Systematic Review
Behavioral Sciences

Assessment of child's dental anxiety/fear and stress during dental treatment: a systematic review by CEDACORE

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Declaration of Interests: The authors certify that they have no commercial or associative interest that represents a conflict of interest in connection with the manuscript.

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https://doi.org/10.1590/1807-3107bor-2022.vol36.0067

Abstract: There is a lack of evidence on the correlation between salivary biomarkers and subjective measures of dental fear and anxiety in children. This systematic review aimed to retrieve the scientific evidence comparing the results of dental anxiety measured by salivary biomarkers with patient-reported outcomes in pediatric dental setting. The PECOS was as follows: population: pediatric patients aged ≤ 18 years; exposure: patient-reported outcome measures, such as scales and/or questionnaires; comparator: salivary biomarkers; outcome: anxiety, fear, phobia or stress during dental treatment; study design: observational studies or controlled trials. Electronic searches were conducted in PubMed, Scopus, Web of Science, and Ovid databases. Studies that compared scales/questionnaires and salivary biomarkers for the evaluation of dental anxiety, fear, and stress in children/adolescents during dental treatment were included. Certainty of evidence was assessed with GRADE. Risk of bias of the included studies was assessed with the Cochrane tool or the University of Adelaide tool. From the 314 studies identified, eight were included. Participants' age ranged from three to 13 years. The most used salivary biomarkers and instruments were cortisol and the Dental Subscale of the Children's Fear Survey Schedule, respectively. Most studies showed a weak correlation between objective and subjective measures. The main issues regarding bias were on allocation concealment, blinding of assessors, follow up, and exposure assessment. Certainty of evidence was low/very low. Evidence of salivary biomarkers and patient-reported outcome measures to investigate anxiety, fear and stress in children during in the dental environment is limited. There was no correlation between subjective and objective measures in almost all included studies.

Keywords: Dental Care for Children; Hydrocortisone; Alpha-Amylases; Chromogranin A; Surveys and Questionnaires.

Introduction

Measurement of dental anxiety, fear, and stress in children is largely based on observed behavior rating scales or questionnaires.[1] However, the accuracy of such scales and questionnaires in determining what

Submitted: March 18, 2021
Accepted for publication: February 2, 2022
Last revision: February 18, 2022

the child actually feels during dental treatments is limited due to their subjectivity, the need for a skilled examiner,[1] and the need for training in the use of the tool.[2-4] Another method of measuring the stress of a child during dental treatment is through saliva. Under certain conditions such as dental treatment, the allostatic systems become deregulated and alterations in saliva occur.[5] Heart rate, blood pressure, electrodermal activity, and salivary cortisol are examples of objective measures to assess dental anxiety/fear/stress in children. Studies have questioned the usefulness of heart rate, blood pressure, and electrodermal activity to investigate anxiety/fear/stress.[6] Conversely, salivary components as biomarkers of physiological characteristics have been widely used in dentistry to assess caries risk, salivary gland function,[7] and stress in children during dental treatments by examining salivary cortisol.[3,8,9]

Both salivary cortisol and subjective (patient-reported outcome measures - PROMs) methods such as scales and questionnaires have been used to evaluate dental anxiety/fear/stress in children.[10] However, despite the large number of assessment instruments, no systematic attempt has been made to compile the studies comparing objective and subjective measures. Such information could be helpful in choosing the tool used evaluate children's dental anxiety/fear/stress during dental appointments. Therefore, the aim of this systematic review was to compare salivary biomarkers with patient-reported outcome measures to assess dental fear or anxiety in children.

Methodology

Protocol and registration

This systematic review complied with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[11] A protocol has been registered in the International Prospective Register of Systematic Reviews (PROSPERO), under registration number CRD42018108929.

Eligibility criteria

The eligibility criteria were chosen using the PECOS (population, exposure, comparator, outcomes and study design) strategy: a) population: pediatric patients aged up to 18 years; b) exposure: patient-reported outcomes measures, such as scales and/or questionnaires; c) comparator: salivary biomarkers; d) outcome: dental anxiety, fear, phobia or stress during dental treatment; and e) study design: observational studies (cross-sectional, cohort or case-control studies) or randomized controlled trials (RCT). No restrictions were placed on language or publication date. Meeting abstracts, editorials, literature reviews, and letters to the editor were excluded. Moreover, studies were not excluded based on their methodological quality.

Information sources

Computerized searches were conducted on May 2020 across four electronic databases: PubMed (National Library of Medicine), Scopus (Elsevier), Web of Science (Thomson Reuters), and Ovid (Wolters Kluwer). The reference lists of the included articles were also screened for the identification of references that might not have been retrieved in the searches in the electronic databases. Finally, a search through Google Scholar limited to the first 300 hits was carried out. Duplicates were removed upon identification. References were managed using EndNote software (EndNote™, Clarivate Analytics, Toronto, Canada).

Search

Keywords and Boolean operators were selected and combined. The following search strategy was used in all databases: pediatric dentistry OR pediatric dentistry OR child OR children OR adolescent OR adolescents OR toddler OR teenager OR infant AND dental stress OR dental anxiety OR dental phobia OR dental fear OR odontophobia AND saliva biomarker OR salivary biomarker OR saliva biomarkers OR salivary biomarkers OR biomarker OR biological markers OR cortisol OR alpha-amylase OR alpha amylase OR nitric oxide OR melatonin OR immunoglobulin-A OR immunoglobulin A OR Ig-A OR Ig A OR chromogranin A.

Study selection

Study selection was performed by two authors, who worked independently. Titles/abstracts were assessed. The studies that met the eligibility criteria

were included. If the titles or abstracts had insufficient information for a decision on inclusion or exclusion, the full text was retrieved for evaluation using the same eligibility criteria. Full texts that fulfilled the eligibility criteria were also included.

Data extraction

For each included study, the following data were extracted: first author's last name and year of publication, sampling (number of groups and description of groups as well as participants' sex and age), description of the methods used for the evaluation of patient-reported outcomes and salivary biomarkers, dental procedures and evaluation times, statistical analysis used, and main results.

Risk of bias in individual studies

Evaluation of the risk of bias of included studies was performed by two review authors independently. The risk of bias in randomized clinical trials was assessed by means of the Cochrane tool. The following items were assessed: sequence generation, allocation concealment, blinding of participants/personnel, blinding of outcome assessment, incomplete outcome data, selective reporting of outcome, and other sources of bias. According to this tool, for each item in the study the risk of bias is classified as of low-quality, high-quality, or unclear.[12]

The risk of bias in cross-sectional studies was evaluated by means of the University of Adelaide tool. The following items were evaluated: clear description of criteria for inclusion in the sample, detailed description of subjects and setting, valid and reliable exposure measurement, objective and standard criteria for the condition measurement, identification of confounding factors, statement on strategies to deal with confounding factors, valid and reliable way for outcome measurement, and use of appropriate statistical analysis. For each item, the response could be yes, if the article had fulfilled the requirements for that item (low risk of bias) and no, if the article had not fulfilled the requirements for that item (high risk of bias). Unclear risk of bias is also an option.[13]

The risk of bias in the follow-up study was assessed using the University of Adelaide tool. This tool allows for the evaluation of the following aspects: whether exposure was measured in a similar manner to assign people to both the exposed and unexposed groups, whether exposure was measured in a valid and reliable way, whether confounding factors were identified, whether strategies for dealing with confounding factors were stated, whether outcomes were measured in a valid and reliable manner, whether follow-up time was specified and was long enough for outcomes to occur, whether follow-up was complete (if not, the reasons for loss to follow up were described and explored), whether strategies to address incomplete follow up were used, and if appropriate statistical analysis was used. For each item, the response could be yes, if the article had fulfilled the requirements for that item (low risk of bias) and no, if the article had not fulfilled the requirements for that item (high risk of bias). Unclear risk of bias was also an option.[13]

Assessment of the certainty of the evidence

The certainty of the evidence was judged according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. GRADE enables the assessment of the quality of the body of evidence based on the evaluation of the following parameters: study design, risk of bias, imprecision, inconsistency, indirectness, and other factors, such as publication bias.[14]

Summary measures

The results regarding the comparison between salivary biomarkers and patient-reported outcome measures were provided with medians, quartiles, means, standard deviations, values of correlation coefficient (rho - Spearman correlation; r – Pearson correlation), and p-values.

Results

Study selection

A total of 314 references were identified. After the removal of 96 duplicates, 218 remained. Among them, 178 studies were excluded after the screening process. The main reasons for exclusion were articles not addressing issues related to salivary biomarkers

and/or patient-reported outcome measures (n = 140), no comparison between salivary biomarkers and patient-reported outcome measures (n = 23), and other reasons, such as age, type of study, and context (n = 15). Among the 40 potentially eligible studies, 32 were excluded after full-text analysis. Thus, eight studies were included in this systematic review, five of which were cross-sectional studies,[15-19] two were prospective cohort studies,[8,20] and one was a randomized clinical trial.[21] Figure shows the search process and reasons for exclusion of references after full-text evaluation.

Study characteristics

The included studies were published in English between 2007 and 2019 and were conducted in Greece,[8] Japan,[15,17] Sweden,[16] India,[18, 21] Turkey,[19] and Saudi Arabia.[20] The sample size of the studies ranged from 20[18,21] to 151 pediatric patients.[20] The age of participants ranged from three to 13 years. In three studies, the respondents were not the children, but the parents/caregiver[17,19] or the dentist.[21]

The most used salivary biomarkers were cortisol (n = 6 studies),[8,16,18-21] followed by alpha amylase (n = 4),[8,15,19,20] and chromogranin A (n = 2).[17,19] No other biomarker was found. The saliva samples were collected at predetermined times, and in almost all studies samples were collected before, during, and/or after the dental intervention.[8,15,17,19-21]

These salivary biomarkers were compared with different instruments used to measure dental fear and dental anxiety in children. Dental fear was

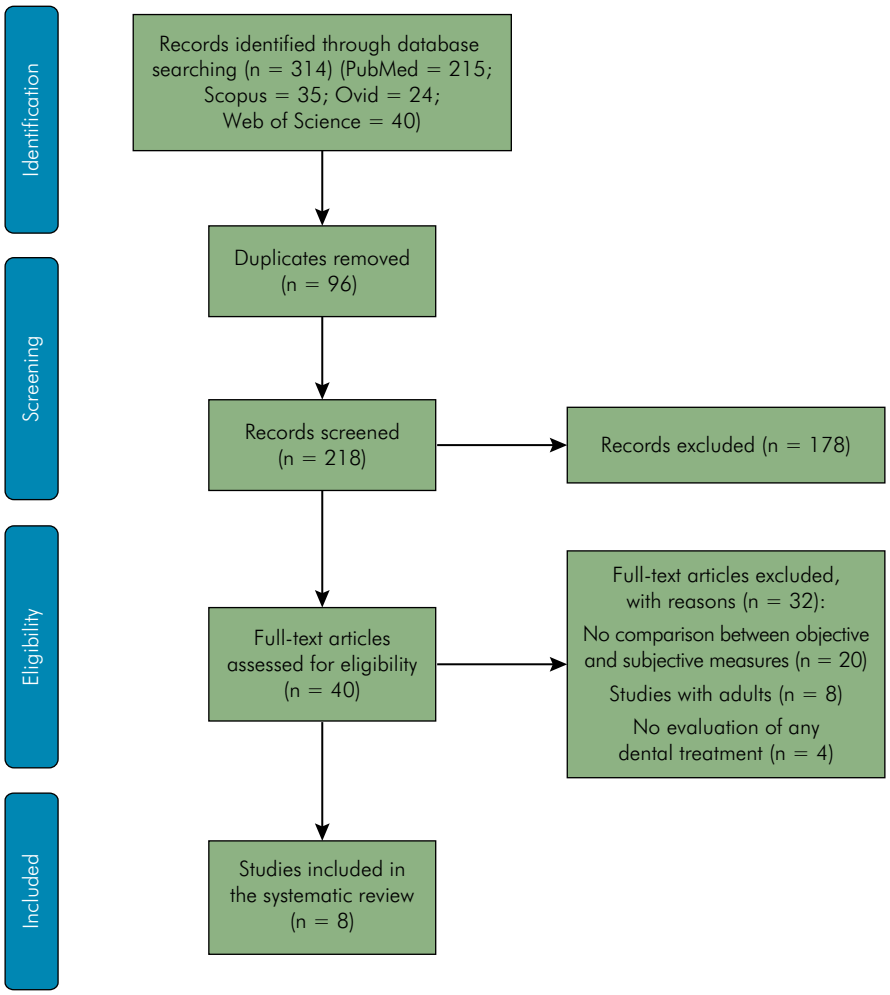

Figure 1. Flow diagram of the study steps.

measured with the Dental Subscale of the Children's Fear Survey Schedule (CFSS-DS).[8,15,17,19,20] Dental anxiety was evaluated using the Corah Dental Anxiety Scale (CDAS)[16,18], the Venham Clinical Anxiety Scale (VCAS),[21] and the Facial Image Scale (FIS).[19] In all included studies, these instruments were completed before the procedure.[19,15-19,21] In two studies, the instruments were also applied after the intervention.[15,21]

In almost all studies, some procedures, such as clinical examination,[8,16,19] prophylaxis,[8,15] restorations,[8,15,21] radiographs,[16] exposure to the noise of caries removal,[17] and other non-invasive dental treatments (orthodontic treatment, topical fluoride application, pit and fissures sealants)[15] were performed. In one study, the dental procedure that was performed was not specified. In this study, the authors stated that they recorded whether or not the dental treatment was successfully completed.[20] In two studies, children underwent restoration and extraction, pulpectomy, or pulpotomy.[19,21] These procedures were performed under sedation[21] or general anesthesia.[19] Study characteristics are described in Table 1.

Risk of bias in included studies

The results of the risk of bias assessment of the randomized clinical trial[21] are provided in Table 2. The main issues regarding unclear risk of bias was for allocation concealment and blinding of assessors. For the longitudinal studies,[8,20] a high risk of bias was found for follow up, given the lack of information that would allow the reader to decide whether or not the follow up had been completed and whether or not strategies to address incomplete follow up had been used (Table 3). In four cross-sectional studies, the item evaluating whether the exposure had been measured in a valid and reliable way presented an unclear risk of bias[18] or a high risk of bias[16, 17,19]

Table 1. Characteristics and results of the included studies.

Author(s), year	Study design	Participants	Dental procedures
		n (age)	
Yıldırım et al, 2018[19]	Cross-sectional	38 (35–72 months)	Restoration, pulpal treatment and extraction under general anesthesia
Yfanti et al, 2014[8]	Prospective cohort	97 (62–124 months)	Clinical examination, followed by prophylaxis or restoration with the use of local anesthesia
Aoyagi-Naka et al, 2013[15]	Cross-sectional	28 children (8–13 years) divided in two groups: the increased amylase group (G1, n = 14) and the decreased amylase group (G2, n= 14)	Orthodontic treatment, prophylaxis, topical fluoride application, composite resin restorations without local anesthesia, and pit and fissure sealants
Blomqvist et al, 2007[16]	Cross-sectional	89 children aged 13 years divided in two groups: control (G1, n = 71); attention deficit hyperactivity disorder (G2, n=18)	Clinical examination and bite-wing radiographs.
Okano et al, 2009[17]	Cross-sectional	37 aged 3–12 years divided in two groups: preschool (G1, n = 15) and school-aged (G2, n=22)	Exposure to the noise of tooth excavation (dental air turbine noise)
Patil et al, 2015[18]	Cross-sectional	20 (4–8 years)	Routine dental examination

Table 2. Quality assessment of the randomized clinical trial.

Author(s), year	Sequence generation	Allocation concealment	Blinding participants/ personnel	Blinding assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Shanmugaavel et al., 2016[21]	Low risk of bias	Unclear risk of bias	Low risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias

Table 3. Quality assessment of the follow-up study.

Variable	Yfanti et al, 2014[8]	AlMaummar et al, 2019[20]
Were the two groups similar and recruited from the same population?	Not applicable	Yes
Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Yes	Yes
Was the exposure measured in a valid and reliable way?	Yes	Yes
Were confounding factors identified?	Yes	Yes
Were strategies to deal with confounding factors stated?	Yes	Yes
Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Not applicable	Not applicable
Were the outcomes measured in a valid and reliable way?	Yes	Yes
Was the follow up time reported and sufficient to be long enough for outcomes to occur?	Yes	Yes
Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	No	No
Were strategies to address incomplete follow up utilized?	No	No
Was appropriate statistical analysis used?	Yes	Yes

Yes: Low risk of bias; No: High risk of bias.

Table 4. Quality assessment of the cross-sectional studies.

Author(s), year	Criteria for inclusion in the sample clearly defined?	Study subjects and setting described in detail?	Exposure measured in a valid and reliable way?	Objective and standard criteria used for measurement of the condition?	Confounding factors identified?	Strategies to deal with confounding factors stated?	Outcomes measured in a valid and reliable way?	Appropriate statistical analysis used?
Yıldırım et al, 2018[19]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
Aoyagi-Naka et al, 2013[15]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Blomqvist et al, 2007[16]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
Okano et al, 2009[17]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
Patil et al, 2015[18]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes

Yes: Low risk of bias; No: High risk of bias.

(Table 4). The level of evidence was very low/low, given the data imprecision (Table 5).

Synthesis of results

Five studies compared a (trait) dental fear subjective measure (CFSS-DS) with a salivary biomarker, such as alpha amylase,[15,19,20] cortisol,[19,20] alpha amylase:cortisol ratio[8] and chromogranin A.[17,19] The CFSS-DS[2] questionnaire measures fear and anxiety and identifies their causes. The scale consists of 15 items related to various aspects of dental treatment. Scores below 31 indicate low anxiety, scores between 31 and 38 denote moderate anxiety, and scores higher than 38 indicate high anxiety regarding dental treatment.[23]

Table 5. Assessment of the certainty of the evidence with GRADE.

Certainty assessment							Certainty
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
7	observational studies	not serious	not serious	not serious	very serious	none	⊕◯◯◯ VERY LOW
1	randomized trials	not serious	not serious	not serious	very serious	none	⊕⊕◯◯ LOW

The pre-treatment median salivary cortisol, alpha amylase, and chromogranin A levels were significantly higher in patients with low CFSS-DS responded by parent (between 15 and 31) compared with those with moderate (between 32 and 39) and high scores (higher than 39) (p = 0.046).[19] Conversely, no difference was observed between individuals with increased and decreased alpha amylase regarding the CFSS-DS mean score (p = 0.19).[15] The CFSS-DS score presented a weak negative correlation with the alpha amylase:cortisol ratio shortly after dental treatment (rho = -0.24). The CFSS-DS score presented a weak negative correlation with alpha amylase:cortisol ratio before dental treatment (rho = -0.15) and a weak positive correlation between 7 and 14 days after treatment at the recall visit (rho=0.02).[8] Another study demonstrated that the levels of salivary alpha-amylase and salivary cortisol three months and one year after dental treatment had a significant association with the level of dental fear (p = 0.029 and p = 0.000, respectively), confirming that phobic patients had the highest levels of salivary amylase and salivary cortisol.[20] There was no correlation between CFSS-DS responded by child/parents and change in chromogranin A level during the exposure to noise of an air turbine in preschool children (rho = 0.00) or schoolchildren (rho = 0.00),[17] but since CFSS-DS is a dental fear (trait) measure, this change was not expected.

Six studies compared subjective measures of dental anxiety, such as the VCAS,[21] the CDAS[16,18] and the FIS[19] with salivary biomarkers, such as cortisol,[16,18,19,21] alpha amylase and chromogranin A.[19] The VCAS is a global scale, which was developed for the behavioral assessment of children during dental treatment. The assessment is done over a period of time and the predominant behavior of the child is noted at the end of the observation period.[24] The scale has six scores with more detailed descriptions of behaviors. The higher scores of the scale are representative of worse behaviors.[24] The reduction in the VCAS score according to pediatric dentistry presented a weak positive correlation with the change in salivary cortisol level in children sedated with intranasal midazolam (rho = 0.213) and with sublingual midazolam (rho = 0.265).[21]

No difference was observed regarding the mean salivary cortisol level among individuals with different levels of anxiety (low, moderate, high and severe) according to the CDAS (p = 0.214).[18] On the other hand, CDAS[25] contains questions about anxiety regarding dental treatment. It consists of four questions, specifically related to aspects of dental care, with five answer options. Only one answer must be selected, and each answer has a score between one and five. A total score ranging from 4 to 20 is achieved when adding the item scores. Scores below 12 indicate low anxiety, between 12 and 14, moderate anxiety, and greater than 14, high dental anxiety.[26] Conversely, another study, in which the CDAS was compared with cortisol, showed a positive correlation both in children with attention deficit hyperactivity disorder (r=0.54) and in children without this disorder (r = 0.28).[16]

No strong correlations were observed between salivary biomarkers and FIS scores.[19] The FIS is a scale used to assess children's self-report dental anxiety according to.[27] This scale comprises a row of five faces ranging from "very happy" to "very unhappy". All faces are scored by assigning a value of 1 to the happiest face and 5 to the saddest face. It is a simple and easy-to-apply scale, in which children are asked

to indicated which face they recognized themselves most at the moment before being referred to the dental office.[27] The results of the included studies are described in Table 1.

Assessment of the certainty of the evidence

Two assessments were performed to compare salivary biomarkers and patient-reported outcome measures for evaluating dental fear or dental anxiety in children. In one assessment, seven observational studies were incorporated. In the second assessment, the randomized trial was incorporated. In both evaluations, there were very serious concerns regarding imprecision and the certainty of the evidence was either very low or low.

Discussion

This systematic review compared salivary biomarkers and patient-reported outcomes for the evaluation of dental fear or dental anxiety in children and found that the correlation between the two measures is limited in almost all included studies. This could be explained by methodological differences, as substantial heterogeneity was found among studies, especially a wide age range and differences in the dental procedures.

Scales and questionnaires assess dental fear and anxiety in several ways; some studies evaluated state dental fear and anxiety, by means of the VPT and FIS, and others evaluated trait dental fear and anxiety, such as using the CFSS-DS. Similarly, there was no child-, parent-, or observer-reported measure that could be used as a standard to compare with salivary biomarkers. Moreover, among the eight included studies, only one was a randomized clinical trial,[21] which also limits the evaluation of the quality of evidence from the retrieved studies. Despite the low risk of bias presented in this randomized clinical trial study,[21] the longitudinal studies[8,20] did not provide information that would allow the reader to decide whether or not follow-up had been complete or if strategies had been in place to deal with incomplete follow-up. In four cross-sectional studies,[16-19] there was unclear or high risk of bias regarding whether the exposure was approached in a valid and reliable manner, suggesting caution during the interpretation of the results.

Nonetheless, there is no question that salivary biomarkers and psychometric indices are important in providing an objective approach for measuring children's physiological reactions and for the subjective assessment of children's dental fear/dental anxiety, respectively. The combination of both types of measures allows a better understanding of dental anxiety and dental fear in children, which contributes to the adequate management of oral health issues by the pediatric dentist. In clinical practice, children's self-report would better reflect their subjective feelings regarding the dental setting. Therefore, especially when salivary tests are not available, the busy clinician may use questionnaires to assess dental fear and anxiety, such as CFSS-DS, Modified Dental Anxiety Scale, CDAS,[10] VCAS,[28] and the FIS.[27]

Most studies showed that the subjective measure CFSS-DS did not correlate with salivary biomarkers.[8,15,17,19] However, in one study, higher levels of salivary markers were observed in children whose parents/guardians had reported low dental fear, which may indicate that parent/guardians had limited knowledge of their children's feelings and emotions.[19]However, in another study, the levels of alpha amylase and salivary cortisol had a significant association with the level of dental fear, especially in patients who self-reported being phobic using the CFSS-DS.[20] Thus, the differences in correlation between objective and subjective measures in these studies might be explained by the use of parent/guardian or child responses.

Regarding parent's/guardian's reporting of children's dental anxiety, there was no positive or significant correlation between subjective measures and objective measures in most studies.[18,19,21] This finding sheds light on the assumption that parents tend to overestimate their children's anxiety.[29] Other studies also found no significant correlation between dental anxiety score (DAS) and salivary cortisol level.[30,31] Krueger et al.[32] found no correlation between dental anxiety and salivary cortisol in adult female individuals, although individuals were significantly more aroused and anxious prior to the treatment appointment. Only one study found a positive and

significant correlation between anxiety reported by the children using the CDAS and cortisol levels as an objective measure prior to the procedure.[16] The children from this study were 13 years old, and although most of them were from a control group, some of the individuals in the sample were diagnosed with attention deficit hyperactivity disorder.[16] We can hypothesize that the methodological differences between the two types of measurements may be the reason for not finding a correlation in some of the cases. On the other hand, in those cases where a correlation does exist, the subjective measure may best reflect the child's state, besides being the easiest to collect in the dental setting.

In all included studies, invasive or/and noninvasive dental procedures were performed on children, which may have an influence on the interpretation of the results, since simple procedures, such as dental prophylaxis are less stressful[9] than invasive procedures.[33] Also, procedures were performed under sedation in one study[21] and under general anesthesia in another study.[18] Thus, the different dental procedures, the non-standardization in the use of general anesthesia or sedation, and the use of different pharmacological techniques could represent a bias that prevents a clear determination of a correlation. This may have influenced the evaluation of the measures, since sedation and anesthesia are stressful procedures and may cause an endocrine change that increases salivary cortisol levels.[34] Moreover, sedation and anesthesia are prescribed for stressful operative procedures, so a significant increase in cortisol levels in these pediatric patients is not unexpected.[35]

Salivary cortisol was the most commonly used objective measure[8,16,18,20,21] and seems to be the most appropriate biomarker for measuring stress and anxiety in the dental setting.[36-38] Determination of cortisol in saliva is useful to assess children' dental stress, not only because the result is reliable, but also because collecting a saliva sample is painless and less invasive and easier than collecting a blood sample. However, there are limitations due to circadian changes such as time of day and day of week. Also, the protein-binding capacity of the biomarker can vary and special devices are needed for sample collection and storage.[39] This systematic review confirms that there is still a lack of agreement between self-reported of anxiety levels and biological stress reactivity[40] or a lack of correlation between cortisol level and anxiety at certain periods of the day.[41]

Although salivary chromogranin, an acid phosphorylated secretory glycoprotein, has been reported as a biomarker for the evaluation of acute stress episodes,[42] only two studies used it for the evaluation of dental anxiety in children,[8,17] and the evidence for a relationship between salivary chromogranin A and dental anxiety has not been established yet.[43]

This systematic review has limitations. First, although every effort was made to find all articles related to the topic, publication bias cannot be ruled out. Second, due to the heterogeneity of the included studies, a meta-analysis was not possible. However, we followed strict criteria to minimize error.[12,13] It should be noted that in some studies, questions about fear/anxiety were directed to parents/caregivers[17,19] or the dentist.[21] Although this assessment of perception cannot be considered a "patient-reported outcome", in the context of pediatric research, proxy measures – PROMs – provide critical information about children. Another limitation was that we were unable to compare children's behavior with the other measures investigated because the included articles did not provide this information. This could be an important variable, as dental anxiety may predict children's behavior during dental treatment[44] and should be further assessed in future studies.

Conclusion

This systematic review found that the evidence of an association between objective salivary biomarkers and subjective patient-reported outcomes of dental fear or dental anxiety in the pediatric dental setting was of low/very low quality. Therefore, the information provided should be used cautiously. Studies of higher quality designed specifically to compare objective and subjective measures are needed.

Acknowledgements

We thank the Newton Fund 2016–2017 (British Council, UK), Fundação de Amparo à Pesquisa

do Estado de Goias, Brazil, and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for the financial support to the workshop that enabled this working group.

We acknowledge the contribution of all CEDACORE (Children Experiencing Dental Anxiety: Collaboration on Research and Education) members in the discussions that underpinned this work.

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