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Could the ratio of the second finger to the fourth finger (2D:4D) be a new morphological marker in predicting preoperative anxiety and postoperative agitation in pediatric patients?

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ABSTRACT

Studies have reported that the ratio of the second finger to the fourth finger (2D:4D) indicating the effects of intrauterine andogene exposure. It is stated that it can be used as a morphological marker in evaluating developmental/ psychopathological disorders. 90 children between the ages of 5-10, who were planned to undergo deciduous tooth extraction under deep sedation, were included in the study. Measurements were made on the second and fourth fingers of children's right and left hands. The behaviors of the patients during the preoperative period (m-Yale Preoperative Anxiety Scale), vascular access insertion and separation from the family were evaluated in determining the anxiety levels of the patients. During the recovery process, agitation status was evaluated using Watcha Scale. And there was no significant relationship found between 2D:4D and these parameters. In conclusion, 2D:4D did not succeed as a morphological marker in predicting preoperative anxiety and postoperative agitation in the preoperative period.

1. Introduction

Anxiety is one of the most important problems we encounter before medical procedures. In general, anxiety can occur in 10-30% of hospitalized patients. This rate increases in preoperative anxiety. It is reported that especially in pediatric patients, the anxiety rate exceeds 60% in the preoperative period, and this rate increases as the age decreases (West et al., 2020). General anesthesia / sedation applications are needed for many medical procedures of children. Many processes such as preparations procedures, preoperative waiting time and invasive procedures are increasing the anxiety level of the children. Apart from these, reasons such as not having full information about the procedure to be performed, anxiety of pain, fear of death are also effective (Meletti et al., 2019). Especially in children, the lack of cooperation and fear of leaving the family increase the level of anxiety. In dental practice, dental anxiety, a more specific and important condition, is encountered. Dental anxiety causes delayed dental treatments and impaired oral hygiene, negatively affecting the patient's oral health. Previous experiences and fear of losing an organ cause serious anxiety especially in children (Dixit and Jasani, 2020).

It has been associated with anxiety level and many complications such as postoperative pain, nausea, behavioral disorders, burnout, and sleep disturbance (Dwairej et al., 2020). This causes an increase in postoperative complications and difficulties for the hospital staff to continue their treatment. It also causes health personnel not to work efficiently and increases hospital costs.

Postoperative agitation, like preoperative anxiety, is a condition that negatively affects healthcare and can cause complications. Postoperative agitation appears as a picture that causes delirium, confusion, disorientation, uncontrolled crying, irritability, and elongation at recovery time (Hino et al., 2017; Ali et al., 2020). In this process, the patient may hurt himself. Additional medications applied to prevent excitation may delay the recovery process. In the preoperative period, some scales and determinant tests can be used to predict postoperative agitation risk and to take precautions against factors that trigger and cause postoperative agitation.

It is known that intrauterine testosterone is effective in determining gender and behavior patterns. Richard et al. investigated the effects of the ratio of the second finger [index finger] to the fourth finger [ring finger] (2D:4D) and have shown a relationship between prenatal sex hormone measurements (amniocentesis and perinatal cord blood) (Ventura et al., 2013; Richards, 2017). Many studies have reported that low 2D:4D ratio is an indicator of intrauterine androgen exposure and may be associated with many diseases (Ribeiro et al., 2016; Eichler et al., 2018; Myers et al., 2018). The relationship between physical, psychological, social and developmental disorders and 2D:4D have been investigated (O'Briain et al., 2017; Butovskaya et al., 2019; Togo et al., 2019).

In this study, the hypothesis is that 2D:4D ratio may be low in patients with high preoperative anxiety and postoperative agitation. If this relationship is determined, the 2D:4D ratio can be used as a morphological marker to predict preoperative anxiety and postoperative agitation. For such patients, regular application of behavioral management techniques, special time allocation, calling to operation when the ambient conditions are at the optimum level and pharmacological techniques can be recommended. It may also be recommended that the physician be cautious for the reasons that increase postoperative agitation.

In this study, it was aimed to investigate whether there is a significant relationship between 2D:4D ratio and preoperative anxiety and postoperative agitation in pediatric patients who are planned to deciduous tooth extraction under deep sedation.

2. Materials and methods

This is a double-blind, randomized study. The study started after the permission of the Ondokuz Mayis University Clinical Research Ethics Committee (B.30.2.ODM.0.20.08/537). This study was carried out in accordance with the Helsinki Declaration Principles. 90 children between the ages of 5-10, ASA I-II, male and female who were planned to deciduous tooth extraction under deep sedation, were included in the study. Patients with high anxiety and incompatibility were directed to tooth extraction under deep sedation. Deciduous teeth that should be removed due to caries or root resorption were included in the study. Patients with skeletal deformity, developmental retardation and mental disability were excluded from the study. First of all, relatives and patients were explained in the waiting room and informed volunteer consent form was approved. Relatives accompanied the patients until the anesthetic drug was given. Anxiety levels of all patients were evaluated using the m-Yale Preoperative Anxiety Scale (m-YPAS) in the preoperative waiting room. Afterwards, finger measurements of the children were made, and patients who did not allow measurement were excluded from the study. Measurements were made on the second and fourth fingers of children's right and left hands. The distance between the basal wrinkle and the fingertip was measured with the help of a ruler (vernier caliper). All measurements were made by the same assistant medical staff. Patients' behaviors were evaluated and recorded during intravenous vascular access and leaving the family and taken to the operating table. Minute heart rate, arterial oxygen saturation, and mean arterial pressure measurements were performed before surgery, after local anesthesia injection and every five minutes in all patients. Patients were administered intravenously (iv) with propofol 1 mg kg-1, midazolam 0.5 mg kg-1, fentanyl 1 μg kg-1. Propofol 0.5 mg kg-1 iv was administered to patients whose Ramsey Sedation Score was less than 5 (Table 1). Articain (40 mL mg-1) was administered to all patients as a local anesthetic. Demographic and intraoperative hemodynamic data were recorded. During the recovery process, agitation status was evaluated using Watcha

Table 1. Ramsey Sedation Score and Watcha Scale.

Ramsey Sedation Score	Response	Watcha Score	Response
1	Patient anxious oragigated or both	0	Asleep
2	Patient cooperative, oriented and tranquil	1	Calm
3	Patient responds to commands only	2	Crying, but can be consoled
4	A brisk response to a light glabellar tab	3	Crying, but cannot be consoled
5	Asluggish response to light glabellar tab	4	Agitated, and trashing around
6	No response		

Scale (WS). Complications, operation time and number of extracted teeth were recorded. No information was given to the patient about the finger measurements, the patient's relative and the physician who made the behavioral evaluations. All tooth extractions were done by the same dentist.

Statistical method

The data were analyzed with IBM SPSS V23. Comparisons by groups were compared with independent samples t-test and ANOVA. Categorical data were analyzed with chi-square test. The significance level was taken as $p<0.05$.

3. Results

Finger measurements were evaluated as mean ± standard deviation and multiple or small. When the average age, weight, procedure duration and number of extracted teeth were evaluated, there was no significant difference between 2D:4D ratios. The patient were aged a median of 7 (5-10) and 42 of these were female and 48 were male.

When the number of teeth extracted from the study was evaluated, it was found to be 5 ± 1 in patients with 2D:4D<1, and 6 ± 1 in patients with 2D:4D≥1 (p=0.664). When the processing times were evaluated, it was found to be 6 ± 1 minutes in patients with 2D:4D <1, and 7 ± 1 minutes in patients with 2D:4D≥1 (p=0.969).

When the preoperative anxiety level was evaluated, the the m-YPAS was found to be 29 (15-48) in patients with right hand 2D:4D ratio less than one, and 28 (16-48) in patients greater than one. (p=0.504). When the left hand was evaluated, 2D:4D ratio was determined as 29 (16-48) in patients with less than one, and 30 (18-46) in patients with greater than one (p=0.732) (Table 2).

When the behavior patterns shown by patients during vascular access insertion were evaluated, there was no significant relationship with right and left 2D:4D. Right hand 2D:4D ratio was determined as 0.96 ± 0.4 in shouting, impregnable patients, 0.98 ± 0.4 in patients with crying anxious, 1.00 ± 0.5 in patients withdrawing his hand, and 0.99 ± 0.5 in inactive calm patients (p=0.068). Left hand 2D:4D ratio was 0.97 ± 0.5 in shouting, impregnable patients, 0.97 ± 0.4 in patients with crying anxious, 0.97 ± 0.5 in patients withdrawing his hand, 0.98 ± 0.4 in inactive calm patients (p=0.863) (Table 3).

Table 2. M-Yale Preoperative Anxiety Scale according to finger ratios.

	Right 2D:4D		Left 2D:4D	
	<1	≥1	<1	≥1
M-Yale Preoperatif Anxiety Scale	29 (15-48)	**28 (16-48)**	29 (16-48)	30 (18-46)
p	0.504		0.732	

Data presented as median (min-max). 2D: 4D; ratio of second finger to fourth finger.

When the behavior patterns shown by the patients during family separation were evaluated, there was no significant relationship with right and left 2D:4D. The ratio of right 2D:4D was 0.98 ± 0.5 in calmly allowed families to leave, and 0.98 ± 0.4 in non-calm (p=0.463); the left 2D:4D ratio was 0.97 ± 0.5 in calmly allowed families to leave and 0.98 ± 0.4 in non-calm (p=0.885) (Table 3).

Table 3. 2D:4D ratios according to the Vascular Access İnsertion, Family Seperation, Watcha Scale.

Vasculer access insertion	**Shouting, impregnable patients (0)**	**Crying anxious (1)**	**Withd-rawing hand (2)**	**Inactive calm (3)**	**p**
Right 2D:4D	0.96±0.4	0.98±0.4	1.00±0.5	0.99±0.5	0.068
Left 2D:4D	0.97±0.5	0.97±0.4	0.97±0.5	0.98±0.4	0.863
Family separation	**Calm**	**Non-calm**			
Right 2D:4D	0.98±0.5	0.98±0.4	-	-	0.463
Left 2D:4D	0.97±0.5	0.98±0.4	-	-	0.885
Watcha scale	**Watcha 1**	**Watcha 2**	**Watcha 3**		
Right 2D:4D	0.98±0.5	0.98±0.4	0.98±0.2	-	0.997
Left 2D:4D	0.97±0.4	0.97±0.4	1±0.4	-	0.724

Data presented as mean ± standard deviation. 2D: 4D; ratio of second finger to fourth finger.

When hemodynamic data was evaluated, it was found that there was no significant difference with the right and left 2D:4D ratios in terms of heart rate, mean arterial pressure and arterial oxygen saturation (Table 4).

When the postoperative agitation status of the

Table 4. Hemodynamic data according to right and left 2D:4D ratios.

	Right 2D:4D<1	**Right 2D:4D≥1**	**p**	**Left 2D:4D<1**	**Left 2D:4D≥1**	**p**
Preoperative HR	**103±13**	100±20	0.213	101±15	101±20	0.724
HR after local anest-hesia	**123±10**	105±13	0.183	103±12	129±12	0.077
Minute 5 HR	**108±13**	**105±14**	**0.342**	**105±13**	**108±13**	**0.665**
Minute 10 HR	**112±11**	102±10	0.638	105±11	112±14	0.607
Preoperative MAP	**82±10**	81±11	0.400	81±10	81±12	0.053
MAP after local anesthesia	**84±12**	**80±11**	**0.392**	**82±11**	**81±13**	**0.106**
Minute 5 MAP	**78±11**	79±12	0.548	78±10	79±12	0.068
Minute 10 MAP	**77±9**	74±10	0.979	74±8	79±12	0.497
Preoperative SpO_2	**99(99-100)**	99(99-100)	0.107	99(99-100)	99(97-100)	0.233
SpO_2 after local anesthesia	**99(99-100)**	99(99-100)	0.638	99(99-100)	99(98-100)	0.454
Minute 5 SpO_2	**99(98-100)**	99(99-100)	0.586	99(99-100)	99(99-100)	0.783
Minute 10 SpO_2	**99(98-100)**	99(99-100)	0.230	98(98-100)	99(99-100)	0.774

Data presented as mean ± standard deviation and median (min-max). 2D:4D; ratio of second finger to fourth finger. HR; heart rate. MAP; mean arterial pressure. SpO2; arterial oxygen saturation.

patients was evaluated, the right hand 2D:4D ratio was 0.98 ± 0.5 in patients with Watcha 1, 0.98 ± 0.4 in patients with Watcha 2, and 0.98 ± 0.2 in patients with Watcha 3 (p=0.997). Left hand 2D:4D ratio, it was 0.97 ± 0.4 in patients with Watcha 1, 0.97 ± 0.4 in patients with Watcha 2, and 1 ± 0.4 in patients with Watcha 3 (p=0.724). There were no patients with Watcha score of 4 and 5 (Tables 1 and 3).

4. Discussion

High anxiety level can cause many problems during the operation and postoperative period. It has been stated that an anxiety-induced neurohormonal response may increase the need for anesthetics during operation and particularly cardiovascular complications. Increased catecholamine and cortisol levels can cause many systemic side effects (Moura et al., 2016; Malik et al., 2018). Similarly, postoperative agitation can cause many problems in children such as general anxiety, separation anxiety, sleep anxiety, eating disorders, disobedience to parents and environmental authority, and apathy in the postoperative period (Cho et al., 2020; Devroe et al., 2020). In addition, dental anxiety especially affects pediatric patients in the procedures applied in dentistry. Dental anxiety is more specific and important, and is a reaction to bad dental experience (Bux et al., 2019). In the preoperative period, it can be tried to be kept under control by keeping pediatric patients in appropriate environments, explaining the procedures to be applied and using behavior management techniques (Appukuttan, 2016). In cases where it is not sufficient, pharmacological methods are frequently used in dentistry applications (Wang et al., 2020). Determining the patients anxiety levels before and appropriately approaching them will have a positive impact on the patients treatment experience and therefore their dental health. The prevalence of preoperative anxiety and postoperative agitation and the frequency of its occurrence can be reduced by taking precautions (Hino et al., 2017; West et al., 2020). Many studies have shown that there is a negative relationship between many psychopathological conditions such as behavioral disorder, suicide, autism, and 2D:4D, and the 2D:4D ratio is less than one in such disorders (O'Briain et al., 2017; Butovskaya et al., 2019; Togo et al., 2019). In a study by Lenz et al. in cadavers, they reported that the rate of 2D:4D was lower in men who died by suicide than those who died normally. They stated that intrauterine androgen exposure may cause suicidal tendencies (Lenz et al., 2016). In another recent study, they did not find a significant relationship between 2D:4D ratio and the aggressive behaviors they display during the video game in college age teens (Hilgard et al., 2019). O'Brian et al. investigated the relationship between aggression-related injuries and 2D:4D ratio in patients who applied to the pediatric emergency department and reported that this rate was lower in girls (O'Briain et al., 2017). We investigated whether 2D:4D ratio can be a morphological marker in predicting preoperative anxiety and postoperative agitation. In this study, the behaviors of the patients during the preoperative period, vascular access insertion and separation from the family were evaluated in determining the anxiety levels of the patients However, no significant difference was determined in terms of these parameters and 2D:4D. This may be related to the average age group of patients included in this study. The anxiety to feel pain, inability to understand the events that develop around and fear of leaving the family were common results in this age group (West et al., 2020). In this study, the addition of dental anxiety to preoperative anxiety may have caused similar anxiety levels in all patients. Studies on the relationship between preoperative anxiety and 2D:4D are insufficient in the literature. Further studies are needed.

In order to predict postoperative agitation in the preoperative period, some scales are tried to be developed in addition to the clinical features of the patient and surgery (Berghmans et al., 2015; Hino et al., 2017; Lerman, 2018). Hino et al. investigated the validity of the scale they created using age, Pediatric Anesthesia Behavior Score, type of operation and duration of operation, and reported that it was effective in predicting postoperative agitation. They also stated that using this scale, preventive measures can be taken (Hino et al., 2017). In this study, it was hypothesized that the 2D:4D ratio may be a morphological marker in predicting postoperative agitation based on the studies we mentioned earlier. However, there was no significant relationship between postoperative agitation and 2D:4D ratio.

This study has some limitations. Some factors that increased the risk of postoperative agitation were not present in this study. Many factors such as long operation time, inhaler anesthetics and risk of postoperative pain were not included in the plan of this study. Deep sedation was provided to patients with intravenous anesthetics and the duration of anesthesia was very short. Local anesthesia was applied to all patients for postoperative analgesia. The relationship between postoperative agitation and 2D:4D ratio can be investigated after general anesthesia with inhaler anesthetics in further studies.

In conclusion, 2D:4D did not succeed as a morphological marker in predicting preoperative anxiety and postoperative agitation in the preoperative period. New studies can be planned considering the limitations of this study.

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