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Split-mouth and parallel-arm trials to compare pain with intraosseous anaesthesia delivered by the computerised Quicksleeper system and conventional infiltration anaesthesia in paediatric oral healthcare: protocol for a randomised controlled trial

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ABSTRACT

Introduction: Local anaesthesia is commonly used in paediatric oral healthcare. Infiltration anaesthesia is the most frequently used, but recent developments in anaesthesia techniques have introduced an alternative: intraosseous anaesthesia. We propose to perform a split-mouth and parallel-arm multicentre randomised controlled trial (RCT) comparing the pain caused by the insertion of the needle for the injection of conventional infiltration anaesthesia, and intraosseous anaesthesia by the computerised QuickSleeper system, in children and adolescents.

Methods and analysis: Inclusion criteria are patients 7–15 years old with at least 2 first permanent molars belonging to the same dental arch (for the split-mouth RCT) or with a first permanent molar (for the parallel-arm RCT) requiring conservative or endodontic treatment limited to pulpotomy. The setting of this study is the Department of Paediatric Dentistry at 3 University dental hospitals in France. The primary outcome measure will be pain reported by the patient on a visual analogue scale concerning the insertion of the needle and the injection/infiltration. Secondary outcomes are latency, need for additional anaesthesia during the treatment and pain felt during the treatment. We will use a computer-generated permuted-block randomisation sequence for allocation to anaesthesia groups. The random sequences will be stratified by centre (and by dental arch for the parallel-arm RCT). Only participants will be blinded to group assignment. Data will be analysed by the intent-to-treat principle. In all, 160 patients will be included (30 in the split-mouth RCT, 130 in the parallel-arm RCT).

Ethics and dissemination: This protocol has been approved by the French ethics committee for the protection of people (Comité de Protection des Personnes, Ile de France I) and will be conducted in full accordance with accepted ethical principles. Findings will be reported in scientific publications and at research conferences, and in project summary papers for participants.

Trial registration number: ClinicalTrials.gov NCT02084433.

Strengths and limitations of this study

- This clinical trial will provide new evidence on pain associated with intraosseous anaesthesia by the computerised QuickSleeper system as compared with conventional infiltration in paediatric oral healthcare.
- The trial is a well powered, multicentre, randomised controlled trial (RCT). It involves a split-mouth trial and a parallel-arm design: patients who do not have symmetrical disorders (therefore are not eligible for the split-mouth RCT) will be included in the parallel-arm RCT.
- Operators cannot be blinded. However, patients will be blinded and the primary outcome—pain reported by the patient—is not likely affected.
- The trial is conducted in three French hospital dental departments specialised in treating children and adolescents, which may affect the generalisability of findings to different settings.

INTRODUCTION

Background and rationale

Local anaesthesia is commonly used in paediatric oral healthcare. Practitioners frequently use intramucosal infiltration anaesthesia, the conventional anaesthesia type. This method is a source of anxiety for the child because of fear of the injection. Also,

the injection can be painful if the product is delivered too quickly in the mucosa.

Recent developments in anaesthesia techniques may allow for decreasing pain during injection: intraosseous anaesthesia with a computerised system delivers local anaesthesia at a constant rate and pressure. In a case series of 50 children receiving intraosseous anaesthesia with the QuickSleeper system, most children felt no pain, or felt only mild discomfort (scores 0–2 for 81.8% and 83.9% of cases with face pain and visual analogue scales (VAS), respectively).[1] Intraosseous anaesthesia represents an interesting alternative to infiltration anaesthesia in that the latency—the time between when the anaesthetic is delivered and the effect produced—is potentially reduced.[2 3] In a randomised split-mouth trial of 30 children in Spain, the latency was 0.48±0.32 min for intraosseous anaesthesia with the QuickSleeper system and 7.10 ±2.23 min with conventional infiltration anaesthesia.[2 4] In addition, deep caries or molar-incisor hypomineralisation (MIH) on the first permanent molar inducing porous, exposed subsurface enamel and dentine may promote bacteria penetration into the dentine, thereby resulting in chronic inflammation of the pulp, which can diminish the effect of anaesthesia.[3–6] Intraosseous anaesthesia could be a good alternative to classical infiltration anaesthesia because the local anaesthetic is injected directly in the cancellous bone adjacent to the tooth needing to be anaesthetised.

Objectives

We hypothesised that intraosseous anaesthesia via the QuickSleeper system may reduce pain during anaesthesia and obtain more rapid local anaesthesia than anaesthesia via the conventional infiltration technique. The main objective is to compare pain with conventional infiltration anaesthesia and intraosseous anaesthesia with the QuickSleeper system for treating first permanent molars with deep caries or MIH (moderate-to-high severity) in children and adolescents. The second objectives are to compare latency, need for additional anaesthesia during the treatment and pain felt during the treatment between the two types of anaesthesia.

Trial design

This study involves a parallel-arm and a split-mouth randomised controlled trial (RCT). Split-mouth RCTs are popular in oral health research.[7–10] As compared with parallel-arm RCTs, the design most frequently used,[11] split-mouth RCTs randomly allocate experimental and control interventions to different areas in the oral cavity (teeth, surfaces, arches, quadrants)[12] and have the advantage that most of the variability in outcome among patients is removed from the intervention effect estimate, for a potential increase in statistical power, each patient being its own control.[8 9] since every patient receives each intervention, the design may also be better suited to determine patient preferences. However, a disadvantage of a split-mouth design is the need to include patients with a symmetrical disorder (eg, carious lesions on at least two first permanent molars). Consequently, many patients are not eligible. Generally, the two types of trials provide similar results, but estimates of the treatment effect may differ between split-mouth and parallel-arm RCTs.[13–15] Therefore, we chose to conduct a split-mouth RCT and a parallel-arm RCT.

METHODS

Study setting

Patients will be included and treated in the Department of Paediatric Dentistry at three University dental hospitals in France: Rennes, Nice and Bretonneau Hospital in Paris.

Eligible criteria

The inclusion criteria are (1) patients 7–15 years old; (2) absence of disease (handicap, autism, cancer, heart disease, sickle cell anaemia); (3) no analgaesic drug use 48 h before randomisation; (4) preserved pulp vitality as determined by clinical and radiographic observations and (5) agreement by patient and parents, or guardians, to participate in the study. Patients with periodontal disease (periodontal pockets or dental mobility) or radiological defects (necrosis, furcation or periapical radiolucency) are not eligible. Treatments concern first permanent molars with deep caries (ie, dentinal lesion involving more than 50% of the entire dentine thickness evaluated by radiographs) or MIH (moderate-to-high severity) and can be conservative or endodontic limited to pulpotomy. Patients and parents/guardians will receive explanations of the two anaesthesia techniques, and anaesthesia will be performed after they provide oral informed consent (see online supplementary files, texts S1–S4).

Each patient will undergo two anaesthesia techniques: conventional, and intraosseous with the QuickSleeper system (hereafter intraosseous anaesthesia). The two anaesthesia types will be performed by the same dentist (one of the four authors). For the split-mouth RCT, eligible patients will receive the anaesthesia treatment on at least two first permanent molars belonging to the same dental arch. Each patient will undergo treatment of a tooth with one of the techniques, and treatment of the homologous contralateral tooth with the other technique. A 7–21 day interval is allowed between one procedure and the other. For the parallel-arm RCT, eligible patients will require treatment with anaesthesia in one first permanent molar. Each patient will be allocated to receive one or the other technique.

Interventions

The topical anaesthesia Xylocaïne visqueuse 2% (AstraZeneca, Rueil Malmaison, France) will be applied for 1–2 min on previously dried mucosa before both anaesthesia techniques. Conventional anaesthesia, that is, para-apical maxillary and locoregional

mandibular anaesthesia, will involve use of 16 and 35 mm long needles, respectively. Intraosseous anaesthesia will be administered by the QuickSleeper system (Dental Hi Tec, Cholet, France) following the instructions of the manufacturer.[16] A 30-gauge, 9 or 13 mm long needle will be used. A three-step procedure will be used for the intraosseous anaesthesia, including (1) anaesthesia of the mucosa by inserting the needle at a 15°–20° angle to the buccal mucosa at the interdental papilla; (2) computerised rotation of the needle to penetrate the cancellous bone at a 30°–45° angle to the main axis of the tooth; and (3) computerised injection of the anaesthetic solution. The anaesthetic solution for both techniques will be 4% articaine with adrenalin, 1:200 000. The volume of anaesthetic solution delivered will be recorded.

Outcomes

Primary outcome measures

At the end of the anaesthesia, patients will be asked to assess the pain they felt during insertion of the needle and injection of the anaesthetic, on a VAS ranging from 0 (no pain) to 10 (very much pain).[17–19]

Secondary outcome measures

Three secondary outcomes will be assessed: (1) latency evaluated by examining the sensitivity of the vestibular sulcus for conventional anaesthesia, or lingual or palatine sulcus for intraosseous anaesthesia by using a probe (an examination will be conducted every minute until the sulcus is insensitive to the probe); (2) the need for additional anaesthesia during the treatment and (3) pain felt during the treatment, evaluated by the VAS at the end of the dental treatment session.

Participant timeline

For the split-mouth RCT, eligible patients will receive the anaesthesia treatment on at least two first permanent molars belonging to the same dental arch. Each patient will undergo treatment of a tooth with one of the techniques, and treatment of the homologous contralateral tooth with the other technique. A 7–21-day interval is allowed between one procedure and the other. For the parallel-arm RCT, eligible patients will require treatment with anaesthesia in one first permanent molar. Each patient will be allocated to receive one or the other technique.

Sample size

Split-mouth RCT

To estimate sample size for the primary outcome—pain felt during insertion of the needle and injection of the anaesthetic according to the VAS—we took into account the correlation induced by the paired nature of the data. In a previous trial, the corresponding SD in the VAS score could be estimated at 1.2.[1] Assuming that the SD is equal in the two randomisation groups and that the correlation between the pain scores for the same patient in the first and second treatment is 0.6, the difference in VAS scores would have a SD of 1.10. With a type I error risk of 0.05, we would need 30 patients to guarantee 80% power to detect a minimum true difference of 0.6 points in mean pain experienced during conventional infiltration and intraosseous anaesthesia.

Parallel-arm RCT

We plan to enrol 130 patients. In fact, under the same assumptions as above (type I error risk 0.05; two-tailed test; SD for VAS score of 1.2; minimum true difference in pain with infiltration and intraosseous anaesthesia of 0.6 points), the sample size to achieve 80% power is 128.

About one in five patient will be randomised to the split-mouth RCT.

Recruitment

The enrolment capacity was estimated to be 10 patients/month for the three hospitals. A 16-month period was planned for including the 160 patients.

This study is currently recruiting participants. Patient recruitment started in January 2015 and we plan to end this study in June 2016.

Assignment of interventions

Sequence generation

We will use a computer-generated, permuted-block randomisation sequence for anaesthesia allocation with two block sizes randomly varied. The random sequences will be stratified by centre (and by dental arch for the parallel-arm RCT). For the split-mouth RCT, the patient will be randomised to receive (1) at the first visit, conventional infiltration anaesthesia and, at the second visit, intraosseous anaesthesia or (2) at the first visit, intraosseous anaesthesia and, at the second visit, conventional infiltration anaesthesia. For the parallel-arm RCT, the patient will be randomised to receive (1) conventional infiltration anaesthesia or (2) intraosseous anaesthesia.

Allocation concealment mechanism

The operator will obtain each randomisation allocation via a centralised, secure web-based interface (RandoWeb). The sequence is thus concealed until the intervention is assigned.

Blinding

Operators cannot be blinded to the randomisation because of the different material used for the two anaesthesia techniques. However, patients will be unaware of which of the two techniques is being used. Thus the blinding is incomplete, but the primary outcome—pain reported by the patient—is not likely affected by lack of blinding of the operator.

Data collection and management

Local investigators will collect the data using a paper form (see data collection forms in online supplementary files, texts S5, S6). The form was pilot tested by the coordinating centre. All outcomes will be measured according

to standardised instruments and processes. Data will be entered electronically by the coordinating centre after transmission of the paper forms. Participant files will be stored in a secure and accessible place and manner.

STATISTICAL METHODS

The unit of analysis will be the tooth for the split-mouth RCT (two permanent first molars belonging to the same dental arch treated per patient) and the patient for the parallel-arm RCT (only one permanent first molar treated per patient). We will compare pain mean scores according to the VAS and mean latency between anaesthesia with conventional injection and intraosseous anaesthesia. We will report the mean differences between groups and the associated 95% CIs. For the split-mouth RCT, with each patient being his or her own control, our statistical analysis will take into account the paired nature of data and the results will be analysed by Student t test for paired samples. We will also compare intervention effect estimates between the split-mouth and parallel-arm RCTs. The analyses will follow the intent-to-treat principle.[20]

Monitoring

A Data Monitoring Committee is not needed because of the short duration of patient participation and known minimal risks. We did not plan any interim analysis or early stopping. Adverse events will be collected and reported according to the usual reported system of the sponsor. Audits may be mandated by the trial sponsor (Assistance Publique—Hôpitaux de Paris) and, if carried out, will be independent of the investigators.

DISCUSSION

To the best of our knowledge, this study is the first to include a split-mouth RCT as well as a parallel-arm RCT to assess how children and adolescents evaluate and accept intraosseous anaesthetic injections. Conducting the two types of trials allows for including all patients meeting inclusion criteria: indeed, patients who do not have symmetrical disorders and therefore are not eligible for the split-mouth RCT are included in the parallel-arm RCT. Consequently, during the period of patient inclusion for the split-mouth RCT, we will also enrol patients for the parallel-arm RCT and thus will not lose eligible patients. Finally, if the two types of trials provide similar results, we can combine the findings of the split-mouth RCT together with those of the parallel-arm RCT in a meta-analysis, which allows for use of all available evidence.

The ease in using the QuickSleeper system is significant for the practitioner, who does not have to stay focused on the amount of pressure needed for the anaesthetic injection and does not need to use force. Moreover, every practitioner knows that pain due to anaesthesia is a failure factor of healthcare. Thus, if trial results show reduced pain with the QuickSleeper system compared with conventional anaesthesia application, clinicians will be helped by evidence-based recommendations concerning the choice of local anaesthesia technique for children and adolescents. For patients, the results may lead to reduced pain during anaesthesia and thus reduced anxiety for healthcare.

ETHICS AND DISSEMINATION

Research ethics approval

Our study protocol received approval from the French ethics committee for the protection of people (Comité de Protection des Personnes, Ile de France I, trial number 13 466) in February 2014, and will be conducted in full accordance with accepted ethical principles (protocol issue date: 8 November 2013, ID number: 2013-A01580-45).

Local investigators will seek verbal consent to participate from children and their parents or guardians. Written information documents will be given to the children and to their parents or guardians. The ethics committee has approved these written summaries (see online supplementary files, texts S1–S4).

The protocol was also approved by the national French authorities regulating confidentiality (Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé, number 14.217)

We will communicate any important protocol modification to the ethics committee (Comité de Protection des Personnes, Ile de France I) and to the trial sponsor (Assistance Publique—Hôpitaux de Paris), and we will report them on ClinicalTrials.gov.

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Contributors All the authors have contributed to the design of the study and the preparation of the draft manuscript. VS-F and FC co-conceived the study, designed the study materials, and applied for ethics, NHS research and development approvals. VS-F conceived the study and its design, participated in its coordination and drafted the protocol in accordance with the International Conference on Harmonisation (ICH) E9 guidelines,[21] the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement,[22] the CONSORT Statement extension for nonpharmacologic treatments,[23] the CONSORT statement extension for abstracts[24] and the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 statement.[25] MM-B and J-LS participated in the methods development and design of the study. All the authors read and approved the final manuscript, and will have access to the final trial dataset.

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Competing interests None declared.

Ethics approval French ethics committee for the protection of people (Comité de Protection des Personnes, Ile de France I, trial number 13466).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The authors will share the data on a platform such as DRYAD.[26]

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