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Homeopathic Combination before Dental Treatment for Anxiety Reduction in Children – Pilot Study

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Abstract

Objectives: We assessed the effectiveness of homeopathic remedy in decreasing children's anxiety before dental treatment by measuring saliva cortisol and α-amylase levels.

Design: The study was of double blinded crossover design. The study group comprised of eleven 5-9 years old children that exhibited anxiety. The homeopathic remedy comprised of a mixture of Ambra grisea 7cH/Arsenicum album 7cH/Gelsemium sempervirens 9cH/Ignatia amara 9cH/alcohol 18%. Two comparable dental restorative treatments were performed. Levels of salivary cortisol and α-amylase were measured on the day of dental treatment at two time points.

Results: Salivary cortisol levels were low in both study and control groups before treatment, but differed during dental treatment: they were elevated in the control but almost didn't change in the homeopathic group. This biomarker suggests lower anxiety in the homeopathic group than in the control group. Post-treatment Facial Image Scale scores in the homeopathic group were not significantly lower than in the pre-treatment. Pulse rate, oxygen saturation, and Houpt score were similar in both the control and the study group.

Conclusions: Although the results were not conclusive, an interesting trend of lower anxiety levels among the homeopathic group compared to placebo was indicated by salivary cortisol and α-amylase levels. Further research is needed.

Keywords: Homeopathic remedy; Children's anxiety; Dental treatment

Introduction

About eleven percent of children and adolescents suffer from dental anxiety [1]. To control behavior and allow safe completion of dental procedures pediatric dentists use pharmacological methods, yet according to the American Academy of Pediatrics (AAP) and American Academy of Pediatric Dentistry (AAPD) guidelines, sedation for pediatric patients has serious associated risks, such as hypoventilation, apnea, airway obstruction, laryngospasm, and cardiopulmonary impairment [2].

Few effective medicaments are available to the dental practitioner for conscious sedation [3]. Combined with nitrous oxide, the sedative drugs of choice in pediatric dentistry are hydroxyzine, midazolam, or chloral hydrate. These drugs have adverse effects that range from hypoventilation to death [4-13].

Homeopathy is being used as an adjuvant to conventional dentistry for handling a number of difficulties, including teething, toothache, surgical trauma, ulcers, dry mouth, periodontitis and anxiety [14-18].

Homeopathic remedies are believed to gain greater potency as they are diluted. The more dilute a homeopathic remedy, the more potent it is considered to be [19,20]. While a systematic literature review found no definite evidence for the efficacy of homeopathy [21], a few studies have proven that some homeopathic remedies are significantly more efficient than placebo [22].

The present pilot study used objective laboratory tests of salivary alpha-amylase and cortisol levels to assess the effectiveness of a homeopathic remedy in decreasing dental anxiety in children when administered before dental treatment.

Cortisol, the main glucocorticoid hormone produced by the adrenal cortex, has a large circadian variation that follows the sleep-wake rhythm with high levels in the morning and low ones at midnight. High serum levels are also found as a reaction to stress. Salivary cortisol is an ultrafiltration of

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plasma cortisol and reflects the levels of biologically active, non-protein bound cortisol in the serum. An advantage of salivary cortisol analysis is the easy, non-invasive sample collection [23].

Salivary α-amylase, locally produced by salivary glands in the oral mucosa, has been proposed as a sensitive biomarker for stress-related changes in the body that reflect the activity of the sympathetic nervous system [24]. Salivary flow rate has no impact on salivary α-amylase levels, as is the case with salivary cortisol. Salivary α-amylase levels change more dramatically than those of salivary cortisol after the same mental stress event. Physical stress also has an impact on salivary α-amylase levels, e.g., the physical stress inflicted by surgical operation affected salivary α-amylase levels in children [24,25].

As secretion of both salivary cortisol and salivary α-amylase increases in states of stress [26,27] and the measurement of their levels in the saliva is a noninvasive procedure, we used cortisol and α-amylase levels in the saliva to assess the effectiveness of homeopathic combination administered before dental treatment in decreasing dental anxiety in children.

Materials and Methods

The study protocol has been approved by the Hadassah Human Subjects Institutional Board (IRB No. 0273-12-HMO) and by the Clinical Trials department at the Ministry of Health. Children whose guardians were interested in the proposed treatment at the Department of Pediatric Dentistry in the Hadassah School of Dental Medicine and that met the inclusion criteria were offered the opportunity to participate in the study. Inclusion criteria were: healthy 5-9 years-old children, not taking any medications, that needed at least two similar dental treatments and who were cooperative but exhibited some degree of anxiety on the initial diagnostic appointment. Exclusion criteria were recent use of other homeopathic remedies or medications.

The purpose and nature of the study were explained to the children and their parents and then their consent to participate was obtained.

Randomly, children received homeopathic combination on the first appointment and a placebo on the second one, while the others received placebo for the first treatment and a homeopathic combination on the second one (crossover study design). Both the patient and the dentist were blind to the remedy administrated.

Sociodemographic data collected included age, gender, ethnicity, parents' education and previous experience with homeopathy.

Homeopathic combination

The homeopathic combination comprised of a mixture of Ambra grisea 7cH/Arsenicum album 7cH/Gelsemium sempervirens 9cH/Ignatia amara 9cH/alcohol 18%. Ambra grisea is applied to excitable, nervous children and thin, nervous patients. Arsenicum album has general symptoms of all-prevailing enfeeblement, exhaustion, and restlessness. Gelsemium sempervirens causes varying degrees of motor paralysis, dizziness, drowsiness, dullness, tired feeling, and mental apathy. Ignatia amara produces a marked hyperesthesia of all the senses and is used homeopathically as one of the main remedies for panic [28,29].

The combination was suggested by a specialist from the Integrative and Complementary Medicine department, Hadassah Hebrew University Medical Centre, Jerusalem, Israel. The combination was prepared by a licensed pharmacist experienced in preparing homeopathic drugs and placebo for studies. All of these ingredients are approved by the Ministry of Health.

Ten drops of the combination were taken in the morning and evening of the day before the treatment, and on the morning of the treatment day, two hours before treatment. Combination and placebo bottles were identical in appearance and their contents had similar taste, they were marked 1 or 2 and the code was kept in signed envelope until the end of the study. Randomization was done by toss of a coin.

Dental treatment

All dental treatment performed at the morning hours (9:00-12:00). Dental treatment was carried out using behavior management techniques. Nevertheless, the patients received inhaled sedation using nitrous oxide when necessary. In cases of no cooperation the dental treatment was stopped, no restrain was used. The patient was monitored using pulse oximeter during the treatment and heart rate and oxygen saturation were recorded every 10 min. The two dental sessions included comparable dental treatments. Only appointments with restorative treatments were included (e.g. cavity restorations). There were no extractions, to avoid saliva contamination at the end of the treatment. The minimal interval between sessions was one week.

Procedures

Salivary cortisol and α-amylase: Saliva was collected using a commercially saliva collecting device (Salivette©; Sarstedt, Rommelsdorf, Germany) on the day of dental treatment at two time points: before the beginning of dental treatment and 15 min after it ended. The Salivette© swab was placed in the patients' mouth for 60 sec and then returned back to the Salivette tube. Centrifugation for 2 min at 1,000xg yielded clear saliva in the conical tube. Saliva was stored at -80°C.

The salivary cortisol and α-amylase levels were measured in the lab using enzyme immunoassay kit according to the manufacture instructions (Saliva Cortisol ELISA kit and Salivary alpha- Amylase ELISA Kit; EUROIMMUN AG, Germany).

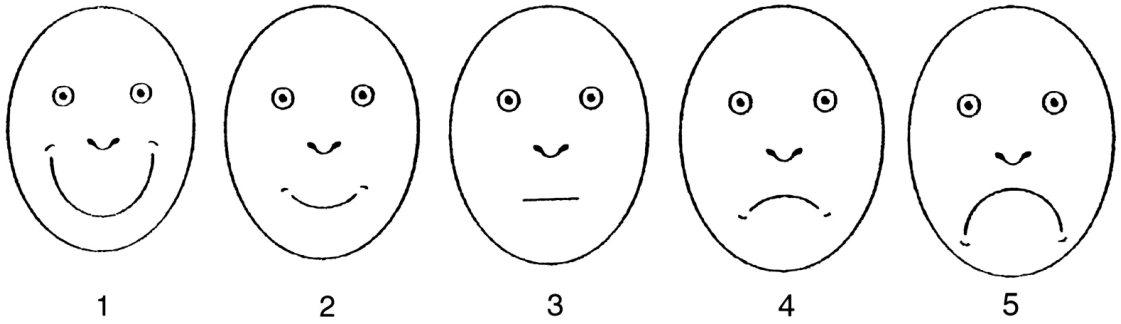

Figure 1: Facial Image Scale with image scores, 1-5 [30].

Calibrators, controls and patients samples were transferred into individual microplate wells. Enzyme conjugate (peroxidase-labelled cortisol, peroxidase- labelled alpha-amylase) and antiserum solution (polyclonal anti-alpha amylase antibody) were pipetted into each well. The microplate wells were incubated on a microplate shaker (400 U/min) at room temperature. After washing, chromogen/ substrate solution was pipetted into each of the wells and the microplates were incubated again. Then stop solution was pipetted into each well and photometric measurements of the color intensity were made at wavelength of 450 nm. "4-parameter logistics" plotting was used for calculation of the standard curve for determination of cortisol and alpha-amylase concentrations in patients' samples.

Facial Image Scale (FIS): FIS [30] is a valid measure of dental anxiety for employment with young children in the clinical context. FIS was used to measure subjective feeling of anxiety at two time points: before the beginning of dental treatment and 15 min after the end of dental treatment. The children were asked to point at which face they feel most like at that moment (Figure 1).

Houpt Scale: The Houpt scale [31] is a reliable tool that measures behavior by rating sleep, movement, crying and overall behavior. In this study a blind observer (specialist in pediatric dentistry) rated only general behavior during the dental treatment.

Rating for overall behavior:

1. Aborted- no treatment rendered
2. Poor- treatment interrupted, only partial treatment completed
3. Fair-treatment interrupted, but eventually all completed
4. Good- difficult, but all treatment performed
5. Very good- some limited crying or movement
6. Excellent- no crying or movement

Statistical analysis

To evaluate quantitative variables between two independent groups Wilcoxon test was applied. Spearman's test was used for multivariable correlations. Statistical significance was set at $p<0.05$.

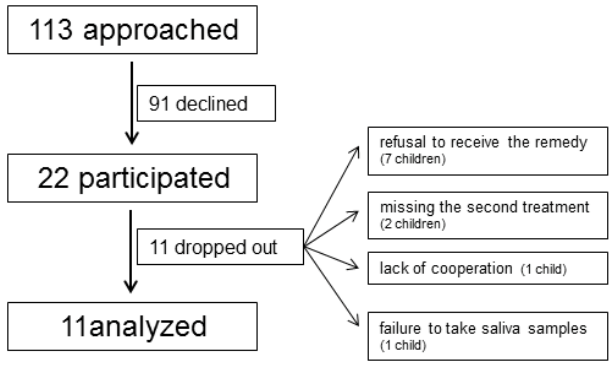

Figure 2: Flow chart.

Results

One hundred and thirteen patients met inclusion criteria and were approached and invited to participate in the study. Ninety one declined, so the initial study group comprised of 22 children. Eleven children dropped out due to refusal to receive the combination (seven children), missing the second treatment (two children), lack of cooperation (in one child from the control group treatment was aborted on the first appointment and continued with oral sedation), and failure to take saliva samples (one child) (Figure 2). The remaining eleven children were 5-9 years old, seven girls and four boys. Mann-Whitney Test verified that the order of remedy taken didn't influence the result.

While both salivary cortisol and α-amylase before and after treatment were lower in the homeopathic combination group, cortisol levels did reflect (although without the desired statistical significance) the effect of homeopathic treatment, while α-amylase levels did not (Table 1). FIS levels, although not statistically significant, also showed a slight difference between the groups. There was no statistically significant difference between the groups in the other measurers (pulse during treatment and Houpt score.

Salivary cortisol level almost didn't change during dental treatment in the homeopathic group, while it was elevated

	Homeopathy	Control	*p*-value
cortisol pre-treatment (ng/ml)	1.38 ± 1.45	2.28 ± 3.09	0.859
cortisol post-treatment (ng/ml)	1.39 ± 2.90	4.37 ± 6.91	0.929
(U/ml) α-Amylase pre-treatment	56.02 ± 45.72	92.09 ± 110.65	0.333
α-Amylase post-treatment (U/ml)	73.36 ± 54.81	102.62 ± 104.42	0.374
FIS pre-treatment	2.18 ± 1.68	1.91 ± 1.22	0.083
FIS post-treatment	2.09 ± 1.30	2.64 ± 1.20	0.154
Pulse	90.0 ± 12.93	90.3 ± 14.03	0.592
Houpt	4.73 ± 0.905	4.55 ± 0.688	0.705

Table 1: Salivary cortisol, α-amylase, FIS score and Houpt score before and after the treatment and pulse rate during treatment.

	Homeopathy	Control	*p*-value
Cortisol Δ	0.11	2.09	0.424
α-Amylase Δ	20.8	0.16	0.169
FIS Δ	-0.09	0.72	0.069

Table 2: Differences between pre and post-treatment values of cortisol, α-Amylase and FIS scale in the homeopathic and control groups.

in the control (Table 2), suggesting higher anxiety in the control group. Post-treatment FIS scale in the homeopathic group was lower than the pre-treatment, suggesting that the children's' anxiety had been reduced during the treatment, while it was elevated in the control group (Table 2).

Pulse rate and oxygen saturation were similar in both the control and the study group during the procedure and all scheduled treatments were completed during each appointment.

Discussion

To the best of our knowledge, this is the first randomized-controlled trial on the possible effects of homeopathic combination administered prior to dental treatment on children's anxiety. This is also the first study using impartial methods to evaluate homeopathic combination efficacy.

Several studies reported that stressful aspects of dental treatment can lead to higher salivary cortisol levels. Increase in salivary cortisol levels was found in 40% to 45% of patients after local anesthesia [32]. Patil et al. [33] found a correlation between salivary cortisol and stress in dental procedure. Salivary samples collected after administration of sublingual midazolam showed a marked decrease in cortisol levels compared to samples taken from the placebo group [26]. No differences were found between salivary cortisol levels at baseline and during routine dental examination [33]. Interestingly, in our study the control group had higher salivary cortisol levels at baseline and during the restoration procedures. A similar correlation between salivary cortisol and alpha amylase levels had been reported for global developmental delay (GDD) children: those who showed less favorable behavior during dental care had higher salivary cortisol and alpha amylase levels than GDD children with more favorable behavior [34].

Study limitations

The small sample size derived from a major difficulty in recruiting participants: Although interest in Complementary and Alternative Medicine (CAM) has increased during the past decade and the attitude of the general public is mainly positive with Israeli respondents greatly supporting a theoretical scenario of CAM integration into primary medical care, when we approached parents, the majority hesitated. Some were unacquainted with CAM therapies, and some asked for time to think it over, thus eliminating the opportunity to participate in the study. Although there has been increased awareness for homeopathic options in the population, we believe compliance would have been better if the parents themselves were seeking the homeopathic approaches, so better compliance may have been achieved in a population that has some prior knowledge of homeopathic remedies for pre-treatment anxiety.

Parents' compliance also influenced the high dropout rate- seven children didn't take the combination at home and two missed the second appointment. Attaining the full effect of the homeopathic combination required the application of the first dose a day before the treatment. Since the combination is to be taken at home, the dentist influence is limited.

Another limitation of the present study is the administration of an identical combination for all the participants although homeopathic remedies are most efficient when tailored to the needs of individual anxiety types.

Although not statistically significant, the results show a tendency for lower anxiety levels among children who received the homeopathic combination compared with children who received placebo**.**

Pulse rate and oxygen saturation were similar in both the control and the study group during treatment, and no adverse effects were recorded. However, adverse effects might be recorded in future studies with increased number of participants.

Conclusion

Our findings should encourage further studies on homeopathic combinations that may reduce the need for conscious sedation in dental treatment of anxious children capable of being cooperative.

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