A comparison of the effect of two doses of oral melatonin with oral midazolam and placebo on pre-operative anxiety, cognition and psychomotor function in children: A randomised double-blind study

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ABSTRACT

Background and Aims: Melatonin (MT), a naturally occurring pituitary hormone has a sleep promoting effect. There are very few studies on pre-operative oral MT (0.2–0.5 mg/kg) in children. We planned a study to assess the efficacy of oral MT in two doses and compare it with oral midazolam and placebo for pre-operative anxiolysis, sedation, maintenance of cognition and psychomotor skills, parental separation behaviour and venepuncture compliance. Methods: This prospective double-blind randomised study was conducted after ethical committee approval on 100 children aged 5–15 years, American Society of Anaesthesiologists physical status I and II undergoing elective surgery at our hospital from January 1, 2014, to December 31, 2014. Mentally disordered children were excluded from the study. They were randomised into four groups of 25 each (A, B, C, D) to receive either oral MT 0.5 mg/kg or 0.75 mg/kg or oral midazolam 0.5 mg/kg or placebo 45–60 min, respectively, before induction. The child’s anxiety, cognition and psychomotor function before and after pre-medication, behaviour during the parental separation and venepuncture were appropriately scored. Kruskal–Wallis analysis of variance for intergroup and Wilcoxon matched pairs tests for intragroup comparisons of data were applied. Results: The four groups were comparable regarding mean age, weight and sex. The anxiety score reductions in the three groups when compared to placebo were statistically significant. Children receiving MT 0.75 mg/kg had maximum anxiolysis and venepuncture compliance (P < 0.05). Cognition was decreased with maximum sedation, successful parental separation and psychomotor impairment in the midazolam group (P < 0.05). Conclusion: Oral MT (0.5 mg/kg and 0.75 mg/kg) in children decreases pre-operative anxiety without impairing cognitive and psychomotor functions, the 0.75 mg/kg dose being most effective.

Key words: Child, cognition, melatonin, midazolam, pre-medication, psychomotor performance

INTRODUCTION

Pre-operative anxiety in children is associated with adverse post-operative outcomes, such as increased distress in the recovery phase, and post-operative regressive behavioural disturbances, such as nightmares, separation anxiety, eating disorders and bedwetting.[1] Allaying this anxiety is of utmost importance for providing a calm and pleasant anaesthetic experience and preventing an adverse impact on the psychological milieu of the child in the future.[2] Benzodiazepines, mainly midazolam are the most commonly used pre-medicants to decrease anxiety.[3]
They can cause delayed recovery from anaesthesia, cognitive and psychomotor impairment in addition to paradoxical reactions.\[4\]

Melatonin (MT), a ubiquitous molecule widely distributed in nature and a hormone produced by the pineal gland at night has clock-phase resetting and sleep-promoting functions in humans.\[5\] MT and its analogues differ from benzodiazepines by exerting a sleep promoting effect by amplifying day/night differences in alertness and sleep quality and by displaying a modest and quite mild sleep inducing effect.\[6,7\]

We planned a study to assess the efficacy of oral MT in two doses (0.5 mg/kg and 0.75 mg/kg) and compare it with oral midazolam (0.5 mg/kg) and placebo with pre-operative anxiolysis, sedation, maintenance of cognition and psychomotor skills as the primary outcome measures and behaviour of the child during separation from parents, child’s compliance during venepuncture and the occurrence of side effects of MT and midazolam as the secondary outcome measures.

**METHODS**

A prospective randomised double-blind placebo-controlled study was conducted in 100 patients of American Society of Anaesthesiologists (ASA) physical status I and II aged between 5 and 15 years and who underwent elective surgery. Children with a history of psychiatric disorders, on anti-psychotic drugs, language or communication difficulties, sleep disorders, renal or hepatic derangement, low intelligence quotient, colour blindness, abnormalities of the right and left hands which precluded them from performing the finger tapping test (FTT) were excluded from the study. Patients were randomly assigned to four Groups A, B, C and D (\(n = 25\) patients/group) according to a computer-generated list. The pharmacist posted in our department did the randomisation and decided the group the patient belonged to. He informed the group to the pre-induction room anaesthesiologist, who administered the drug orally, that is, either 0.5 mg/kg midazolam (Group A) or 0.5 mg/kg MT (Group B) or 0.75 mg/kg MT (Group C) or placebo (Group D) via similar looking measuring cups to the child. We used aqueous preparation of midazolam (preservative free) 1 ml of which was equivalent to 5 mg midazolam (‘Mezolam®’ from Neon Labs, Mumbai). It was mixed with freshly drawn raw liquid honey. Commerially available MT syrup (‘Fast acting liquid MT’ from Life extension pharmaceuticals, Lauderdale, obtained online) was used for the study. Each 1 ml had MT equivalent of 3 mg. A volume of 5 ml of multivitamin syrup (‘Kidicare®’ from Meyer Vitabiotics, Mumbai) was used as the placebo. Both the patient and the investigator were unaware of the identity of the administered drug. We ensured parental (preferably maternal) presence, a good social conversation, and reassurance with the children in all the groups in the pre-operative period.

The modified Yale Pre-operative Anxiety Scale (mYPAS), and objective tests for cognition like colour cancellation test (CCT), psychomotor performance tests such as FTT were explained to the patients on the pre-operative day during pre-anaesthesia assessment and they were asked to do it in a sample test.\[8,9\]

The mYPAS is an observational state anxiety measure for children comprising 27 items in 5 domains that contemplate the child’s relationship with its environment, namely, activity, state of arousal, vocalisation, expression of emotions and interaction with family members. It has demonstrated high reliability and validity for measuring children’s anxiety pre-operatively.\[8,9]\n
The mYPAS-m total score was calculated. Each domain received a partial score based on the punctuation observed divided by the number of categories of that domain. The score of each domain was added to the others and multiplied by 20. Higher scores indicated more anxiety.

Observer’s sedation score\[10\] was used to assess sedation. It is rated from 5 to 1 where 5 = ready responsiveness to name, 4 = lethargic response, 3 = response when name is called out loudly, 2 = response only with mild prodding, 1 = no response to prodding and 0 = no response to noxious stimuli indicating deep sedation.

Cognition was assessed by the CCT which consists of 150 circles in red, blue, yellow, black and grey. The participants were required to cancel only the red circles as fast as they could. Time taken in seconds to complete the test comprised the score.\[11\] CCT results are reported as the number of seconds required to complete the task; therefore, higher scores reveal greater impairment.

Psychomotor function was assessed using the FTT. Subjects were asked to tap the mounting key on a
finger-tapping instrument as rapidly as possible using the index finger of the preferred hand. A comparable set of measurements was then obtained with the non-preferred hand, each trial lasting for 10 s.\(^{11,12}\) The average number of taps counted manually for each hand comprised the score due to the non-availability of finger tapping boards.

The heart rate and oxygen saturation were recorded by attaching conventional monitors.

The patient was shifted to a quiet room near the operation theatre 2 h pre-operatively. The drug was given to the patient by the pre-induction room doctor, 60 min before induction time in similar looking measuring cups. No other pre-medication was given.

Before giving the drug, the patient’s anxiety, sedation, cognition and psychomotor levels were assessed using mYPAS, OSS, CCT and FTT scores, respectively, by the investigator. The child was asked to relax and sleep following the intake of syrup. After 30 and 60 min, the patient was assessed with the same parameters and the tests were repeated again. At the end of 60 min the behaviour of the child during separation from parents and during venepuncture was recorded. Occurrence of side-effects of MT such as headache, dizziness, nausea and drowsiness and side-effects of midazolam such as dizziness, vertigo, ataxia, disorientation, amnesia and prolongation of reaction time-impairment of psychomotor skills were also noted.

The sample size was determined based on previous studies.\(^{13}\) A sample of 25 was taken to provide a power of 90% with a confidence interval of 99% with respect to mYPAS based on the assumption that placebo could have an effect in producing anxiolysis in 20% of patients, whereas MT and midazolam in at least 50% of patients. The data were analysed using Statistical Package for the Social Sciences version 20.0 software (SPSS Inc., 233 South Wacker Drive, 11th Floor Chicago, IL, USA). Chi-square test was used for analysing categorical data such as age, gender and ASA grade. Nonparametric data were analysed using Kruskal–Wallis analysis of variance test, Mann–Whitney U-test and Wilcoxon matched pairs test. \(P < 0.05\) was considered statistically significant.

### RESULTS

The four groups were comparable regarding age, sex, gender, weight and ASA status [Table 1]. The majority of the surgeries were related to the ear, nose and throat, hypospadiasis and hernias. There were no dropouts in any of the groups since our study ended with intravenous cannulation irrespective of whether the surgery took place or not.

With respect to the changes in mYPAS scores before, 30 and 60 min after pre-medication, they were significant in all the four groups \((P < 0.05)\) [Table 2]. However, during the intergroup comparison, a statistically significant difference in mYPAS scores was seen when MT in 0.5 and 0.75 mg/kg doses and midazolam were compared with placebo \((P = 0.00001)\). When 0.5 and 0.75 mg/kg MT were compared with each other, there was no significant difference \((P = 0.17)\) in mYPAS anxiety scores after giving the pre-medication. However when MT 0.5 mg/kg and 0.75 mg/kg were compared with 0.5 mg/kg midazolam [Figure 1], the results were significant with MT 0.5 mg/kg \((P = 0.0407)\) and highly significant with MT 0.75 mg/kg \((P = 0.0001)\).

The sedation scores in all the groups after pre-medication were statistically significant \((P < 0.05)\), but the increase in sedation was greatest in midazolam group and the least in placebo [Table 1]. When midazolam was compared with MT 0.5 mg/kg and 0.75 mg/kg [Figure 2] sedation scores were highly significant \((P = 0.00001)\) for both, but there was no statistically significant difference when MT 0.5 and 0.75 mg/kg doses were compared with placebo \((P = 0.4669, P = 0.6276, \text{respectively})\). This shows that like placebo, both doses of MT did not produce sedation in children whereas the children were significantly sedated in the midazolam group.

The CCT scores were increased in the MT and placebo groups 60 min after premedication, whereas they were

| Table 1: Demographic and other basic data of the patients of the four groups |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| **Patient characteristics**     | **Group A**     | **Group B**     | **Group C**     | **Group D**     |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| **Number of cases**             | 25              | 25              | 25              | 25              |
| **Drop outs**                   | 0               | 0               | 0               | 0               |
| **Age (years)**                 | 11.04±2.92      | 10.72±2.41      | 11.04±2.70      | 9.16±2.62       |
| **Gender**                      | male: 12:13     | female: 12:13   | 16:9            | 11:14           |
| **Weight (kg)**                 | 32.28±8.34      | 30.28±5.78      | 30.32±7.64      | 23.36±7.34      |

\(\text{Group A – Patients receiving midazolam 0.5 mg/kg; Group B – Patients receiving melatonin 0.5 mg/kg; Group C – Patients receiving melatonin 0.75 mg/kg; Group D – Patients receiving placebo; SD – Standard deviation}\)
decreased in the midazolam group [Table 3]. Hence, the clinically important P value of statistical significance was seen only in the midazolam group (P = 0.00001).

The comparison of the mean difference between the midazolam and placebo and MT groups for CCT scores [Figure 3] was highly significant (P = 0.00001), but there was no significant difference when the MT 0.5 and 0.75 mg/kg groups were compared with placebo (P = 0.8159, P = 0.9923, respectively).

The FT scores in the dominant and non-dominant hands were decreased in midazolam group whereas they were increased in the MT and placebo groups 60 min after pre-medication [Table 3]. There was a highly significant difference when midazolam was compared to the other groups [Figure 4] for FT scores (P = 0.00001), but there was no statistically significant difference when MT 0.5 and 0.75 mg/kg doses were compared with placebo for FT scores (P = 0.1595, P = 0.2253). There was no statistically significant difference in the FT scores between MT 0.5 and 0.75 mg/kg groups (P = 0.5936).

A significant decrease in heart rate was observed in midazolam group compared to MT and placebo group 60 min after pre-medication (P < 0.05), whereas no statistically significant difference was noted in any of the four groups in the oxygen saturation values at any point of time.

During parental separation 88%, 72%, 80% and 0% of the children in Groups A, B, C and D, respectively, were free of anxiety. Although most effective anxiolysis was seen with midazolam, there was no statistically significant...
significant difference when the mean scores were compared with that of MT 0.5 mg/kg and 0.75 mg/kg groups ($P > 0.05$).

MT 0.75 mg/kg group had maximum number of patients with successful venepuncture compliance. When MT 0.75 mg/kg was compared with midazolam and MT 0.5 mg/kg, the results were not statistically significant ($P = 0.6371$, $P = 0.1238$, respectively).

DISCUSSION

Melatonin, a naturally occurring pituitary hormone, exerts natural hypnotic effects through activation of the MT1 and MT2 MT receptors.\cite{14} It has been reported to cause pre-operative anxiolysis and increase in levels of sedation without impairing orientation.\cite{3,15} There are a few studies on pre-operative oral MT (0.2–0.5 mg/kg) in children. One of these\cite{16} has shown oral MT (0.5 mg/kg) to be ineffective as a pre-medicant in children. The others have observed positive results with oral MT (0.25 mg/kg and 0.5 mg/kg).\cite{13,17}

We chose children from 5 to 15 years age group so that they were able to comprehend and perform the tests required for the study. In a related study, the researchers used oral MT in the dose range of 0.1, 0.25 or 0.5 mg/kg.\cite{13} In another study, 20 mg of oral MT was used in children undergoing brainstem audiometry and was found to be safe;\cite{18} even higher doses of MT (up to 80 mg) were found to be safe in children.\cite{19} Hence, we chose MT in doses of 0.5 mg/kg and 0.75 mg/kg.

The peak effect of exogenous MT ranges from 60 to 150 min. The peak action of oral midazolam ranges between 30 and 90 min.\cite{3} Hence, we gave both the drugs 60 min before induction. We did not include a rescue anxiolytic in our study since most related researchers\cite{13,16,18,20-22} have not done so.

The primary outcome measures in our study were the effects of oral MT in two doses (0.5 and 0.75 mg/kg), midazolam 0.5 mg/kg and placebo on pre-operative anxiety, sedation, cognitive and psychomotor function. Our results showed that oral midazolam 0.5 mg/kg and MT 0.5 mg/kg produced effective anxiolysis. This was comparable to the results of some previous researchers.\cite{13} However, this was in contrast to some studies\cite{21} wherein the researchers used oral MT (3 mg, 6 mg) and another study\cite{22} where a maximum oral MT dose of 0.4 mg/kg was used and no significant anxiolytic effect of oral MT was found when compared to either midazolam or placebo. This was probably because the dose of MT which they used was lesser compared to ours. In our study, midazolam produced the highest degree of sedation when compared to MT and placebo. MT, like placebo, did not produce any sedation in our study. This outcome was comparable to the results of studies by other researchers.\cite{16,21} Our study showed that MT in doses 0.5 and 0.75 mg/kg did not produce sedation compared to the midazolam group. Hence, we can say that patients pre-medicated with MT would require less pre-operative monitoring (no sedation) than patients pre-medicated with midazolam (moderate to deep sedation). Our study results showed a significant increase in the time in seconds taken for CCT after pre-medication in midazolam group compared to MT and placebo. These were in agreement with the results of a similar study done in children\cite{7} and a study done in adults using the Trieger dot test.\cite{13}

Our secondary outcome measures were the behaviour of the child during separation from parents, the child’s compliance during venepuncture and the occurrence of side effects of MT and midazolam. The parental separation score\cite{23} used in our study was different from the scores used in other studies\cite{13,22} where the mYPAS was used for evaluation of parental separation. In one of these studies,\cite{13} it was observed that children in the
MT 0.25 mg/kg and 0.5 mg/kg or midazolam 0.25 mg/kg and 0.5 mg/kg groups exhibited less anxiety compared to placebo and this was similar to our results. However in the other study,[22] wherein oral MT was compared in doses of 0.05 mg/kg, 0.2 mg/kg and 0.4 mg/kg with oral midazolam 0.5 mg/kg, it was reported that the groups did not differ significantly in their separation anxiety and this was similar to our study results; nevertheless the mean age of the children in these studies[13,22] was 3.5 ± 0.6 and 5.1 ± 2.35 years, respectively, whereas it was 10.49 ± 2.66 years in our study. No research has yet been carried out on the effect of age and emotionality on the effectiveness of MT administered, although the effects of midazolam have been shown to vary with the age and temperament of the child,[24] nevertheless, we suggest research on this topic.

Our study had several unique features. To date, ours is the only study among published literature, wherein MT has been used in a dose of 0.75 mg/kg in children for pre-medication. Most researchers on MT have not assessed cognition and psychomotor function using tests specific for them. The effects on these functions were simply noted down as observations in a few studies.[13] However, we used the CCT to assess the cognition of children. This test has been used in many psychiatric studies not related to MT.[12] Thus, since it was not possible to compare our study results regarding this aspect with other studies, we have compared our study results with those of studies done in adults.[25,26] Studies have shown that the heart rate decreases when the patient is calm or less anxious.[11] We monitored the heart rate and found that midazolam produced a maximum decrease in mean heart rate compared to the other groups; we also studied compliance to venepuncture after receiving oral MT. Our study findings support the use of MT in a dose of 0.75 mg/kg for effective pre-operative anxiolysis without sedation or cognitive and psychomotor dysfunction in children.

Most studies on pre-medication in children include assessment of parameters such as acceptance of face mask, post-operative analgesia, nausea, vomiting and agitation in addition to response to intravenous cannulation; our study ended at intravenous cannulation. Other parameters could not be assessed because variable anaesthetic techniques were used in our patients with intravenous cannulation as a common step to all.

Our study has some limitations. As the drugs were available in the syrup form, we experienced a difficulty in accurately measuring and administering the drug according to body weight. We used placebo as a pre-medication in one group. It may appear that there was a total lack of anxiolysis in children belonging to this group; however, children older than 4–6 years are easy to communicate with.[27] Research has shown that a lower level of parental anxiety and maternal presence helps in overcoming anxiety in a child.[20,29] We ensured parental (preferably maternal) presence but it was not possible for us to maintain uniformity in the level of parental anxiety. Furthermore, we manually counted the number of finger tappings as we did not have the finger tapping boards which are ideally used for automatically counting the number of finger taps.

CONCLUSION

Oral MT at 0.75 mg/kg appears to be the most effective drug for allaying pre-operative anxiety in children followed by MT 0.5 mg/kg and oral midazolam 0.5 mg/kg, in that order. Oral MT in the doses of 0.5 mg/kg and 0.75 mg/kg does not cause sedation or cognition and psychomotor dysfunction unlike oral midazolam at 0.5 mg/kg.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Perry JN, Hooper VD, Masiongale J. Reduction of preoperative anxiety in pediatric surgery patients using age-appropriate teaching interventions. J Perianesth Nurs 2012;27:69-81.
2. Kain ZN, Caldwell-Andrews AA, Mayes LC, Weinberg ME, Wang SM, MacLaren JE, et al. Family-centered preparation for surgery improves perioperative outcomes in children: A randomized controlled trial. Anesthesiology 2007;106:65-74.
3. Patel T, Kurdi MS. A comparative study between oral melatonin and oral midazolam on preoperative anxiety, cognitive, and psychomotor functions. J Anaesth Analg Clin Pharmacol 2015;31:37-43.
4. Liu DP, Lu WI. Practical oral sedation in dentistry. Part II – Clinical application of various oral sedatives and discussion. Compend Contin Educ Dent 2006;27:500-7.
5. Gorfine T, Zisapel N. Melatonin and the human hippocampus, a time dependent interplay. J Pineal Res 2007;43:80-6.
6. Yousaf F, Seet E, Venkatraghavan L, Abridhani A, Chung F. Efficacy and safety of melatonin as an anxiolytic and analgesic in the perioperative period: A qualitative systematic review of randomized trials. Anesthesiology 2010;113:968-76.
7. Ahmed RA, Samarkandi A, Al-Mansouri SM, Al Obeidan SA. Sedation characteristics of melatonin and midazolam for premedication of adult patients undergoing cataract surgery under local anaesthesia. Saudi J Anaesth 2007;1:6.
8. O’Sullivan M, Wong GK. Preinduction techniques to relieve anxiety in children undergoing general anaesthesia. Contin
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9. Guaratini AA, Marcolino JA, Teixeira AB, Bernardis RC, Passarelli ML, Mathias LA. A transversal study on preoperative anxiety in children: Use of the modified Yale scale. Rev Bras Anestesiol 2006;56:591-601.

10. Mason KP. Pediatric Sedation Outside of the Operating Room: A Multispecialty International Collaboration. 2nd ed. New York: Springer; 2012. Available from: http://www.springer.com/us/book/9781493913893. [Last accessed on 2015 Nov 05].

11. Oomen A. Assessment of attention and the profile of hyperkinetic children on psychological assessment. In: Hirisave U, Oomen A, Kapur K, editors. Psychological Assessment of Children in the Clinical Setting. 3rd ed. Bengaluru: NIMHANS; 2011. p. 47-60.

12. Kar BR, Rao SL, Chandramouli BA. Cognitive development in children with chronic protein energy malnutrition. Behav Brain Funct 2008;4:31.

13. Samarkandi A, Naguib M, Riad W, Thalaj A, Alotibi W, Aldammas F, et al. Melatonin vs. Midazolam premedication in children: A double-blind, placebo-controlled study. Eur J Anaesthesiol 2005;22:189-96.

14. Kurdi MS, Patel T. The role of melatonin in anaesthesia and critical care. Indian J Anaesth 2013;57:137-44.

15. Marseglia L, D’Angelo G, Manti S, Aversa S, Arrigo T, Reiter RJ, et al. Analgesic, anxiolytic and anaesthetic effects of melatonin: New potential uses in pediatrics. Int J Mol Sci 2015;16:1209-20.

16. Berrin I, Tozgul B, Haluk B. Premedication with melatonin vs midazolam in anxious children. Pediatric Anesth 2008;18:635-41.

17. Gitto E, Marseglia L, D’Angelo G, Manti S, Crisafi C, Montalto AS, et al. Melatonin versus midazolam premedication in children undergoing surgery: A pilot study. J Paediatr Child Health 2015. Doi: 10.1111/jpc.13007. [Epub ahead of print]

18. Schmidt CM, Knief A, Deuster D, Matulat P, Am Zehnhoff-Dinnesen AG. Melatonin is a useful alternative to sedation in children undergoing brainstem audiometry with an age dependent success rate – A field report of 250 investigations. Neuropediatrics 2007;38:2-4.

19. Zhidanova IV, Wurtman RJ, Morabito C, Piotrovksa VR, Lynch HJ. Effects of low oral doses of melatonin, given 2-4 hours before habitual bedtime, on sleep in normal young humans. Sleep 1996;19:423-31.

20. Johnson K, Page A, Williams H, Wassemer E, Whitehouse W. The use of melatonin as an alternative to sedation in uncooperative children undergoing an MRI examination. Clin Radiol 2002;57:502-6.

21. Sury MR, Fairweather K. The effect of melatonin on sedation of children undergoing magnetic resonance imaging. Br J Anaesth 2006;97:220-5.

22. Kain ZN, MacLaren JE, Herrmann L, Mayes L, Rosenbaum A, Hata J, et al. Preoperative melatonin and its effects on induction and emergence in children undergoing anesthesia and surgery. Anesthesiology 2009;111:44-9.

23. Funk W, Jakob W, Riedl T, Taeger K. Oral preanesthetic medication for children: Double-blind randomized study of a combination of midazolam and ketamine vs midazolam or ketamine alone. Br J Anaesth 2000;84:335-40.

24. Kain ZN, MacLaren J, McClain BC, Saadat H, Wang SM, Mayes LC, et al. Effects of age and emotionality on the effectiveness of midazolam administered preoperatively to children. Anesthesiology 2007;107:545-52.

25. Naguib M, Samarkandi AH. The comparative dose-response effects of melatonin and midazolam for premedication of adult patients: A double-blinded, placebo-controlled study. Anesth Analg 2000;91:473-9.

26. Naguib M, Samarkandi AH. Premedication with melatonin: A double-blind, placebo-controlled comparison with midazolam. Br J Anaesth 1999;82:875-80.

27. Lakshmi V. Preanaesthetic evaluation and premedication in paediatrics. Indian J Anaesth 2004;48:347-54.

28. Messeri A, Caprilli S, Busoni P. Anaesthesia induction in children: A psychological evaluation of the efficiency of parents’ presence. Paediatr Anaesth 2004;14:551-6.

29. Jennisin NK, editor. The Hundred Thousand Kingdoms. 1st ed. New York: Orbit Books; 2010. p. 36.

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