
16. Dal T, Sazak H, Tunç M, Şahin Ş, Yılmaz A. A comparison of ketamine-midazolam and ketamine-propofol combinations used for sedation in the endobronchial ultrasound-guided transbronchial needle aspiration: a prospective, single-blind, randomized study. J Thorac Dis 2014; 6(6): 742-51.
17. Malviya S, Voepel-Lewis T, Tait AR. Adverse events and risk factors associated with the sedation of children by nonanesthesiologists. Anesth Analg 1997; 85(6): 1207-13.
18. Szostakiewicz KM, Tomaszewski D, Rybicki Z, Rychlik A. Intraoperative awareness during general anaesthesia: results of an observational study. Anaesthesiol Intensive Ther 2014: 46(1): 23-8.
19. Ghoneim MM, Block RI, Haffarnan M, Mathews MJ. . Awareness during anesthesia: risk factors, causes and sequelae: a review of reported cases in the literature. Anesth Analg 2009; 108(2): 527-35.