IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 2 Ser.19 (February. 2020), PP 09-13
www.iosrjournals.org

Comparative study of Different Doses of Oral Transmucosal Fentanyl Citrate for Preoperative Sedation in Paediatric Patients Undergoing Patent Ductus Arteriosus ligation

Vikas Gupta[1], Puja Vimesh[2], RasmeetKour[3]
[1]*Lecturer Cardiothoracic Anaesthesiology,GovtSuperspeciality Hospital Jammu*
[2]*Associate Professor & Head,Department of Cardiothoracic Anaesthesiology,GovernmentSuperspeciality Hospital, ,Jammu*
[3]*Lecturer , Department of Cardiothoracic Anaesthesiology,Govt. Superspeciality Hospital, ,Jammu*
Corresponding Author: Puja Vimesh, Associate Professor & Head,Department of Cardiothoracic Anaesthesiology, GovernmentSuperspeciality Hospital, ,Jammu

Abstract
Oral Transmucosal Fentanyl Citrate (OTFC) is a labelled Paediatric Sedative. These are available in different colours for different doses and sweetener added to these so that the children suck these easily. Doses greater than 20 micrograms/Kg are associated with a high incidence of postoperative nausea and vomiting and respiratory depression. We studied the safety and efficacy of OTFC in different doses compared with placebo group.
Method: *Sixty patients of ASA I and II for Patent Ductus Arteriosus Ligation were randomized into three equal groups.Children between age four to ten years were included in the study. Those patients having associated other congenital cardiac anomalies and history of hypersensitivity to the drug used for study were excluded from the study.*
Children were randomized into three groups.OTFC were given 40 minutes before start of surgery.
Group I : OTFC Lollipop 10-15micrograms/Kg
Group II: OTFC Lollipop 15-20 micrograms/Kg
Group III : Placebo Lollipop
Result: *Sedation was maximum in group II patients with mild respiratory depression. Group I showed no preoperative activity at separation of Child from Parents, introduction of intravenous canula and putting anaesthesia mask on patient.There was minimal respiratory depression.Recovery times were similar in the three groups.. Preoperative Pruritis, nausea &vomitingoccurred significantly more in Group II as compared to Group I.*
Conclusion: *OTFC in the dose of 10-15 micrograms/Kg was effective to reduce preoperative activity of child at separation from parents to Operartion Theatre, introduction of intravenous canula and putting anaesthesia mask on patient as compared to Placebo Group.*
Key words: *Oral Transmucosal Fentanyl Citrate Lollipop, Premedication ,Paediatric Patients , Patent ductus arteriosus ligation*

Date of Submission: 18-02-2020 Date of Acceptance: 02-03-2020

I. Introduction

The goals of preanesthetic medication in children include allaying patient anxiety and facilitating the induction of anaesthesia. The Fentanyl Citrate Lollipops were developed and used as preanaesthetic medication as well as analgesic before painful diagnostic and therapeutic procedures (1,2)

The present study was undertaken to compare dose of oral transmucosal Fentanyl 10-15 microgram/Kg Lollipops and 15-20 microgram/Kg Lollipops to Placebo Lollipops with preoperative sedation, anxiety ,cooperation, preanaesthtic induction and side effects.

II. Material and Methods

This study was conducted in the department of Cardiothoracic Anaesthesiology and Intensive Care Unit of Government Superspeciality Hospital, Government Medical College Jammu, a tertiary care hospital during March 2014 - October 2018. All the patients of isolated Patent Ductus Arteriosus with American Society of Anaesthesiologists (ASA) status I and II admitted for Ligation of Patent Ductus Arteriosus were included in

the study. All the parents of patients were informed about the purpose of the study and written consent was obtained from them after seeking approval from the hospital ethics committee to conduct this study.

Randomization:

The patients in the study were randomized to receive either OTFC Lollipops 10-15 ug/kg, 15-20 u/kg or Placebo Lollipops. The procedure was performed with the help of table of random numbers.

Sample size:

20 patients in each group

Each child accompanied by his/her parents approximately 40-60 minutes before scheduled Operation was brought to the Holding area adjacent to the operating Room.Following examination of patient's oral mucosa, baseline systolic and diastolic blood pressure,heartrate,respiratory rate and oxygen saturation were measured. Patient then received either the placebo, 10-15ug/kg or 15-20ug/kg dose of OTFC unit lollipops and were asked to suck these rapidly without biting or chewing; the time of their complete consumption was recorded.

The SpO2 was continuously measured ,the heart rate, systolic and diastolic blood pressure ,and respiratory rate were remeasured every 10 minutes throughout the preanaesthetic evaluation period until the children were taken to Operating Room. Activity, Anxiety, and Cooperation Scores ,evaluating the effectiveness of the premedication as per scoring system(Table 1) ECG electrodes and pulse oxymeter were attached for monitoring Heart rate and oxygen saturation. An intravenous canula of appropriate size was inserted in the right dorsum of the hand and intravenous infusion of Isolyte P was started.Anaesthesia was induced with incremental doses of sevoflurane (1-8%) and nitrous oxide (60%) in Oxygen via facemask. Ventialtion at first was spontaneous, then assisted ,and finally controlled as the patient lost consciousness. Speed of induction , as determined every 15 to 20 seconds from start of induction to the loss of consciousness was recorded. The presence of airway obstruction, secretions and laryngospasm if any were recorded. Intravenous Ondansetron 2 mg followed by 0.5-1 mg of midazolam , tramadol 1mg/Kg were given. Induction started with intravenous Propofol 2mg/Kg ,once the eye lash reflex was abolished intravenous Vecuronium 0.08mg/Kg was given and patient was ventilated with with Sevoflurane 1% and Oxygen 100%. Patient was intubated with appropriate sized endotracheal tube. Right radial artery was canulated for arterial tracing. Patient was catheterized for monitoring Urine output. Chest opened by left postero-lateral Thoracotomy. Systolic Arterial Blood Pressure was brought down to 60-70 mm of Hg with the help of titrated doses of intravenous Nitroglycerine (NTG) using Infusion pump. Patent Ductus Arteriosus was dissected and looped with number 1 Silk and Triple ligation done at systolic pressure of 50 mm Hg.Blood Pressure maintained at preoperative level by titrating the NTG. Intercostal nerve block given intraoperatively using preservative free 2% Lignocaine (not to exceed 5mg/Kg diluted with normal saline). Chest was closed and patient put back to supine position. All inhalational agents except for Oxygen 100% were stopped. Reversal with neostigmine and glycopyrrolate (according to the weight), the child was extubated once the patient fulfilled the weaning criteria.

The incidences and times of occurrences of Pruritis and nausea (as volunteered by the patient) and vomiting were recorded in preoperative Holding Area, Operation Theatre.

Data were analysed for statistical significance using Chi Square test.

III. Result

Data from 60 patients were evaluated, 20 received OTFC Lollipop 10-15 ug/Kg (Group I), 20 received OTFC Lollipop 15-20 ug/Kg (Group II), and 20 received a placebo Lollipop (Group III) The groups were comparable with respect to age ,weight,sex distribution, ASA physical status distribution, baseline vital signs and oxygen saturation and duratioin of anaesthesia.

All oral mucosal observations before and after consumption of OTFC and placebo units were recorded as normal.

Mean arterial pressure,heart rate and respiratory frequency did not change significantly overtime in all the three groups. Oxygen satuaration in group I and III did not decrease significantly from baseline to measurement taken 30 minutes later;however the mean Oxygen saturation for the three groups never decreased to less than 96% exceptfor 2 patients in OTFC group II.

In Preoperative Holding Area at the end of 40 minutes there were 4 children in Group I, 2 in Group II and 15 in Group III who were Irritable ,Crying and uncooperative with p value less than .001 which was highly significant.(Table 2) Pruritus was observed in 14 children in Group II and in 7 patients in Group I while only one child in group III developed Pruritus with p value less than .001 which was highly significant.(Table 3)Preoperative nausea and vomiting was observed in 5 children in group I,13 in group II and 2 in group III which was also considered highly significant as p value was less than .001.(Table 4)

In Operation Theatre before Induction there were 2 children in Group I, 4 in Group II and 9 in Group III who were Irritable ,Crying and uncooperative with p value less than .03 which was significant.(Table 5) Pruritus was observed in 8 children in Group II and in 4 patients in Group I while only one child in group III developed Pruritus with p value less than .02 which was significant.(Table 6)

Nausea and vomiting was observed in 3 children in group I,7 in group II and 1 in group III which was also considered significant as p value was less than .04 (Table 7)

Table 1
Scoring Schedule for Preoperative Activity (Sedation), Anxiety, cooperation, Anaestheticinduction,and emergence
Preoperative Activity
1. Asleep,not readily arousable
2. Asleep,slowly responds to verbal command
3. Drowsy,readily responds to verbal Commands
4. Awake,calm and quiet
5. Awake and active

Preoperative Anxiety
1. None
2. Little(demonstrates some fear or uneasiness but does not cry)
3. Moderate(clearly fearful,cries but becomes quiet with reassurance)
4. Excessive(crying,uncooperative,does not become quiet with reassurance)

Preoperative cooperation
1. Cooperative
2. Mildly resistant
3. Resistant

Induction
1. Excellent(patient unafraid,fullycooperative,compliant,not at all resistant;an uneventful induction)
2. Good (mostly cooperative,compliant,some anxiety or crying but becomes quiet with reassurance)
3. Fair(moderate fear of crying,not quiet with reassurance)
4. Poor(combative,crying,resistant,need for restraint;a stormy induction

Emergence
1. Quiet
2. Occasional crying
3. Crying but able to be quited
4. Thrashing,unable to be quieted

Table 2: Preoperative Irritable and Crying Children with different doses of OTFC Lollipops at end of 40 minutes in Preoperative Holding Area

	GroupI(n20) 10-15ug/kg		Group II(n20) 15-20ug/kg		GroupIII(n20) Placebo	
	n	%	n	%	n	%
Crying&Uncooperative	4	25	2	10	15	75
Crying absent	16	80	18	90	5	25

Statistical Inference Chi Square 21.5 p<.001,Highly Significant

Table 3: Preoperative Pruritus with different doses of OTFC Lollipops at end of 40 minutes in Preoperative Holding Area

	GroupI(n20) 10-15ug/kg		Group II(n20) 15-20ug/kg		GroupIII(n20) Placebo	
	n	%	n	%	n	%
Pruritus present	7	35	14	70	1	5
Pruritus absent	13	65	6	30	19	95

Statistical Inference Chi Square 18.2 p<.001,Highly Significant

Table 4: Preoperative Nausea and Vomiting in Children with different doses of OTFC Lollipops at end of 40 minutes in Preoperative Holding Area

	GroupI(n20) 10-15ug/kg		Group II(n20) 15-20ug/kg		GroupIII(n20) Placebo	
	n	%	n	%	n	%
Nausea & Vomiting present	5	25	13	65	2	10
Nausea &Vomiting absent	15	75	7	35	18	90

Statistical Inference Chi Square 14.5 p<.001,Highly Significant

Table 5: Relationship of different factors with OTFC Lollipops & Placebo in Operation Theatre before induction

	GroupI(n20) 10-15ug/kg		Group II(n20) 15-20ug/kg		GroupIII(n20) Placebo	
	n	%	n	%	n	%
Crying&Uncooperative	2	10	4	20	9	45
Crying absent	18	90	16	80	11	55

Statistical Inference Chi Square 6.93 p<.03, Significant

Table 6

	GroupI(n20) 10-15ug/kg		Group II(n20) 15-20ug/kg		GroupIII(n20) Placebo	
	n	%	n	%	n	%
Pruritus present	4	20	8	40	1	5
Pruritus absent	16	80	12	60	19	95

Statistical Inference Chi Square 7.26 p<.02, Significant

Table 7

	GroupI(n20) 10-15ug/kg		Group II(n20) 15-20ug/kg		GroupIII(n20) Placebo	
	n	%	n	%	n	%
Nausea & Vomiting present	3	15	7	35	1	5
Nausea &Vomiting absent	17	85	13	65	19	95

Statistical Inference Chi Square 6.23 p<.04, Significant

IV. Discussion

An Ideal premedicant for patients undergoing Patent Ductus Arteriosus ligation would relieve preoperative anxiety,provide sedation, facilitate induction of anaesthesia,and be dispensed easily by the health care personnel and have minimal side effects.

Oral Transmucosal Fentanyl is a sweetened solid matrix mounted on a handle.The Fentanyl lollipops are available in 200ug(Grey), 400ug(green),600ug(red),800ug(pink),1200ug(yellow) and 1600ug(orange). 25% of the total dose of fentanyl lollipop is rapidly absorbed across the buccal mucosa for the early onset of anxiolytic and analgesic effect.The optimum dose of OTFC as a premedicant is frequently quoted as 15-20ug/kg (3,4,5),although some authors recommended 10-15ug/kg(6). Several studies have compared OTFC with placebo and found it produced significantly less perioperative anxiety(6-11)

We chose to compare OTFC 10-15ug/kg and 15-20ug/kg with placebo. There have been two main concerns raised regarding the use of OTFC, namely the incidence of respiratory depression and vomiting. An effective antiemetic would enable children to have a lower incidence of postoperative vomiting.

There was no clinically significant respiratory depression in our study.Studies which have reported respiratory depression have used OTFC with doses more than 20ug/kg(3,12) and/or used in cardiac patients(7,12), including children with cyanotic heart disease.

Clinically no significant problems were noted with smaller doses i.e. less than 20ug/kg (,6,8,i0,11,13)

The incidence of nausea and vomiting has been vary variable.As with all other opiates OTFC can cause vomiting and again the incidence seems to be dose related(3,14,15) with greater incidence at doses more than 20ug/kg(16,17)

In our study we found that preoperative nausea and vomiting with OTFC in group I & II were 25%,65% while group III (Placebo) it was 10%,which was highly significant p value <.001.

Pruritus in Preoperative Holding Area in group I was 35%,group II 70% and Group III 5%.This was also highly significant p value <.001.

The ideal paediatricpremedicant should be acceptable or preferably appealing to children.It should have a predictable onset and a reliable anxiolytic effect . It should be safe and have no ,or minimal, upsetting side effects and cause no postoperative sequelae. OTFC goes a long way in fulfilling these requirements.

In our study we found that OTFC 10-15ug/kg was safe and have minimal side effects and may be particularly useful in children who are uncooperative and transbuccal route of absorption offers an advantage in extremely anxious children who are prone to retching and vomiting especially after an unpleasant tasting premedicant (18)

References

[1]. Schecter NL, Weisman SJ, Rosenblum M, et al. The use of oral transmucosal fentanyl citrate for painful procedures in children. Paediatr 1995;95:335-39

[2]. Schutzman SA, Liebelt E, Wisk M, Burg J. Comparison of oral transmucosal fentanyl citrate and intramuscular mepridine,promethazine,and chlorpromazine for conscious sedation of children undergoing laceration repair. Ann Emerg Med 1996;28:385-90

[3]. Streisand, JB, Stanley, TH, Hague, B, Van Vreeswijk, H, Ho, GH, Pace, NL. Oral transmucosal fentanyl citrate premedication in children. *Anesthesia and Analgesia*1989; 69: 28– 34.

[4]. FradkinDM,Scott-Warren VL, Vashisht R, Rolfe SE. An Evidence Based Guideline for the Preoperative Sedation of Children. J Pediatr Neonatal Care 2015;2(6)

[5]. KarSK,Ganguly T, Dasgupta C.S, et al.Preoperative Anxiety in Pediatric Population: Anesthesiologist's Nightmare. Transl Biomed.2015,6:4

[6]. Ashburn, MA, Streisand, JB, Tarver, DS, *et al.*Oral transmucosal fentanyl citrate for premedication in paediatric outpatients. *Canadian Journal of Anaesthesia*1990; 37: 857– 66.

[7]. Freisen, RH, Carpenter, E, Madigan, CK, Lockhart, CH. Oral transmucosal fentanyl citrate for pre-anaesthetic medication of paediatric cardiac surgery patients. *Paediatric Anaesthesia*1995; 5: 29– 33.

[8]. Nelson, PS, Streisand, JB, Mulder, S, Pace, NL, Stanley, TH. A comparison of oral transmucosal fentanyl citrate and an oral solution of meperidine, diazepam and atropine for premedication in children. *Anesthesiology*1989; 70: 616– 21.

[9]. Feld, LH, Champeau, MW, Van Steennis, CA, Scott, JC. Pre-anesthetic medication in children. A comparison of oral transmucosal fentanyl citrate vs. placebo. *Anesthesiology*1989; 71: 374–77.

[10]. Freisen, RH, Lockhart, CH. Oral transmucosal fentanyl citrate for pre-anesthetic medication of pediatric day surgery patients with and without droperidol as a prophylactic anti-emetic. *Anesthesiology*1992; 76: 46– 51.

[11]. Stanley, TH, Leiman, BC, Rawal, N, *et al.*The effects of oral transmucosal Fentanyl citrate premedication on pre-operative behavioural responses and gastric volume and acidity in children. *Anesthesia and Analgesia*1989; 69: 328– 35.

[12]. Goldstein-Dresner, MC, Davis, PJ, Kretchman, E, Siewers, RD, Certo, N, Cook, R. Double-blind comparison of oral transmucosal fentanyl citrate with oral meperidine, diazepam, and atropine as pre-anesthetic medication in children with congenital heart disease. *Anesthesiology*1991; 74: 28– 33.

[13]. Schechter, NL, Weisman, SJ, Rosenblum, M, Bernstein, B, Conard, PL. The use of oral tansmucosal fentanyl citrate for painful procedures in children. *Pediatrics*1995; 95(3): 335– 39.

[14]. Epstein, RH, Mendel, HG, Witkowski, TA, Waters, R, Guarniari, KM, Marr, AT, Lessin, JB. The safety and efficacy of oral transmucosalfentanyl citrate for pre-operative sedation in young children. *Anesthesia and Analgesia*1996; 83: 1200–05.

[15]. Steisand, JB, Busch, MA, Egan, TD, Smith, BG, Gay, M, Pace, NL. Dose proportionality and pharmacokinetics of oral transmucosal fentanyl citrate. *Anesthesiology*1998; 88: 305– 09.

[16]. Stanley, TH, Hague, B, Mock, DL, *et al.*Oral transmucosal fentanyl citrate (lollipop) premedication in human volunteers. *Anesthesia and Analgesia*1989; 69: 21– 27.

[17]. Streisand, JB, Hague, B, Van Vreeswijk, H, *et al.*Oral transmucosal fentanyl premedication in children. *Anesthesia and Analgesia*1987; 66: S1– S191.

[18]. Reitz, CS, Tobias, J. Anesthetic management of children with recurrent viral laryngeal papillomatosis: a case report. *Journal of American Association of Nurse Anesthetists*1996; 64 (4): 362–68.

Puja Vimesh,etal."Comparative study of Different Doses of Oral Transmucosal Fentanyl Citrate for Preoperative Sedation in Paediatric Patients Undergoing Patent Ductus Arteriosus ligation." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(2), 2020, pp. 09-13.