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Does adding clonidine to local anesthetic reduce pain and emergence agitation (confusion and aggression that can occur when a person is coming round from general anesthesia) in children and young adults undergoing cleft lip and cleft palate repair surgery?

Submission date
19/12/2019

Recruitment status
No longer recruiting

Registration date
16/01/2020

Overall study status
Completed

Last Edited
05/02/2020

Condition category
Surgery

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Cleft lip and palate is caused in early development of a fetus when the two sides of the face do not join properly. This leaves a gap in the upper lip and/or the roof of the mouth, which can make it difficult for a child to eat and speak, as well as being potentially disfiguring. Clefts can be repaired surgically.
The idea for this study originated from volunteers of Operation Smile (a charity that provides cleft lip and palate repair surgery). They noticed that emergence agitation (confusion and aggression that can occur when a person is waking up from a general anesthetic) was associated with complications after surgery. Cleft repair surgery can be a painful procedure that might need high doses of opioid pain relief during and after surgery. Opioid treatment has its own potential side effects including sedation (reduced consciousness), drowsiness, nausea and breathing problems.
All participants received general anesthesia so that they were unconscious during the surgery and regional anesthesia (a technique that involves numbing the part of the face that will be operated). This study aims to investigate whether adding clonidine (a drug with pain-relieving and sedating properties) to the local anesthetic solution used for regional anesthesia is associated with better results after surgery in terms of reducing emergence agitation and complications.

Who can participate?
Children and young adults aged over 6 months who need cleft lip and/or palate repair surgery

What does the study involve?
The participants were randomly allocated to one of two groups. Both groups received cleft repair surgery as usual following general anesthesia and a regional anesthesia technique (a technique that involves numbing the part of the face that will be operated). One group received only a local anesthetic drug as local anesthesia solution and the other received local anesthesia and clonidine as part of this solution. The researchers recorded how many patients had complications and emergence agitation as well as how much opioid pain relief they needed in each group.

What are the possible benefits and risks of participating?
It is possible that clonidine will reduce pain and complications, so patients in that group might benefit. All patients in the study are expected to benefit from cleft repair surgery, but they are also at risk of the pain and complications that can follow this surgery.

Where is the study run from?
Operation Smile (USA)

When is the study starting and how long is it expected to run for?
November 2013 to October 2014

Who is funding the study?
Operation Smile (USA), the Government of Assam (India), the National Rural Health Mission (India) and the Sir Dorabji Tata Trust (India)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
19.03.2014

Study information

Scientific Title
Clonidine as an adjuvant to bupivacaine for suprazygomatic maxillary nerve blocks in cleft lip and palate repair. A randomized, prospective, double-blind study

Study objectives
Clonidine as an adjuvant to bupivacaine for suprazygomatic maxillary nerve blocks in cleft lip and palate repair might reduce the incidence of emergence agitation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/03/2014, Operation Smile India Institutional Ethics Committee (Mumbai, India; no telephone number; no email address), no reference number

Study design
Single-centre randomized prospective double-blind study

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Please see attached files for participant information sheets in Assamese and English.

Health condition(s) or problem(s) studied
Suprazygomatic maxillary nerve block in cleft lip and palate repair

Interventions

Patients were randomized after general anesthesia induction using a computerized randomized sequence in a 1:1 ratio in two parallel arms to receive bilateral suprazygomatic maxillary nerve blocks with either a bupivacaine/clonidine mixture for the clonidine group (CLG) or bupivacaine alone in the control group (CG).

Following aseptic preparation of the skin, the suprazygomatic maxillary nerve blocks were performed by an independent anesthesiologist using a 27-gauge 38-mm needle. The needle was first inserted at the frontozygomatic angle, perpendicular to the skin, and advanced until the greater wing of the sphenoid was contacted. The needle was then partially withdrawn, reoriented in an anteroinferior direction (20° anterior and 10° inferior) and advanced 35-38 mm. Local anesthetic solution was injected following negative aspiration at 0.15 ml/kg (maximum of 5 ml per side). The CG received bupivacaine 0.25% with epinephrine 1:200,000. Clonidine 3 mcg /kg (maximum 150 mcg) was added to the anesthetic solution in the CLG.

Fentanyl 0.5 mcg/kg IV was given to treat elevations in BP or HR (>20% above baseline) which was repeated after 5 minutes if hemodynamics did not improve. After two doses of fentanyl, 50-100 mcg/kg of intravenous nalbuphine were administered if tachycardia or hypertension were persistent.

Propofol 1 mg/kg IV was given to treat emergence agitation (EA) immediately after extubation.

Intravenous nalbuphine (50 mcg/kg) was given every 15 minutes as rescue analgesia until pain score was ≤3/10.

Intervention Type
Procedure/Surgery

Primary outcome measure
Emergence agitation. Trained nurses scored the child’s level of agitation using the Watcha scale every 15 min during the first 45 min post-anesthesia. The Watcha Scale is a four-point scale with the highest overall sensitivity and specificity. A child with a score of >2 can be considered to have emergence agitation or delirium.

Secondary outcome measures
1. Pain score assessed at 0, 15, 30, 45, 60 min (every 15 min during the first hour), 90, 120, 150, 180 min (every 30 minutes until the patient was discharged from PACU), and at 4, 8, 12, 16, 20 and 24 h. The FLACC scale (Face, Legs, Activity, Cry, Consolability) was used to assess pain intensity in pediatric patients unable to report pain for themselves. In older patients pain was assessed using a numerical scale from 0 to 10 or by visual analogue scale (VAS), depending on patient characteristics.
2. Perioperative opioid use assessed by reviewing the anesthesia sheet and the patient's records during the entire perioperative period
3. Intraoperative hemodynamics assessed using anesthesia monitoring (non-invasive blood pressure and heart rate) by reviewing anesthesia records during the intraoperative period
4. Respiratory complications during the first 24 h assessed using SpO2 and clinical assessment during the postoperative period in the PACU and ward
5. Nerve block-related complications during the first 24 h assessed using intraoperative monitoring (local anesthetics toxicity and clonidine side effects), and clinical assessment (numbness, vascular puncture, aspiration test, hematoma formation, eye deviation, excessive drooling). Residual block-related complications were assessed at a 30-day follow-up visit by clinical assessment (hematoma formation, numbness, infection).

Postoperative assessments were performed every 15 min during the first hour, every 30 min until the patient was discharged from PACU, and every 4 h during the first 24 h postoperatively. Residual block-related complications were assessed at a 30-day follow-up visit.

Overall study start date
15/11/2013

Completion date
31/10/2014

Eligibility

Key inclusion criteria
1. Children or young adults aged 6 months or older
2. Scheduled for cleft lip or cleft palate surgery under general anesthesia between September and October 2014

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
124 patients were included.

Total final enrolment
124

Key exclusion criteria
1. Lack of consent from patients or their parents
2. Allergy to local anesthetics
3. Coagulation disorders
4. Local infection or lesion at the proposed puncture site
5. Language difficulties
6. Cognitive disorders

Date of first enrolment
01/09/2014

Date of final enrolment
30/09/2014

Locations

Countries of recruitment
India

Study participating centre
Guwahati Comprehensive Cleft Care Center (GC4)
Mahendra Mohan Choudhury Hospital
Guwahati
India
781001

Sponsor information

Organisation
Operation Smile

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Sponsor type
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Funder(s)

Funder type
Charity

Funder Name
Operation Smile

Funder Name
Government of Assam

Funder Name
National Rural Health Mission

Funder Name
Sir Dorabji Tata Trust

Results and Publications

Publication and dissemination plan
Preliminary data for this study were presented as a poster presentation at the SPPM 4th Annual Meeting, March 2, 2017, in Austin, TX and at the ESRA-SPAIN 23rd Annual Meeting, September 27-29, 2017, in Madrid, Spain. The abstract won the Bosenberg Regional Anesthesia Award at the 2017 meeting of SPA/AAP Pediatric Anesthesiology, March 3-5, 2017, Austin, TX.
The results are also planned to be published in an anesthesia or craniofacial surgery journal.

2017 poster and abstract presented at Pediatric Anesthesiology 2017 (part of the Society for Pediatric Pain Medicine 4th Annual Meeting) in http://www2.pedspainmedicine.org/meetings/2017winter/guide/posters/uploads/545--BOS-1.pdf and http://www5.pedsanesthesia.org/meetings/2017winter/guide/posters/abstract.iphtml?id=545&tbs=3

Intention to publish date
30/01/2020

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet		08/01/2020	05/02/2020	No	Yes
Participant information sheet		08/01/2020	05/02/2020	No	Yes