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Research Article

The Effect of Preanesthetic Administration of Melatonin, as a Premedication, on Anxiety of Children Undergoing Tonsillectomy

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ABSTRACT

Introduction: Undergoing surgical operations and entering into the operating room are common causes of anxiety and fear in everybody's life. This issue is especially important in children, when staff try to separate them from their parents; because they may not cooperate before the surgery and this may create adverse mental and psychological complications in the future. Sedatives can reduce children anxiety. Melatonin is an indoleamine hormone secreted naturally by the pineal body. It has some receptors in various parts of the body, including the central nervous system. The aim of this study was to investigate the effect of preanesthetic administration of melatonin, as a premedication, on anxiety of children undergoing Tonsillectomy.

Research method: This study was conducted on 80 children aged 2-8 years who were classified according to the American Society of Anesthesiologists, as ASA 1 and 2. Simple random sampling method was used on the basis of even and odd days, when surgeries were conducted. The study population included all children who were candidates for tonsillectomy in the Peymanieh Hospital, from September 2016 to May 2017. All children fasted for 6-8 hours before entering the operating room. Data were collected using demographic information form and the Anxiety Score Scale. Data were analyzed in SPSS 21, using Mann-Whitney and t-tests.

Results: The mean age of the patients in the melatonin and control groups were 5.23 ± 2.08 and 6.07 ± 2.52 years, respectively. The Mann-Whitney test results showed that there was a significant difference between the melatonin and control groups in terms of the anxiety scores of children when entering the operating room for tonsillectomy (p-value <0.001). In the melatonin group, 40% of the children suffered from grade 1 anxiety, 33.3% grade 2 and 26.7% suffered from grade 3 anxiety. In the control group, 50% of the children suffered from grade 4 anxiety, 20% grade 3 and 16.7% suffered from grade 5 anxiety and the rest of the participants suffered from various grades of anxiety.

Conclusion: Melatonin administration was effective in reducing children's anxiety levels when entering the operating room for tonsillectomy.

Keywords: melatonin, children, anxiety, tonsillectomy.

INTRODUCTION

Anxiety is a natural, adaptive response to the stress induced by surgery that may occur at any time during the preoperative period (1). Each surgery is always associated with an overt or covert, normalor abnormal emotional response. Patient may consider surgical experience as a threat to the normal course of life and even to life itself (2).Undergoing surgical operations and

entering into the operating room are common causes of anxiety and fear in everybody's life. This issue is especially important in children, when staff try to separate them from their parents; because they may not cooperate before the surgery and this may create adverse mental and psychological complications in the future (3).

Relaxation and feel of comfort before entering the operating room are two of the major objectives of anesthesia (4). Pediatric surgery, especially in those aged 1 to 7 years old, is one of the most frequent cases of elective surgery. Child's entry into the unfamiliar environment of operating room causes anxiety and severe restless. Certainly, such stress is not easy to tolerate by child and will cause numerous health problems in the future. On the other hand, the child's restlessness leads to parents' anxiety and leaves negative impact of surgery and anesthesia on their mind. Considering the importance of the issue, obviously, overcoming this problem and making the child calm are very important steps in starting and performing a successful anesthesia (5). Tonsillectomy is one of the most common surgical procedures among children which can be associated with many complications.Studies show that parents' anxiety makes it difficult to separate children from them.To reduce anxiety in children, in addition to meeting children and parents before the surgery, providing necessary explanations and answering to parents' questions and ensuring them on lack of pain during and after the surgery, various methods such as Teddy models and video tapes are also used (6).There are different views among experts on the effects of preoperative anxiety and the result during and after the surgery, especially on recovery after surgery. However, the majority of them believe that preoperative anxiety is usually characterized with personal feelings such as feeling of pressure, restlessness, anxiety and despair. In addition, preoperative anxiety at the lower to moderate levelsimproves behaviors in the postoperative period (7);however, high levels of anxiety before the surgery will create unpleasant psychological an physiological consequences (8-10). Regarding child anxiety and fear, Brown writes that the problems of anesthesia personnel, regarding the anesthesia of 2-6 years old children include fear, worry and lack of cooperation (11).Marlow, In this regard, suggests that surgery, especially for children, is a severe stressful experience and they may not understand the cause of surgery and may think that it is an unfair attack on their body (12). In the case of lack of control over anxiety, it will disrupt the process of anesthesia induction (13 and 14). It is also associated withsome physical and mental consequences that may later manifest in the mind and behavior of children. Some of these consequences include: undue fear of medical staff, insomnia, nightmares and even urinaryand fecal incontinence (15 and 16). Sedatives can reduce children anxiety. Melatonin is an indoleaminehormone secreted naturally by the pineal body. It has some receptors in various parts of the body, including the central nervous system. Melatonin is used to treat sleep disorders in healthy children and in those with neurological, mental and other medical conditions, to prevent idiopathic scoliosis in adolescents, to reduce oxidative stress in sepsis or respiratory distress in infants, as an anti-inflammatory, anti-anxiety, analgesic and also sedative drug before diagnostic procedures and finally, it is used in preoperative anesthesia. Youssef et al. and Gitto et al. reported no significant complication in children (17 and 18). No action is usually taken in the operating room to prevent child's anxiety before the surgery and in most cases the child is restless and anxious when entering the operating room. In the case of lack of control over anxiety, it will disrupt the process of anesthesia induction. It is also associated with some physical and mental consequences that may later manifest in the mind and behavior of children. Some of these consequences include: undue fear of medical staff, insomnia, nightmares and even urinary and fecal incontinence. Thus, appropriate medication should be used to calm the child before asurgery. Therefore, the aim of this study was to investigate the effect of preanesthetic administration of melatonin, as a premedication, on anxiety of children undergoing Tonsillectomy.

METHODOLOGY

This was a pretest-posttest clinical trial. The study population included all children who were candidates for tonsillectomy in the Peymanieh Hospital, Jahrom. Using simple random sampling 80 children aged 2-8 years admitted to the Peymanieh Hospital, Jahrom for tonsillectomy were selected. Simple random sampling method was used on the basis of even and odd days, when surgeries were conducted. Participants were then randomly divided into two groups of A and B (n1= n2= 40). After obtaining permission from the research deputy and the ethics committee of Jahrom University of Medical Sciences, the researcher outlined the research objectives for all the participants and their parents and participants signed informed written consent forms. The participants were also assured about the confidentiality of their information and using suitable drugs in the research.

Patients were divided into A (Melatonin) and B (control) groups. Drugs were given to both groups 30 minutes before the surgery. Patients in group A received 0.5 mg/kg of body weight, oral melatonin as anesthetic premedication and those in group B or the control group received the placebo. The inclusion criteria included: children aged 2-8 years old, ASA (American Society of Anesthesiologists) class 1 or 2 and tonsillectomy candidates and the exclusion criteria included: unwillingness to participate in the study, those with a history of taking central nervous system medications, those with a central nervous system disorder, those who need an emergency surgery and those under the age of two. An anesthetist administered the drug; however, he played no role in the process of interviewing and in data collection and analysis. After administering the drug, the Anxiety Score Questionnaire was used to measure the children's vital signs (including respiratory rate, heart rate per minute and blood pressure) and their anxiety levels. An experienced senior Anesthesia student, who had no information on the type of drug received by the patients, completed the questionnaire. The demographic questionnaire consisted of age, gender, the number of family members, parents' job and parents' education. The Anxiety Score Questionnaire was used to measure children's anxiety levels.

Score 1: agitated, sticking to parents or crying.

Score 2: awaken, not sticking to parents, may moan, but does not cry.

Score 3: calm and easy, sitting or lying down with open eyes.

Score 4: Sleepy and easy, sitting or lying down with closed eyes, yet responds to mild stimuli.

Score 5: asleep with closed eyes, can be wakened, but does not respond to mild stimuli.

Scores 4 and 5 indicated the effectiveness of the used drug in relaxing the patient and reducing the anxiety level and the time interval between taking the drug and reaching score 4 was recorded. Data were analyzed using descriptive statistics (mean, standard deviationand confidence interval), Chi-square, Fisher's exact and t-tests.

RESULTS

The mean age of patients in the melatonin group and the control group was 5.23 ± 2.08 and 2.57 ± 6.07 years, respectively. The two groups were similar in terms of age and gender. The Mann-Whitney test results, presented in Table 1,showed that there was a significant difference between the melatonin and control groups in terms of the anxiety scores of children when entering the operating room for tonsillectomy (p-value <0.001). The mean scores of anxiety were (m = 4) and (m = 2) for the melatonin and control groups, respectively. Higher anxiety scores indicated more effective intervention. This means that anxiety levels were lower in the melatonin group and melatonin administration was effective in reducing children's anxiety levels when entering the operating room for tonsillectomy. In the melatonin group, 40% of the children suffered from grade 1 anxiety, 33.3% grade 2 and 26.7% suffered from grade 3 anxiety. In the control group, 50% of the children suffered from grade 4 anxiety, 20% grade 3 and 16.7% suffered from grade 5 anxiety and the rest of the participants suffered from various grades of anxiety. Table 1 shows the frequency of various grades of anxiety

during tonsillectomy in the melatonin and control groups.

Table 1: The frequency of various grades of anxiety during tonsillectomy in the melatonin and control groups

Score	Group	
	Control	Melatonin
1	12(40)	1(3.3)
2	10(33.3)	3(10)
3	8(26.7)	6(20)
4	0(0)	15(50)
5	0(0)	5(16.7)

The t-test results, presented in Table 2, showed that there was no significant difference between the melatonin and control groups in terms of systolic blood pressure levels,in the pre-operative stage and at times 10 and 30 minutes after the surgery($p> 0.05$). The results of ANOVA test with repeated measures, presented in diagram 2, showed that in the melatonin group,the systolic blood pressure levels did notsignificantly changefrom the pre-operative stage up to 30 minutes after beginning the surgery($p> 0.05$).However, in the control group, the systolic blood pressure levels significantly changed from the pre-operative stage up to 30 minutes after beginning the surgery($p <0.05$). In this group, an increasing trend was observed in the systolic blood pressure levels from pre-operative stage up to 10 minutes after the surgery; however, a declining trend was observed afterwards. Table 2 compares the mean systolic blood pressure levels at different times for the melatonin and control groups.

Table 2: Comparison of systolic blood pressure levels in the two groups

	Group				p-value
	Melatonin		Control		
	Mean	SD	Mean	SD	
Bpsystol. Preoperative	95.90	8.84	95.03	10.71	0.734
Bpsystol. Start operation	95.77	6.70	97.73	11.34	0.417
Bp systole.10min	94.70	7.99	99.13	10.14	0.065
Bp systole.30min	92.97	6.93	94.43	7.65	0.472
Trend -p-value	0.259		0.049		

The t-test results showed that there was no significant difference between the melatonin and control groups in terms of diastolic blood pressure levels, in the pre-operative stage and 10 minutes after the surgery ($p> 0.05$). However, a significant difference was observed during the surgery and 30 minutes after the surgery ($p <0.05$). The diastolic blood pressure levels were higher in the melatonin group during the surgery and 30 minutes after the surgery. The results of ANOVA test with repeated measures showed that in the melatonin and control groups, the diastolic blood pressure levels did not significantly changefrom the pre-operative stage up to 30 minutes after beginning the surgery ($p> 0.05$). The t-test results showed that there was no significant difference between the two groups in terms of heart rate during the surgery and 10 and 30 minutes after the surgery ($p> 0.05$). The results of ANOVA test with repeated measures showed that in the melatonin group, the heart rate did not significantly change from the pre-operative stage up to 30 minutes after beginning the surgery ($p> 0.05$). In the control group, the heart rate significantly changed from the pre-operative stage up to 30 minutes after beginning the surgery ($p <0.05$). In this group, an increasing trend was observed in the mean heart rate from the pre-surgical stage to the surgery itself; however, a declining trend was observed afterwards. The t-test results showed that there was no significant difference between the melatonin and control groups in terms of respiratory rate, during the surgery and 10 and 30 minutes after the surgery ($p> 0.05$). However, a significant difference was observed in the pre-operative stage ($p <0.05$); where, the mean of respiratory rate in the melatonin group was higher than the control group. The results of ANOVA test with repeated measures showed that in the melatonin group, the respiratory rate significantly changed from the pre-operative stage up to 30 minutes after beginning the surgery ($p< 0.05$). In this group, a declining trend was observed in the mean respiratory rate from the pre-surgical stage to 30 minutes after the surgery. In the control group, the respiratory rate did not significantly change from the pre-operative stage up to 30 minutes after beginning the surgery ($p> 0.05$). The t-test results showed that there was a significant difference between the melatonin and control groups in terms of the arterial O2 saturation levels, in the pre-operative stage and during the surgery ($p< 0.05$). The

arterial O2 saturation levels were higher in the control group in the pre-operative stage. However, no significant difference was observed at times 10 and 30 minutes after the surgery (p> 0.05). The results of ANOVA test with repeated measures showed that in the melatonin group, the arterial O2 saturation levels significantly changed from the pre-operative stage up to 30 minutes after beginning the surgery (p< 0.05). In this group, a declining trend was observed in the arterial O2 saturation levels from the pre-surgical stage to 30 minutes after the surgery. In the control group, the arterial O2 saturation levels did not significantly change from the pre-operative stage up to 30 minutes after beginning the surgery (p> 0.05). The t-test results showed that there was a significant difference between the melatonin and control groups in terms of systolic blood pressure levels, at the beginning of the recovery process (p< 0.05). The systolic blood pressure levels were higher in the control group, at the beginning of the recovery process. However, at other times, no significant difference was observed between the two groups in terms of systolic blood pressure levels (p> 0.05). The results of ANOVA test with repeated measures showed that in the melatonin and control groups, the systolic blood pressure levels did not significantly change from the pre-operative stage up to 30 minutes after the recovery process (p> 0.05). The t-test results showed that there was a significant difference between the melatonin and control groups in terms of diastolic blood pressure levels, at the beginning of the recovery process (p< 0.05). The diastolic blood pressure levels were higher in the melatonin group, at the beginning of the recovery process. However, at other times, no significant difference was observed between the two groups in terms of diastolic blood pressure levels (p> 0.05). The results of ANOVA test with repeated measures showed that in the melatonin and control groups, the diastolic blood pressure levels did not significantly change from the pre-operative stage up to 30 minutes after the recovery process (p> 0.05). The t-test results showed that there was no significant difference between the two groups in terms of heart rate at the beginning of the recovery process and at times 5, 10, 15 and 30 minutes after the recovery process (p> 0.05). The Friedman test results showed that in the melatonin group, the heart rate significantly changed at the beginning of the recovery process up to 30 minutes after the recovery process (p <0.05).In this group, an increasing trend was observed in the heart rate at the beginning of the recovery process up to 5 minutes after the recovery; however, a declining trend was observed afterwards. In the control group, the heart rate significantly changed at the beginning of the recovery process up to 30 minutes after the recovery process (p <0.05). In this group, a declining trend was observed in the heart rate at the beginning of the recovery process up to 30 minutes after the recovery. The t-test results showed that there was no significant difference between the two groups in terms of respiratory rate at the beginning of the recovery process and at times 5, 10, 15 and 30 minutes after the recovery process (p> 0.05). The Friedman test results showed that in the melatonin and control groups, the respiratory rate did not significantly change at the beginning of the recovery process up to 30 minutes after the recovery process (p >0.05). The t-test results showed that there was no significant difference between the two groups in terms of the arterial O2 saturation levels, at times 5, 10, 15 and 30 minutes and after the recovery process (p> 0.05). However, a significant difference was observed at the beginning of the recovery process (p <0.05); where, the arterial O2 saturation levels in the control group were higher than the melatonin group. The Friedman test results showed that in the melatonin group, the arterial O2 saturation levels significantly changed at the beginning of the recovery process up to 30 minutes after the recovery process (p <0.05). In this group, an increasing trend was observed in the arterial O2 saturation levels at the beginning of the recovery process up to 5 minutes after the recovery. In the control group, the arterial O2 saturation did not significantly change at the beginning of the recovery process up to 30 minutes after the recovery process (p >0.05).

DISCUSSION

Performing any surgical operation requires proper precisionand follow-up, both before and after the surgery; because surgery can cause different states. On the other hand, many factors affect the quality of a surgical operation.Anxiety is among these factors. Both preoperative and postoperative anxieties can result intangiblecomplications.These complications include simple cases such dissatisfaction with the operation or fear of re-surgery in the future or serious complications such as surgery failure and disorders such as bleeding, worsening the condition of wounds, unsatisfactory vital signs etc. Therefore, by reducing anxiety levels, medical team can reduce problems and dissatisfactions before, during and after surgeries. This is because, regardless of its subsequent unpleasant mental states, anxiety can create different pathologies and can thus reduce the success rate of a good surgical procedure (19). The present study was conducted on this basis and investigated the anxiety-alleviating effects of melatonin in children undergoing tonsillectomy. The results of the study are interpreted as following:

Based on the results, melatonin was effective in relaxing and reducing children's anxiety when entering the operating room fortonsillectomy surgery.There was a significant difference between the melatonin and control groups in terms of children's anxiety scores when entering the operating room. Previous studies have also emphasized the need to reduce patients' anxiety levels in surgical operations.Lonescu et al. investigated administration of melatonin, as a premedication, before performing cholecystectomy surgery and measured anxiety levels and recovery times. In their study, the anxiety levels and recovery time were significantly reduced in the melatonin group. This is consistent with the results of the present study, in which a reduction in anxiety levels was observed in the melatonin group (20). In the present study, there was no significant difference in the mean heart rate of melatonin and control groups; however, the preoperative mean heart rate was higher in the melatonin group. It has been probably due to the short time interval between drug administration and beginning the surgery. The declining trend of heart rate, during and after the operation, further supports this idea. In the present study, there was no significant difference between the melatonin and control groups, in terms of the respiratory rate; however, the preoperative mean respiratory rate was higher in the melatonin group and a declining trend was observed during the surgery and the recovery process. This is consistent with the results of study of RaziehFallah who has investigated the effect of melatonin and gabapentin on reducing the anxiety of lumbar puncturesurgery.According to their study, respiratory rate and heart rate had declining trends during lumbar puncture surgery (21). In the present study, the mean arterial O2 saturation was higher in the control group before and at the beginning of surgery. An increasing trend was observed in arterial O2 saturation of the melatonin group; however, no significant difference was observed in this regard in the control group. Marzban investigated the anxiolytic effect of melatonin in cataract surgery, usingphacoemulsification procedure. According to hisstudy, in the melatonin group, heart rate and blood pressure rate had declining trends and the mean arterial O2 saturation had a more declining trend in the midazolam group. In the melatonin group, there was no declining trend in the mean arterial O2 and this is consistent with the results of the present study (22). In addition, in the present study, there was no significant difference between the mean systolic and diastolic blood pressure levels, in the two study groups. In the melatonin group, a declining trend in the systolic and diastolic blood pressure levels was observed during and after the surgery; however, an increasing trend was observed in the control group. In the present study, the diastolic blood pressure levels were higher in the melatonin group. This increase was not caused by melatonin; because, a declining trend was seen afterwards. Sanie et al. investigated the effect of melatonin and clonidine in reducing the anxiety of elective cesarean section surgery and the positive effects of melatonin in reducing anxiety and systolic and diastolic blood pressure levels was

observed. This is consistent with the results of the present study (23). In the present study, children in the melatonin group stayed for a shorter time in the recovery room.Accordingly, due to the reaction of their body to consciousness, their heart rate and respiratory rate had increasing trends initially and decreased after their full consciousness. In addition, samarkandi investigated the effects of melatonin and midazolam at a University in Riyadh. The lowest recovery time and the lowest anxiety levels were observed in the melatonin group which is consistent with the results of the present study (24).

CONCLUSION

All the above studies have proven the anxiolytic and sedative effects of melatonin before and after surgeries. In the present study, patients' heart rate, respiratory rate and blood pressure levels decreased, without lowering the arterial O2 saturation levels. It seems that melatonin can effectively reduce these vital signs and the anxiety levels in children, during and after the Tonsillectomy procedure. In addition, this drug has decreased the recovery time and vital signs show changes in this regard.

SUGGESTIONS

The review of the research literature indicated that very few studies have investigated the effect of melatonin on anxiety levels. Therefore, it is suggested to conduct further studies in this area.It is also suggested to give the drug to patients at earlier times. As noted above, before surgeries, heart rate levels were higher in the melatonin group and over time, a declining trend was observedin the beneficial effect of melatonin. Therefore, melatonin seems to be more effective, if it is given at earlier times, before the surgery. The systolic blood pressure levels were higher beforesurgeries in the melatonin group. This issueis likely to be resolved through enlarging the sample size and conducting further studies. In addition, the diastolic blood pressure levels were higher in the melatonin group that is likely to be resolved by extending the age group.

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