Pediatric Sedation in Dutch Dental Clinics: The Influence of Guideline Modifications on Adverse Events

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Article

Pediatric Sedation in Dutch Dental Clinics: The Influence of Guideline Modifications on Adverse Events

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Abstract: *Background:* Dental fear and uncooperative behavior can hinder dental treatment quality. Pediatric Procedural Sedation and Analgesia (PPSA) is used to facilitate treatment when coping capacity is exceeded. Out-of-hospital PPSA has been associated with more adverse outcomes compared to hospital-based settings. Updated Dutch PPSA guidelines have increased costs and raised concerns about the accessibility to specialized high quality dental care for children in the Netherlands. This study aims to investigate the impact of the updated 2017 guideline on the occurrence rate of adverse events during PPSA of twelve Dutch dental clinics. *Methods:* Data of 25,872 children treated at twelve dental clinics between 1997 and 2019 were analyzed. A logistic two-level mixed-effects model is used to estimate the updated guideline's impact on adverse events. *Results:* The OR of the occurrence rate of an adverse event adjusted for age, weight, and duration of treatment was 0.75 (95% CI 0.64 – 0.89) after the implementation of the updated guidelin. This outcome was significant with a P=0.001, indicating a protective effect. *Conclusion:* Our findings demonstrate a significant reduction in adverse events after the implementation of the updated guideline and highlight the importance of adherence to evidence-based in out-of-hospital dental clinics.

Keywords: dental anesthesia**;** pediatric dentistry**;** evidence-based practice

Introduction

A quarter of the Dutch population is afraid of the dentist, the prevalence of an excessive fear of the dentist is 3,7% [1]. Dental fear and uncooperative behavior during dental treatment can make the treatment difficult and reduces the quality. When dental fear and uncooperative behavior make dental treatments impossible or when the treatment plan exceeds the coping capacity of children, Pediatric Procedural Sedation and Analgesia (PPSA) can be used to make this treatment possible [2,3]. PPSA has three main goals: prevention or relief of pain and anxiety, facilitating the procedure and patient safety [2,3]. Although rare, PPSA has not been without adverse events (AE) and mortality in the past [4–6].

The incidence of severe adverse events during in-hospital pediatric sedations is estimated in 1/10,000 [7]. This estimate differs greatly compared to out-of-hospital pediatric sedations. In 2000 Coté published his articles on 'adverse sedation events in pediatrics'. The conclusion Coté made was

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"adverse outcomes (permanent neurologic injury or death) occurred more frequently in a nonhospital-based facility, whereas successful outcomes (prolonged hospitalization or no harm) occurred more frequently in a hospital-based setting" [7,8].

In a 2006 review study, Cravero J. et al. described several adverse events during PPSA outside the operating room. Airway obstruction was reported in 93.2 of 10,000 sedations, allergic reaction was reported in 3.0 of 10,000 sedations and an oxygen saturation of less than 90% was reported in 154.4 of 10,000 sedations [6]. In the dissertation of Leroy P. entitled "Improving Procedural Sedation and/or Analgesia in Children," was a concerning issue highlited. Despite the presence of well-established safety guidelines, three severe incidents occurred during PPSA in children. Tragically, two of these incidents resulted in fatalities, while one child suffered permanent damage. Leroy P. also noted that these events were not isolated incidents but rather indicative of a more widespread problem involving non-compliance with established safety guidelines [9]. This underscores the critical need for the development of guidelines specifically tailored for PPSA in settings outside the traditional operating room.

Patient safety and the awareness of adverse events have steadily increased in Europe leading to a number of patient safety initiatives [10,11] like "the safety management system" that ran from 2008 to 2012 in the Netherlands [12]. Evidence-based best practice and patient safety initiatives led to improvements of PPSA guidelines and practices [7,13–15] and resulted in a decline of anesthesia related mortality [16]. The most recent PPSA guideline published in 2017, recommended two anesthesiologists and a ventilator to be present during out of hospital PPSA [7]. Pre-2017 guidelines recommended having one anesthesiologist and did not mention the necessity of a ventilator present. This modification subsequently led to higher costs of out of hospital PPSA and raised the concern that specialized and high-quality healthcare would become less accessible [18].

Until today we are not sure whether this costly change in procedure has any effect on adverse events. To address this uncertainty, this natural experiment study aims to estimate the influence of the updated guideline on the occurrence of adverse events during PPSA as recorded in the anesthesia complication database of twelve participating Dutch dental clinics. Data were from children between 2 and 18 years of age, adjusted for age, body weight and duration of treatment.

Methods

Setting and participants

The data used in this study were collected between 1997 and 2019 from 12 dental clinics performing PPSA outside the hospital and was retrospectively analyzed for this study. The total dataset contained 25,872 children. This study was approved by the pediatric dental group pedodontology and anesthesiology (Kindertand-groep pedodontologie en anesthesiologie), for the use of a randomized anesthesia complication database. This study was designed as a natural experiment study, because the circumstances surrounding the implementation of the 2017 guideline were beyond our control [19].

All children referred to these specialized dental clinics were screened in those dental clinics by an anesthesiologist and a dentist. The ASA classification system (American Society of Anesthesiologists) was used to assess the pre-anesthesia medical co-morbidities [20]. Children ranging from 2 to 18 years with the ASA classification I and II were eligible for PPSA. Children aged under two and over eighteen, or with ASA classification III and upwards, were referred to a general hospital for sedation and were not included in this study.

Procedure

Children were referred by their own dental practice, school dentist or pediatrician to one of the specialized dental clinics for Propofol sedation. Before the guideline was updated, the designated team for dental treatment and Propofol sedation consisted of a pediatric dentist, an anesthesiologist, a designated dental assistant, nurse anesthetist and a designated assistant in the recovery ward. After the guideline was updated a second anesthesiologist was added.

In all dental clinics, a uniform protocol was adhered to for administering Propofol sedation. This protocol remained consistent even following the update of clinical guidelines. According to this

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protocol, patients weighing less than 20 kg received a dosage of 5 mg/kg of Propofol, those in the weight range of 20-30 kg were administered 4 mg/kg of Propofol, individuals weighing 30-40 kg received 4 mg/kg of Propofol, and those exceeding 40 kg were given 3 mg/kg of Propofol. Subsequently, the maintenance dose was initiated at 20 mg/kg/h and was subsequently reduced to 10 mg/kg/h after the initial hour of administration.

The protocol used for the selection of the children did not change after the guideline was updated. All dental clinics within this study followed the guidelines set by the NVA and if needed included children on clinical insight of the anesthesiologist and dentist. After the dental treatment plan was completed, the children were referred back to their own dental clinic.

Ethical considerations

The database used for this retrospective study consists of data from 25,872 children collected between 1997 and 2019. Given the large number of children and the time in which the data were collected, it is "reasonably impossible to ask for permission" for the use of the data [21].

The children treated in the dental clinics in this study are considered vulnerable. Children may have been neglected by their parents or legal guardians leading to the necessity of extensive dental treatment. For this reason, “a selective response is expected to preclude reliable outcomes” [21]. Written permission was given by the pediatric dental group pedodontology and anesthesiology (Kindertand-groep pedodontologie en anesthesiologie) for the use of the database. Individual subjects could not withdraw from this study.

Data collection

In the practice of PPSA in the Netherlands, it is a legal requirement to record any adverse events [24]. In this study, adverse events were tracked using a specialized anesthesia complication database, which included specific predetermined variables such as the clinic code, treatment date, patient's age, treatment duration, the total amount of Propofol administered, the patient's weight, height, and Body Mass Index (BMI). These adverse events encompassed scenarios such as more than three failed intravenous attempts, issues with the laryngeal mask, oxygen desaturation below 90%, subcutaneous administration of Propofol, allergic reactions, and various other miscellaneous adverse events.

Data analysis

The data were analyzed with RStudio version 2022.12.0+353. Descriptive statistics were used to summarize the baseline characteristics of the study population. The following packages were used in R studio; ‘tableone’ for descriptive statistics, ‘lme4’ for constructing the model, ‘DHARMa’ for checking the model’s assumptions. Table 1 provides an overview of baseline variables per clinic. The data is expressed in mean (SD) for continuous variables with a normal distribution and median (IQR) for continuous variables with no normal distribution. Categorical variables are expressed in percentages.

Table 1. baseline variables of analyzed dental clinics before guideline 2017.

Clinic number	clinic 2	clinic 3	clinic 4	clinic 5	clinic 6	clinic 7	clinic8	clinic 9	clinic 11	Total
N children	7133	3256	1219	816	2272	498	384	1365	199	17142
Age (median, IQR)	4 (3 – 5)	4 (3 – 6)	4 (4 – 6)	4 (3 – 5)	5 (4 – 6)	5 (4 – 6)	5 (4 – 6)	5 (4 – 7)	4 (4 – 6)	4 (3 – 6)
Weight in Kg (median, IQR)	18 (16 – 21)	18 (16 - 23)	18 (16 – 23)	18 (16 – 21)	20 (17 – 24)	19 (16 – 23)	19 (17 – 23)	20 (17 – 26)	20 (17 – 24)	18 (16 – 22)

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Length in cm (median, IQR)	110 (103 – 120)	113 (105 – 124)	112 (104 – 126)	108 (102 – 116)	114 (106 – 124)	113 (105 – 122)	111 (104 – 122)	117 (107 – 129)	112 (105 – 120)	112 (104 – 123)
BMI (median, IQR)	15 (14 – 17)	15 (14 – 16)	15 (14 – 16)	16 (14 – 17)	15 (14 – 17)	16 (14 – 17)	16 (15 – 17)	15 (14 – 17)	16 (15 – 17)	15 (14 – 17)
Propofol in mg (median, IQR)*	490 (392 – 610)	485 (387 – 603)	529 (420 – 670)	510 (420 – 620)	550 (450 – 678)	481 (370 – 630)	492 (422 – 580)	504 (400 – 641)	570 (464 – 700)	500 (400 – 626)
Treatment time (median, IQR)**	60 (47 – 73)	55 (42 – 65)	67 (50 – 90)	75 (60 – 90)	60 (50 – 70)	70 (60 – 86)	50 (45 – 60)	60 (50 – 75)	65 (60 – 78)	60 (50 – 75)
Recorded Adverse Events (%)	496 (7.0)	172 (5.3)	92 (7.5)	29 (3.6)	108 (4.8)	31 (6.2)	25 (6.5)	51 (3.7)	9 (4.5)	1013 (5.9)

* Mean Propofol dosage per session in milligrams
** Mean duration of PPSA in minutes

Table 1. baseline variables of analyzed dental clinics after guideline 2017.

Clinic number	clinic 2	clinic 3	clinic 4	clinic 5	clinic 6	clinic 7	clinic8	clinic 9	clinic 11	Total
N children	935	471	330	163	877	156	185	833	723	4673
Age (median, IQR)	5 (4 – 6)	5 (4 – 7)	6 (4 – 9)	4 (3 – 6)	5 (4 – 6)	5 (4 – 6)	5 (4 – 6)	6 (4 – 7)	4 (4 – 6)	5 (4 – 7)
Weight in Kg (median, IQR)	20 (17 – 23)	20 (17 - 26)	21 (17 – 30)	19 (16 – 23)	20 (17 – 25)	21 (18 – 25)	21 (17 – 25)	21 (18 – 27)	20 (17 – 24)	20 (17 – 25)
Length in cm (median, IQR)	110 (104 – 120)	114 (105 – 128)	119 (106 – 137)	110 (102 – 122)	114 (106 – 125)	119 (110 – 128)	116 (106 – 124)	119 (109 – 130)	110 (103 – 120)	114 (105 – 125)
BMI (Median, IQR)	16 (15 – 17)	16 (15 – 17)	15 (14 – 17)	15 (14 – 17)	16 (15 – 17)	16 (14 – 17)	16 (15 – 17)	15 (14 – 16)	16 (15 – 18)	16 (15 – 17)
Propofol in mg (median, IQR)*	510 (424 – 630)	505 (419 – 626)	500 (400 – 658)	510 (434 – 600)	475 (386 – 580)	510 (420 – 617)	532 (456 – 644)	520 (420 – 660)	520 (421 – 630)	505 (411 – 625)
Treatment time	65 (55 – 75)	55 (45 – 65)	60 (45 – 75)	70 (60 – 85)	60 (50 – 65)	70 (55 – 80)	55 (50 – 65)	65 (55 – 80)	60 (45 – 70)	60 (50 – 75)

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(median, IQR)**										
Recorded Adverse Events (%)	49 (5.2)	23 (4.9)	19 (5.8)	4 (2.5)	15 (1.7)	2 (1.3)	10 (5.4)	37 (4.4)	31 (4.3)	190 (4.1)

* Mean Propofol dosage per session in milligrams
** Mean duration of PPSA in minutes

The model was pre-defined. The selection of variables in the study was determined by expert judgment, clinical experience, and existing literature, rather than through statistical methods. Not all clinics implemented the updated guideline in the same year. The implementation of updated guideline in each clinic was recorded and dichotomized. Since a cluster effect within the Dutch dental clinics was expected [22], it was decided to use a logistic two-level mixed effects model with a random intercept and fixed slope to estimate the influence of the updated pediatric sedation guideline on the occurrence of adverse events, using a binominal distribution for adverse events (dependent variable). An estimate of nine clinics is calculated as fixed effect and reported in OR with a 95% CI. The random effects were reported as variance and standard deviation of the odds and chance of an adverse event per clinic. For the regression coefficient b value, the Wald test indicates the significance of the association with the outcome. The P value for statistical significance is set at $P<0.05$. Log-link function was used to interpret the odds of adverse events and to define the odds ratio for effect of the guideline, adjusted for weight of the child and duration of treatment.

Missing data

Multiple imputation was applied if the variables were >5% missing. A correlation matrix and a correlation plot were made to assess whether patterns of missing data could be attributed to missing completely at random (MCAR) or missing at random (MAR). The correlation matrix was used to analyze whether there were pairs of variables with missing data. Additionally, a matrix plot was used to determine whether there were relations between the missing variables. The determination was made by assessing whether the missing data exists because of the variable itself, to rule out the data is not Missing Not at Random (MNAR). A complete case analyzation would be made with variables that are MNAR.

Results

The total anesthesia complication dataset contained 25,872 children, from 12 dental clinics collected between 1997 and 2019. Three clinics did not work with, or not exclusively with the updated guideline of 2017. A contrast is needed before and after the updated guideline to estimate the influence of the updated Pediatric sedation guideline on adverse events. As a result, these clinics were not included in the study. The total number of children analyzed in the remaining nine clinics was 21,759.

Of the 21,759 observations, information about treatment time was missing 39 times (0.18%), and about weight 18 times (0.08%), both less then 5 percent. Information about height and BMI were missing 9027 times (41.5%). Multiple imputations were considered for the variables, but as expected, we found a relationship in the matrix plot between the missing variables length and BMI in a number of dental clinics. These were not randomly distributed among the dental clinics. As result no multiple imputations were applied for these variables. A complete case analyzation was made with the variables treatment time, weight and age.

In the logistic two-level mixed effects model, when adjusting for age, weight, and treatment duration, the odds ratio (OR) for the occurrence of adverse events was 0.75 (95% CI 0.64 - 0.89) following the implementation of the updated guideline, as compared to the period before its implementation (as shown in Table 2). This result was statistically significant with a p-value of 0.001. Furthermore, among the nine dental clinics under consideration, a variance of 0.05 and a standard

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deviation of 0.23 were observed in the occurrence of adverse events. On average, the odds of experiencing an adverse event per clinic were 0.04, corresponding to a 3.81% probability (as indicated in Table 3).

Table 2. The ratio of odds of an adverse event before and after the updated guideline.

	OR	95% CI	Z value	P value
OR of an adverse event *	0.75	0.64 - 0.89	-3.24	0.001

Reference categories:
- odds of adverse events after updated guideline
- odds of adverse events before updated guideline

* Adjusted for treatment time, age, and weight.

Table 3. Odds of an adverse event, before and after the updated guideline. Chances of an adverse event, before and after the updated guideline.

Adverse events per clinic *	odds	Percentage
Clinic no. 2	0.05	4.90%
Clinic no. 3	0.04	3.84%
Clinic no. 4	0.05	4.79%
Clinic no. 5	0.03	2.61%
Clinic no. 6	0.03	3.18%
Clinic no. 7	0.04	3.71%
Clinic no. 8	0.05	4.60%
Clinic no. 9	0.04	3.39%
Clinic no. 11	0.04	3.96%
Overall adverse events in all clinics *	0.04	3.81%

* Adverse events, before and after the updated guideline together, adjusted for treatment time, age, and weight.

Discussion

This natural experiment aimed to assess the impact of an updated guideline on the incidence of adverse events during the administration PPSA within the context of twelve participating Dutch dental clinics, using data from an anesthesia complication database. The findings revealed a significant protective effect associated with the implementation of the updated guideline, resulting in a statistically significant reduction in the occurrence of adverse events. Specifically, the odds of experiencing adverse events decreased by 25% (OR 0.75) following the guideline update, in comparison to the period preceding the update (Table 2). This demonstrated a significant decline in the occurrence of adverse events following the guideline's implementation. Furthermore, it is worth noting that substantial variability in the occurrence of adverse events was observed among the nine clinics, indicating the potential presence of a cluster effect within these clinical settings (Table 3). This underscores the importance of considering clinic-specific factors when evaluating the impact of clinical guidelines.

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Bainbridge et al. described in their systematic review that anesthetic-related mortality has steadily declined over 50 years in developed countries, with a higher rate of improvement found in these regions. They emphasized the importance of evidence-based best practice in reducing anesthetic-related mortality in developing countries [16]. In this study, we found a steady accumulation of evidence-based guidelines in developed countries, as we could observe in the implementation of the updated PPSA guideline of 2017 in Dutch dental clinics. The protective influence of the updated guideline may be part of the proliferation of evidence-based guidelines and safety initiatives [16].

A strength of this study is that we were able to use a natural experiment study design. A natural experiment can be seen as a robust alternative to an RCT [19]. Natural experiments use real-life systems rather than creating a system designed or modified for the purpose of research such as in an RCT [23], creating a greater external validity. A natural experiment study design has a greater generalizability, which contributes to our insight in the 'real world' occurrence of out of hospital PPSA related adverse events in Dutch dental clinics. The use of a large dataset also allows for adequate statistical power. In the final model we analyzed nine of the twelve clinics, with a total of 21,815 children and 1203 adverse events, allowing adequate statistical power.

When evaluating the findings of this study, the presence of a potential learning effect needs to be acknowledged. Dental clinics that joined the study at a later stage had the advantage of tapping into the collective experience, enhanced clinical expertise, and assimilated knowledge and best practices gained from previously participating clinics in pediatric sedation. This accrued knowledge might have played a role in reducing adverse events independently of the impact of the updated guidelines. Consequently, this factor has the potential to introduce a confounding element into the established association between the implementation of the guidelines and the observed reduction in adverse events. Despite this potential confounder, it is important to underscore the robustness of this study. It provides valuable insights into the impact of the updated guidelines on adverse event rates in dental clinics, serving as a significant contribution to the field. The consideration of the learning effect enhances the study's credibility, as it demonstrates a comprehensive approach to accounting for potential sources of influence on the observed outcomes.

From the anesthesia complication dataset, which predominantly encompasses adverse events defined in less precise terms, this can be considered as a limitation. In contrast, the Pediatric Sedation Research Consortium [6,25,26] employs meticulously defined criteria for adverse events. Notably, the only adverse event sharing an identical definition with the consortium's criteria is desaturation below 90%. Conversely, adverse events such as those involving more than three intravenous attempts, complications with the laryngeal mask, subcutaneous Propofol administration, allergic reactions, and miscellaneous adverse events are less congruent with the definitions employed by the consortium [26]. This divergence in adverse event definitions poses a challenge when attempting to draw direct comparisons with outcomes reported by the consortium. To enhance the quality of future research, a potential solution lies in standardizing the definitions of adverse events within a forthcoming complication database. Such standardization would facilitate more robust and meaningful comparisons in future studies, solidifying the study's contribution to the field.

Conclusion

Commencing this study, we harbored uncertainties regarding the potential impact of the costly procedural change on adverse events. Our study outcomes, however, unequivocally reveal a significant reduction in adverse events after the implementation of the updated guideline and highlight the importance of adherence to evidence-based guidelines in improving patient safety and the quality of care provided during pediatric procedural sedation and analgesia in out-of-hospital dental clinics. Our study underlines the necessity of considering the complex underlying mechanisms that play a role in the development and implementation of evidence-based practice and safety initiatives on the occurrence of adverse events. This insight emphasizes the far-reaching implications for the broader healthcare landscape, solidifying the study's significance and highlighting its

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contribution to advancing the field and ultimately reinforcing the imperative of evidence-based practices in healthcare.

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Informed Consent Statement: The use of patient data is subject to conditions and privacy legislation, such as the European General Data Protection Regulation (Europese Algemene Verordening Gegevensbescherming (AVG). The starting point for the use of personal data for scientific research is that patients must, in principle, give permission. The data can only be regarded as anonymous if the conversion of the data in the used dataset to a person requires an unreasonable use of time and resources (1). The use of personal data in the dataset of 'kindertand' is anonymized, the data is not directly traceable to a person. Nevertheless, the data is subjected to privacy legislation. In retrospective research, the Medical Treatment Agreement Act (Wet op de geneeskundige behandelovereenkomst, WGBO) contains two exceptions. If it is "reasonably impossible to ask for permission" or "when asking permission from involved patients "cannot reasonably be required", then the data of that person may still be used for research (1). The exceptions to the consent requirement when using data apply when the patient has died or is untraceable due to relocation or other reasons and apply to research involving very large groups of patients (2) or when such a selective response is expected to preclude reliable outcomes (3). The database used for this retrospective study contained data of 25,872 patients collected between 1997 and 2019. Given the large number of patients and the time in which the data was collected, it is "reasonably impossible to ask for permission" for the use of the data (2). The children treated in children's dental practices are vulnerable. In the dental practices in this study, a proportionate part of the children has been neglected by their parents or legal guardians. For this reason, "a selective response is expected to preclude reliable outcomes" (3). Written permission is given by Kindertand-Anesthesie for the use of the database for this study. Individual subject cannot withdraw from this study.

(1) European General Data Protection Regulations (Europese Algemene Verordening Gegevensbescherming, AVG), preambule, paragraaf 26

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Data Availability Statement: Restrictions apply to the availability of these data. Data was obtained Kindertand, Pediatric Dental Practice, Milletstraat 28, 1077 ZE Amsterdam, The Netherlands and are available from Catherine de Jong, cath.de.jong@xs4all.nl with the permission of Kindertand, Pediatric Dental Practice.

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