Moderate sedation helps improve future behavior in pediatric dental patients – a prospective study

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Abstract: There is little evidence on the long-term effects of pharmacological management in children undergoing dental treatment. This study aimed to assess children's behavior in consecutive dental sessions following oral rehabilitation using different pharmacological regimens for behavioral control. Participants were preschoolers who were previously treated for caries under one of the following: no sedative, oral sedation with midazolam, oral sedation with midazolam/ketamine, or general anesthesia. The children's behavior in the follow-up sessions was assessed using the Ohio State University Behavioral Rating Scale (OSUBRS); higher scores represented less cooperative behavior (range 5–20). Follow-up assessments were conducted on 50 children under four years old for up to 29 months. Data were analyzed by the Friedman/Wilcoxon tests and Cox regression model. OSUBRS mean (standard deviation) scores for the whole sample decreased from 11.9 (5.4) before treatment to 6.8 (3.2) at the final recall session (p < 0.001). Moderate sedation with midazolam (OR 2.9, 95%CI 1.2–6.9) or midazolam/ketamine (OR 4.3, 95%CI 1.6–11.4) improved children's future behavior. The general anesthesia group (n = 4) had a small sample size and the results should be considered with caution. Although invasive dental treatment negatively affected the child's behavior in the dental chair, they became more cooperative over time. Moderately sedated children showed better prospective behavior than those in the non-sedation group.

Keywords: Dental Caries; Restraint, Physical; Conscious Sedation; Anesthesia, General; Dental Care for Children.

Introduction

At present there is an extensive debate over the best method of behavioral management of preschool-aged children undergoing dental treatment[1,2,3,4,5]. Protective stabilization, moderate sedation, and general anesthesia are advanced behavioral control techniques indicated during the dental treatment of early childhood caries. These methods offer advantages and disadvantages during and immediately after the procedure[6]. However, retrospective studies have shown conflicting results with regard to the long-term behavior of children during dental treatment, with some studies reporting better long-term acceptance of dental treatment by children with the tell-show-do method compared with moderate sedation or

general anesthesia[7]. Others have reported equally improved behavior among children who underwent restraint or general anesthesia at short-term recall visits[8], as well as no differences between general anesthesia and sedation[9]. Moreover, no differences were observed between non-pharmacological control and sedation[10], and better results were obtained with general anesthesia compared with sedation[11].

Many children require invasive dental treatment due to early childhood caries. According to the final report of a large epidemiological survey on the oral condition of Brazilians[12], children aged 5 years had an average of 2.4 primary teeth with caries, and fewer than 20% of these had been treated in 2010. This disease continues to remain a major public health problem in many countries, with 9% (621 million people worldwide) of the global population[13] and 19.5% of American children[14] between ages 2 and 5 years affected by untreated caries in the primary teeth in 2010.

Dentists often wonder how to provide maximum benefit during pediatric dental treatment while simultaneously minimizing the risk of an unpleasant dental experience that may traumatize the child. Adults with dental phobia report suffering from dental treatment in their childhood[15,16,17], and data from different countries show that the prevalence of dental anxiety in adulthood varies between 13.5%[17] and 36.9%[18]. Likewise, approximately 20% of Brazilian patients exhibit moderate to severe anxiety associated with dental treatment[19].

Therefore, the aim of this prospective study was to compare the long-term behavior of children who underwent advanced behavioral techniques (non-pharmacological control, moderate sedation, or general anesthesia) while receiving treatment for dental caries. Our hypothesis was that pharmacological approaches would facilitate children's cooperation with the dentist in follow-up sessions by potentially diminishing their distress during dental treatment.

Methodology

Study design

This prospective study stems from a randomized clinical trial (NCT00902395) that compared patient behavior among four different groups during follow-up dental visits after completion of invasive dental procedures in children under four years of age. Children were treated for early childhood caries and were assigned to different treatment groups: no sedative, oral sedation with midazolam, oral sedation with midazolam/ketamine, or general anesthesia. This study was approved by the Institutional Review Board (IRB) of the Universidade Federal de Goiás (Protocol number: 219/09) and followed the ethical principles of the Declaration of Helsinki. Informed consent was obtained from parents after a thorough discussion about the objectives, procedures, risks, and benefits of the study.

Participants

Fifty-six children under four years old who completed the trial were recruited for the follow-up phase. They were initially included in the trial if they were cleared by pediatric professionals to receive moderate sedation or general anesthesia. That is, patients that were healthy (American Society of Anesthesiologists, Physical Status I), demonstrated negative behavior in previous dental appointments, and were in need of extensive dental treatment[6]. Children were also included if they had no physical or mental disabilities and had never had any dental treatment. They were excluded from the follow-up phase if their parents refused to attend the periodic examinations, but data from children who attended the dental sessions for at least one year were kept for analysis.

The sample size for this study was calculated based on a previous study[7] that reported that 78% of 146 children aged 3–13 years showed good cooperation five years after dental treatment, 18% required moderate sedation, and 4% underwent general anesthesia. A minimum sample size of 10 children per group was needed to obtain 5% and 80% power for a two-sided hypothesis test.

Proceedings of the randomized clinical trial phase

Six children participated in a pilot study to test the trial protocol; no changes were needed. Although the entire trial protocol has been described previously[1],

it is important to emphasize some aspects of the study to improve understanding.

During the recruitment stage, a pediatrician and an anesthesiologist assessed the children's general health and a pediatric dentistry assessed their oral health. Children were definitely included in the trial if the physicians and the dentist agreed upon the need for sedation.

Children were randomly assigned to the intervention groups by shuffling opaque sealed envelopes. One member of the research team shuffled the envelopes, pulled one out, and allocated the children to one of four study groups: no sedation (control group) (n = 17); moderate sedation with midazolam (Dormire®, Cristália, São Paulo, Brazil; dose 1 mg/kg, maximum 20 mg) administered orally (n = 16); moderate sedation with the association of midazolam (0.5 mg/kg, maximum 20 mg) and ketamine (S+ Ketamin®, Cristália, São Paulo, Brazil, 3 mg/kg dose, maximum 50 mg) administered orally (n = 13); and general anesthesia with sevoflurane, propofol, fentanyl, and premedication with midazolam (n = 4). All children, except the general anesthesia group, were treated under protective stabilization where the child was wrapped in a sheet fixed with tape.

After randomization, if a parent did not agree with the intervention, the child was excluded from the study. Also, parents were aware that they could forgo their children's participation in the study at any time. In Brazil, protective stabilization without sedation is more common than pharmacological techniques for behavior management in children undergoing dental treatment. Therefore, the IRB did not identify any ethical issues with the randomization process or the performance of extensive dental treatment under protective stabilization.

The children were aged under 4 years when participating in the trial study, and had a mean decayed, missing, and filled teeth index of 6.9 (standard deviation 'SD' 4.9) (Table 1). One of three certified pediatric dentists performed the surgical-restorative dental treatments for each child in as many sessions as were needed (6.2, SD 4.3), except in the case of general anesthesia, in which the whole treatment was completed in one extended session (Table 1). The sessions without medication and with sedation

were carried out at an outpatient level, and the children were accompanied by an adult throughout the session. The general anesthesia sessions were carried out in a day-hospital type surgical center. Children received comparable invasive dental procedures (Table 1). Local anesthetic (2% lidocaine + 1:100000 epinephrine, maximum 4.4 mg/kg) was administered to all groups in all sessions.

One of the two anesthesiologists were responsible for administering the sedatives and general anesthesia, as well as for monitoring the patients. During sedation, each child's oxygen saturation and heart rate were monitored by the 3800 pulse oximeter (Datex Ohmeda Inc., Madison, Wisconsin), and during general anesthesia the children received additional electrocardiography and capnography monitoring.

Follow-up procedures

The follow-up sessions (or recall appointments) commenced approximately 4 months after completion of the dental treatment and were performed at intervals of approximately 4 months, depending on the participant's attendance. The total follow-up was planned to be completed in 24 months. The mean age of the children at the beginning and end of follow-up were 34.0 (SD 6.5) and 52.1 (5.7) months old, respectively.

At each follow-up session, the children underwent a standardized dental check-up that was identical to the initial dental visit (trial phase) where the baseline behavior of the child was determined and a treatment plan established. One of four certified pediatric dentists examined the child without the use of protective stabilization and in the presence of an accompanying adult. All pediatric dentists were trained to use distraction and tell-show-do techniques during the dental examination. The dentist first performed a professional prophylaxis with a rubber cup, followed by a dental intraoral examination using a dental mirror and an exploratory probe under adequate lighting. The child was discharged after a topical application of fluoride varnish.

The child's behavior at baseline (before dental treatment) and follow-up sessions was recorded by the same dentist (observer), who was different from the pediatric dentists in charge of the dental exams. The

Table 1. Children's demographic information and dental sessions' characteristics by the experimental group.

Characteristics	Experimental group – n or mean (standard deviation)				Total sample
	No sedative	Midazolam sedation	Midazolam/ketamine sedation	General anesthesia	
Baseline session (before the dental treatment)					
n	17	16	13	4	
Child's age, months	28.1(6.0)	25.4(5.7)	28.9(6.1)	29.3(9.7)	27.5(6.2)
Male	10	11	7	1	29
Dental exam length, minutes	12.9(4.0)	10.6(1.7)	11.5(3.2)	11.3(2.5)	11.7(3.1)
dmft	5.8(3.6)	6.8(5.2)	5.6(3.5)	16.3(6.8)	6.9(4.9)
OSUBRS, sum*	12.5(5.3)	13.8(4.7)	11.3(5.2)	9.5(4.1)	12.4(5.0)
Dental treatment					
Appointments needed for completion of treatment	3.0(1.7)	3.0(1.5)	2.7(2.0)	1.0	3.2(1.7)
Procedures					
Restoration only	14	10	9	1	34
Pulp therapy and restoration	1	2	2		5
Exodontia and restoration	1	3	1	3	8
Exodontia, pulp therapy and restoration	1	1	1		3
Follow-up 1					
n	17	16	13	4	50
Time elapsed from baseline, months	5.8(1.8)	6.8(2.1)	6.4(2.3)	8.5(2.6)	6.5(2.2)
Child's age, months	33.8(5.6)	32.3(6.3)	35.2(6.4)	37.8(10.4)	34.0(6.5)
Dental exam length, minutes	10.2(2.2)	10.0(1.8)	11.9(2.5)	12.5(2.9)	10.8(2.4)
OSUBRS, sum*	10.8(4.0)	8.6(4.7)	8.4(4.7)	12.0(5.9)	9.6(4.6)
Follow-up 2					
n	17	16	13	4	50
Time elapsed from baseline, months	9.5(2.1)	10.3(2.1)	10.5(2.5)	12.8(7.7)	10.3(2.4)
Child's age, months	37.5(6.1)	35.6(6.2)	39.3(6.0)	42.0(10.7)	37.7(6.6)
Dental exam length, minutes	12.7(5.3)	11.9(4.0)	10.8(1.9)	12.5(8.3)	11.9(4.0)
OSUBRS, sum*	10.2(5.0)	8.1(4.4)	7.7(4.4)	6.8(2.2)	8.6(4.6)
Follow-up 3					
n	17	16	13	4	50
Time elapsed from baseline, months	12.1(2.4)	14.0(2.4)	14.4(2.9)	16.5(9.7)	14.1(2.7)
Child's age, months	41.4(5.9)	39.4(6.3)	43.2(5.9)	45.8(11.1)	41.6(6.6)
Dental exam length, minutes	10.6(1.7)	10.9(2.0)	10.8(2.8)	11.3(2.5)	10.8(2.1)
OSUBRS, sum*	9.7(4.4)	7.7(4.3)	5.9(2.5)	6.3(2.5)	7.8(4.1)
Follow-up 4					
n	13	13	4	0	30
Time elapsed from baseline, months	17.1(1.2)	18.3(2.1)	15.5(2.4)	-	17.4(2.0)
Child's age, months	44.1(5.7)	44.6(5.3)	45.0(2.4)	-	44.4(5.1)
Dental exam length, minutes	9.6(3.8)	9.6(3.2)	12.5(2.9)	-	10.0(3.5)
OSUBRS, sum*	8.1(2.9)	5.5(1.0)	5.0(0)	-	6.5(2.4)
Follow-up 5					
n	13	13	4	0	30
Time elapsed from baseline, months	21.2(2.0)	22.7(2.8)	19.0(2.4)	-	21.5(2.7)
Child's age, months	48.1(5.7)	49.0(5.7)	48.3(2.2)	-	48.5(5.3)
Dental exam length, minutes	11.2(2.2)	10.5(3.0)	11.3(2.5)	-	10.9(2.5)
OSUBRS, sum*	7.8(2.6)	5.2(0.4)	5.0(0)	-	6.3(2.2)
Follow-up 6					
n	12	12	4	-	28
Time elapsed from baseline, months	25.3(2.0)	26.3(1.7)	22.3(3.8)	-	25.3(2.5)
Child's age, months	52.7(5.8)	52.7(5.8)	48.8(5.3)	-	52.1(5.7)
Dental exam length, minutes	11.7(3.6)	12.5(3.4)	12.5(2.9)	-	12.1(3.2)
OSUBRS, sum*	8.3(4.0)	5.8(2.1)	5.0(0)	-	6.8(3.2)

dmft: decayed, missing, filled teeth; *Sum of the highest scores observed in five periods related to key procedures, using the Ohio State University Behavioral Rating Scale (OSUBRS). Sums ranged between 5 and 20; the higher the OSUBRS sum, the worse the child's behavior

observer was an experienced dentist trained in the proper use of the scale based on 15 minute-extracts of videos recorded during the children's dental treatments. Simultaneously, the observer also scored the children's behavior every minute according to the Ohio State University Behavioral Rating Scale (OSUBRS)[20] through observation of the movements of the head and extremities, crying, and physical resistance. The observer scored the same video files again one week later, and the intra-rater agreement was found to be satisfactory (weighted Kappa 0.8). The OSUBRS is comprised of four mutually exclusive scores: 1) behavior without crying and without movements (quiet behavior); 2) behavior with crying and no movements; 3) behavior with movements without crying; 4) behavior with crying and movements (resistance behavior).

For data collection, the OSUBRS method was adapted to facilitate in situ observation instead of recording a videotape. The observer was unmasked, took part in the entire dental consultation, and scored the child's behavior according to the highest OSUBRS score detected during the periods related to key procedures, including when the child entered the clinic, the professional prophylaxis, the intraoral examination, topical fluoride varnish application, and at the end of the dental procedure. The sum of the OSUBRS scores registered in each of the 5 periods in a session was calculated to determine a total score/session (minimum 5, maximum 20).

Statistical analyses

Data were tabulated using IBM SPSS version 19.0 software and quality-checked. Frequencies of OSUBRS scores and measures of dispersion were calculated. The Friedman's and Wilcoxon tests were used to compare the changes in the sum of OSUBRS scores observed in each follow-up session. Significance was set at $p < 0.05$.

Survival analysis was chosen to analyze the length of time required for children to show cooperative behavior in a routine recall appointment (follow-up session as described earlier) as a function of predictor variables. Survival analysis was chosen instead of regression or ANOVA because it allows censored values such as cases lost to follow-up. The event of

interest was the first time a child reached "quiet" behavior (OSUBRS score = 1) at 100% of the five evaluation points during follow-up sessions (sum of OSUBRS scores = 5). The response variable was the amount of time that elapsed between the baseline consultation and the end of follow-up sessions or the censorship of cases. The censored cases were those that had abandoned follow-up visits or exhibited resistance behaviors (crying and/or movement).

Cox's proportional hazard model evaluated explanatory variables for quiet behavior including gender, age, and type of behavioral intervention. This model is a multiple regression analysis applied to survival analysis. Using Cox's model an estimate of the role of independent variables that act multiplicatively on risk is obtained. The assumption was that different individuals have certain traits that are proportional to each other and that the ratio among these risk functions does not vary over time.
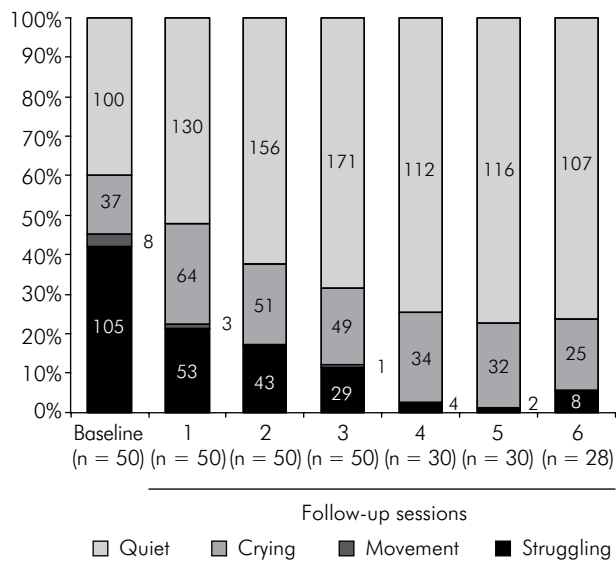
Results

The parents of 50 children provided consent, while the parents of 6 children refused to participate in the follow-up phase. Children were followed-up for up to 29 months, with a mean follow-up time of 25.3 months (SD 2.5). None of the children included in the study required additional operative care in the period between completion of treatment and the final follow-up session. Details of each consultation and the demographic characteristics are shown in Table 1. The Friedman test showed statistically significant differences between the sums of OSUBRS scores in different consultations ($p < 0.001$). Post-hoc comparisons (Wilcoxon) showed that children's behavior improved over time, with it being more negative at baseline than at the first follow-up ($p = 0.001$), exhibiting no significant changes from follow-up sessions 1–3 ($p > 0.05$), enhanced changes at follow-up 4 ($p = 0.019$), and no further changes of significance through the end of the study ($p > 0.05$).

The frequencies of the different OSUBRS scores are shown in Figure 1. The five time points for each session (entering the office, prophylaxis, examination, fluoride application, and the end of the consultation) were investigated separately. The percentage of "quiet" scores tended to increase over time, from 40.0% at

baseline to a peak of 77.3% in the fifth session. At the end of the follow-up period, 76.4% of children exhibited 'quiet' behavior at all five time points. Once a child reached a quiet behavior during the whole session, s/he kept this behavior in the on-going sessions.

Survival analysis of the 'gender', 'age at baseline', and 'intervention' variables showed that the children most likely to display totally quiet behavior during follow-up were those who received sedation with midazolam (2.9 times more likely) and those who received midazolam + ketamine (4.3 times as likely). Other variables showed no significant results (Table 2). The survival table (Figure 2) showed that 50% of children in the midazolam-ketamine group displayed 'quiet behavior' 10 months after the baseline consultation, and this percentage was lower for the other groups (approximately 37% for midazolam, 25% for general anesthesia, and 17% for the group that received no medication).

Discussion

Our results demonstrate that children who received moderate sedation during surgical-restorative dental treatment for early childhood caries behaved more positively during follow-up sessions than those patients who did not receive sedation. In general, child behavior in the dental office improves along with increasing psychomotor development[21,22]. This investigation provides scientific evidence that the use of sedatives can diminish the negative impact of invasive dental treatments compared with the exclusive use of protective stabilization (without sedative).
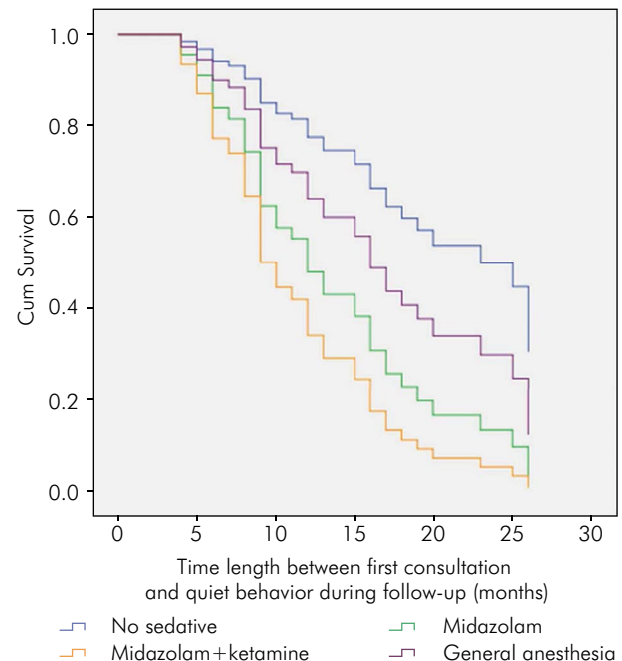

Figure 1. Relative and absolute frequencies of OSUBRS* scores obtained during the different follow-up sessions representing the highest behavioral score observed at 5 key intervals.

Table 2. Cox regression model for independent variables explaining quiet behavior (OSUBRS score = 1; scores assessed at 5 intervals during follow-up dental exams).

Independent variable	Odds Ratio (95% Confidence Interval)	p
Gender		
Female	1.0	0.705
Male	1.1 (0.6 – 2.3)	
Age at baseline (months)	1.0 (1.0 – 1.1)	0.221
Intervention		
No sedative	1.0	
Midazolam	2.9 (1.2 – 6.9)	0.017
Midazolam+ketamine	4.3 (1.6 – 11.4)	0.004
General anesthesia	1.8 (0.4 – 7.0)	0.427

Overall chi-square 11.469, p = 0.043; OSUBRS: Ohio State University Behavioral Rating Scale.

Figure 2. Life table for quiet behavior during the follow-up session after dental treatment rendered according to one of the intervention groups.

We anticipated the use of midazolam would lead to improved behavior during follow-up sessions due to the ability of this sedative to promote anterograde amnesia. Midazolam-induced amnesia could have led to better medium-term behavior in this study because the children likely did not remember the dental procedure. One study has shown that midazolam produces amnesia ten minutes after oral administration[23]. Another pediatric dentistry-based study showed that 80% of children under 72 months of age were unable to recall figures shown after administration of midazolam[24].

In this study, the group that received ketamine and midazolam exhibited better behaviors during follow-up sessions than the others. Like midazolam, ketamine has the ability to promote anterograde amnesia[25]. In addition to amnesia, ketamine is expected to reduce pain perception and improve a child's comfort level during invasive procedures[26,27].

The long-term results from the addition of ketamine as a sedative can be explained by the phenomenon of "implicit memory". Midazolam affects patient memory as far as perceptual recognition and facilitation are concerned[28]. That is, children sedated with a moderate level of midazolam remain responsive to verbal and physical stimuli but do not recognize images seen after administration of the sedative (explicit memory). Meanwhile, patients continue to store information on what is happening during sedation (implicit memory), which has a direct effect on subsequent behavior. Therefore, with the addition of ketamine, we hypothesize that the better behavior of the group receiving this both ketamine and midazolam can be explained by the reduced perception of pain. Thus, those children would have an implicit memory of greater comfort during dental treatment.

The group of children who received no sedative were less cooperative over time compared to the groups who received at least some sedation. Crying and movement in these children indicated the no-sedative group considered dental treatment to be unpleasant. However, another study[10] did not document any differences in the behavior of children 2 to 34 months following dental treatment where children were sedated; the study compared different sedation methods: midazolam and nitrous oxide, chloral hydrate and nitrous oxide, and no pharmacological agents. Their study[10], however, was retrospective and not controlled.

The results for the general anesthesia group should be viewed with caution due to the small sample size. One prospective 5-year follow-up study found that more than one-half of children between 0 and 13 years old that had received general anesthesia showed a total lack of cooperation and/or fear during subsequent dental visits.[29] Retrospective studies of children treated under general anesthesia and mild sedation, not including midazolam, found no differences in future behaviors 13 months and 18 months, respectively, after completion of dental treatment[11,30]. In our study, the results of the general anesthesia group did not differ from those of the non-medicated group. Additional studies to evaluate the future behavior of children who receive general anesthesia as compared to those sedated with midazolam are needed.

The sums of OSUBRS scores significantly decreased over time. Studies with different protocols indicate that child behavior during dental visits generally improves with psychomotor development[21,22]. This improvement is facilitated if children have not experienced painful or unpleasant procedures or by having recurring visits to the dentist.[22] Patient age at the onset of dental care also influences child behaviour[31]. Nonetheless, our results indicate age at baseline visit did not influence patient behavior. This is probably because sedatives exert a greater influence on behavior than age during treatment.

It should be emphasized that, regardless of the benefits demonstrated in this study, sedation should not be used indiscriminately. The dentist, i.e. certified pediatric dentist, should have specific knowledge and training to be responsible for sedation of children during dental treatment[32]. In Brazil, training in sedation is rarely addressed in undergraduate and graduate programs. Furthermore, some drugs cannot be used without the supervision of an anesthesiologist; ketamine, for example, is categorized as a general anesthetic[1].

Despite our efforts to control for variables in this study, there were some limitations with this study. The investigator, pediatric dentists, anesthesiologists, and the caretakers of patients were aware of the type of intervention each child received. Intervention

masking was not proposed because general anesthesia was initially included in the experimental study. In addition, while a follow-up rate of 100% within the first year, the final follow-up rate was 56.0%.

As the survival analysis showed a remarkable difference in child's behavior around the tenth month of follow-up, the results of the sedation groups compared to no sedation might be generalized to other patient groups. However, due to small sample size, the results of the general anesthesia group should not be generalized[33].

Conclusion

Overall, this study contributes to the field of child behavior management. The dental treatment of early childhood caries under moderate sedation was shown to significantly improve the future behavior of children during subsequent recall appointments 4 to 29 months after completion of treatment. Moderate sedation can be a valuable tool in reducing the suffering of toddlers and preschoolers during dental treatment. Nonetheless, pediatric dentists must receive special training to administer sedation.

Acknowledgements

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