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Comparative Evaluation of Oral Transmucosal Fentanyl Citrate and Nasal Transmucosal Midazolam Spray as Premedication in Children

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Abstract

Context: Premedication is an integral part of anaesthetic management. An ideal premedicant drug is anxiolytic, analgesic, sedative and amnestic. It should fulfill the aims of premedication, be safe for the patient and be easily administered.

Aims: To evaluate and compare the efficacy of oral transmucosal fentanyl citrate lollipop and intranasal midazolam spray as a premedication in children by a non-invasive route and to evaluate post-operative sedation score.

Settings and design: Our study was conducted in Government Medical College, Jammu, J&K. It was a comparative clinical trial done in 3 groups (40 subjects in each). The study was approved by the Ethical committee of the Institute.

Methods and material: Children aged 5 to 10 years undergoing surgery in general anaesthesia were included in our study. Informed written consent was obtained from the parents of each child before adding the child in the study.

Statistical analysis used: Data was collected on 120 children. Variables were reported as mean and standard deviation. The difference in mean values across the groups was assessed by One-Way Analysis of Variance (ANOVA). Statistical significance of qualitative variables was assessed with the use of chi-square test. Intergroup comparisons were made post-hoc by Bonferroni's t-test.

Results: Children who were given oral transmucosal fentanyl citrate (15 µgm/kg) were better sedated in the pre-operative period, had less apprehension at venipuncture, had better mask acceptance, were calmer at emergence and post-operative period, as compared to those who were given nasal transmucosal midazolam spray (0.2 mg/kg) or nasal saline spray.

Conclusions: It was concluded that oral transmucosal fentanyl citrate, in the dose of 15 µg/kg, is superior to nasal transmucosal midazolam spray (0.2 mg/kg) in providing preoperative sedation, decreasing anxiety at the time of placement of anaesthesia mask and intravenous cannulation and lowering the level of agitation at emergence.

Keywords: General anaesthesia; Premedication; Children

Introduction

Children suffer from severe anxiety and apprehension when they are separated from their parents or family members for the induction of anaesthesia. Fear of a child is accentuated by many factors like separation from parents, operation equipments, operation theatre lights, face masks and intravenous cannulation and may affect the smoothness of induction, emergence from anaesthesia. An ideal premedicant drug should be anxiolytic, analgesic, sedative and amnestic. It should be safe, easy to administer and should not produce undue depression of cardiovascular, respiratory and central nervous systems. Special care should be taken in extremes of age that is in children and elderly patients. There are several non-pharmacological means to minimize child's anxiety like preadmission tours, videos and preoperative clinic visits by the anaesthesiologist to establish rapport with the child. Pharmacological agents are more efficient to provide sedation and promote smooth induction. Sedative premedication is often helpful in this regard. Oral premedication decreases patient anxiety on induction significantly more than parental presence.

Subjects and Methods

The present study was conducted to compare the efficacy of oral transmucosal fentanyl and nasal transmucosal midazolam as premedicants in children, after attaining approval of the Ethical Committee of the institute. The study included 120 children of either sex aged between 5-10 years belonging to ASA grade I and II undergoing elective surgery under general anaesthesia. An informed written consent was signed by each parent before including the participant in the study.

Exclusion criteria

1. History of hypersensitivity to any of the study drugs.
2. Developmental delay.
3. History of chronic illness.
4. Children who refuse to take the drug.

Children were randomly allocated either of the study groups so as to minimise chances of erroronemous results. All the patients, Irrespective of the group which they were allotted, were given the

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routine premedication with injection glycopyrrolate 5µg/kg i.m. Hence, every child included in the study received routine premedication regimen used in the institute and those in the study groups, were given additional premedicants (fenatnyl/midazolam).

Children who were taken in group 1, were given oral transmucosal fenatnyl 15 µgm/kg; those in Group 2 were given midazolam nasal spray 0.2 mg/kg and those in Group 3 were given nasal saline spray 0.5 ml/kg.

Each group consisted of 40 children. The study drugs were given 30 minutes before induction of anaesthesia.

Variables like heart rate, blood pressure, SpO_2 and degree of sedation according to a 5-point scale were recorded before administration of the study drug and thereafter at intervals of 10 minutes up to 30 minutes. The child was taken inside the operation theatre at 30 minutes, intravenous line was started and reaction to i.v. cannulation was noted by a 4-point scale [1]. 100% oxygen was given to the child via facemask and the mask acceptance by the child was noted according to a 5-point scale [2]. Preoxygenation with 100% oxygen was done for 3 minutes followed by induction of anaesthesia with injection sodium thiopentone 5 mg/kg i.v. and tracheal intubation was done after giving injection succinylcholine 1.5 mg/kg i.v.

Vitals were noted every 10 minutes intraoperatively and anaesthesia was maintained with nitrous oxide 66%, oxygen 33%, halothane and IPPV. Injection atracurium 0.5 mg/kg i.v. was given as the loading dose and subsequent doses were given as $1/4^{th}$ of the loading dose for muscle relaxation. Analgesia was provided by diclofenac suppository 3 mg/kg body weight after induction of anaesthesia.

At the end of the surgery the child was reversed with injection neostigmine 0.05 mg/kg i.v. and injection glycopyrrolate 0.01 mg/kg i.v. Tracheal extubation was done and the patient was assessed for the level of postoperative agitation using a 4-point scale at emergence and thereafter monitoring of vitals (heart rate, systolic blood pressure, diastolic blood pressure, SpO_2, sedation score) was done every 30 minutes till 6 hours [3].

Plan of analysis

Sedation score and hemodynamic variables were reported as mean and standard deviation and the difference in mean values across the groups was assessed by One-Way Analysis of Variance (ANOVA). Statistical significance of qualitative variables was assessed with the use of chi-square test. Intergroup comparisons were made post-hoc by Bonferroni's t-test. All analysis was in accordance to intention to treatment principal, p-value<0.05 was considered as statistically significant. All 'p' values reported were two-tailed.

Results

The study groups did not vary significantly in terms of statistics with regard to patients' age, weight or the duration for which the surgery continued (Table 1).

Degree of sedation after giving premedication

[SCORE 1=Asleep; not readily arousable, 2=Asleep; responds slowly to verbal commands. 3=Drowsy; readily responds to verbal commands. 4=Awake; calm and quiet. 5=Awake and active] The mean values for sedation score were comparable in the three groups before giving premedication to the children (p-value>0.05) (Table 2).

In group 1, sedation score showed a gradual decrease and was 5 ± 0 at 5 minutes, 4.95 ± 0.22 at 10 minutes, 4.20 ± 0.52 at 20 minutes and 3.70 ± 0.56 at 30 minutes after giving the study drug which was less than the sedation score before administration of the drug (5 ± 0) (Table 3).

In group 2, the sedation score decreased from baseline value of 5 ± 0 to 4.90 ± 0.22 at 5 minutes after premedication to 4.70 ± 0.46 at 10

GROUP	AGE mean ± SD (in years)	Weight mean ± SD (kg)	Duration of surgery (in minutes)
1	6.40 ± 1.42	18.40 ± 2.12	65.96 ± 5.35
2	6.53 ± 1.27	17.93 ± 2.70	68.80 ± 7.50
3	6.60 ± 1.07	18.27 ± 3.05	66.03 ± 7.95
	p-value>0.05	p- value -0.782	p-value-0.08

The mean difference is significant at p-value<0.05 and highly significant at p-value<0.001.

Table 1: Comparison of mean age and mean weight in the three groups.

Variable	Group 1 Mean ± SD	Group 2 Mean ± SD	Group 3 Mean ± SD	p-value	Remarks
Sedation Score	5 ± 0	5 ± 0	5 ± 0	*	*
Heart rate (beats/min)	114.27 ± 17.04	115.40 ± 10.84	119.93 ± 9.13	0.199	NS
SBP (mmHg)	119 ± 11.54	116.87 ± 11.84	115.93 ± 16.21	0.662	NS
DBP (mmHg)	79.67 ± 6.76	75.67 ± 7.20	76.67 ± 7.65	0.080	NS
SpO_2 (%)	99.90 ± 0.30	99.83 ± 0.37	99.87 ± 0.34	0.756	NS

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; SpO_2: % Saturation of haemoglobin with oxygen; NS: Not Significant
The mean difference is significant at p-value<0.05 and highly significant at p-value<0.001.
*Comparison could not be made because of similar values in groups 1, 2 and 3.

Table 2: Comparison of sedation score hr, sbp, dbp and spo_2 in the three groups before giving premedication.

Time (in minutes)	Group 1 Mean ± SD	Group 2 Mean ± SD	Group 3 Mean ± SD	p-value	1versus2	1versus3	2versus3
5	5 ± 0	4.90 ± 0.22	5 ± 0	*	*	*	*
10	4.95 ± 0.22	4.70 ± 0.46	4.97 ± 0.15	<0.001	0.002 (S)	0.60 (NS)	<0.001 (HS)
20	4.20 ± 0.52	4.38 ± 0.59	4.92 ± 0.26	<0.001	O.14(NS)	<0.001(HS)	<0.001(HS)
30	3.70 ± 0.56	4.08 ± 0.66	4.90 ± 0.30	<0.001	0.006(S)	<0.001(HS)	<0.001(HS)

The mean difference is significant at p-value<0.05 and highly significant at p-value<0.001.
*Comparison could not be made because of similar values in groups 1 and 3.

Table 3: Sedation score in the three groups after giving premedication.

Time (in minutes)	Group 1 Mean ± SD (beats/min)	Group 2 Mean ± SD (beats/min)	Group 3 Mean ± SD (beats/min)	p-value	p-value (1 versus 2)	p-value (1 versus 3)	p-value (2 versus 3)
5	94.75 ± 8.92	107 ± 13.90	107 ± 10.46	<0.001	<0.001 (HS)	<0.001(HS)	*
10	93.13 ± 8.75	106 ± 13.70	106.50 ± 11.19	<0.001	<0.001(HS)	<0.001(HS)	0.85(NS)
20	90.55 ± 7.36	105 ± 13.90	106.50 ± 12.24	<0.001	<0.001(HS)	<0.001(HS)	0.60(NS)
30	88.68 ± 6.12	105 ± 13.60	106.90 ± 13.04	<0.001	<0.001(HS)	<0.001(HS)	0.52(NS)

The mean difference is significant at p-value<0.05 and highly significant at p-value<0.001.

Table 4: Significance of heart rate (beats/minute) changes in the three groups after giving premedication.

Time (in minutes)	Group 1 Mean ± SD (mmHg)	Group 2 Mean ± SD (mmHg)	Group 3 Mean ± SD (mmHg)	p-value	p-value (1 versus 2)	p-value (1 versus 3)	p-value (2 versus 3)
5	118.50 ± 8.54	104 ± 10.80	105.50 ± 7.07	<0.001	<0.001(HS)	<0.001(HS)	0.46(NS)
10	117.30 ± 9.14	103 ± 10.80	105 ± 7.62	<0.001	<0.001(HS)	<0.001(HS)	0.34(NS)
20	114.90 ± 8.05	104 ± 10.30	104.70 ± 8.22	<0.001	<0.001(HS)	<0.001(HS)	0.73(NS)
30	114.30 ± 9.4	104 ± 10.50	105.50 ± 9.95	<0.001	<0.001(HS)	<0.001(HS)	0.51(NS)

The mean difference is significant at p-value<0.05 and highly significant at p-value<0.001.
S: Significant; HS: Highly Significant; NS: Not Significant.

Table 5: Intergroup comparison of sbp (mm Hg) at various intervals after giving premedication.

Time (in minutes)	Group 1 Mean ± SD	Group 2 Mean ± SD	Group 3 Mean ± SD	p-value	p-value (1 versus 2)	p-value (1 versus 3)	p-value (2 versus 3)
5	67.55 ± 7.70	62.70 ± 4.54	67.18 ± 5.64	<0.001	<0.001(HS)	0.80(NS)	<0.001(HS)
10	66.25 ± 7.38	62.20 ± 4.38	67 ± 6.67	<0.001	0.003(S)	0.63(NS)	<0.001(HS)
20	63.50 ± 6.91	62.20 ± 4.26	67.20 ± 6.69	<0.001	0.31(NS)	0.01(S)	<0.001(HS)
30	62.98 ± 6.98	61.90 ± 4.3	66.78 ± 7.58	<0.001	0.40(NS)	0.02(S)	<0.001(HS)

The mean difference is significant at p-value<0.05 and highly significant at p-value<0.001.

Table 6: Significance of changes in dbp (mmhg) after giving premedication.

Time (in minutes)	Group 1 Mean ± SD	Group 2 Mean ± SD	Group 3 Mean ± SD	p-value	p-value (1 versus 2)	p-value (1 versus 3)	p-value (2 versus 3)
5	98.90 ± 0.89	100 ± 0.22	99.20 ± 0.82	<0.001 (HS)	<0.001(HS)	0.12(NS)	<0.001(HS)
10	98.70 ± 0.88	99.70 ± 0.51	98.90 ± 0.84	<0.001(HS)	<0.001(HS)	0.29(NS)	<0.001(HS)
20	98.80 ± 0.81	99.80 ± 0.41	98.93 ± 0.79	<0.001(HS)	<0.001(HS)	0.46(NS)	<0.001(HS)
30	98.60 ± 0.70	99.80 ± 0.48	98.98 ± 0.62	<0.001(HS)	<0.001(HS)	0.01(S)	<0.001(HS)

The mean difference is significant at p-value<0.05 and highly significant at p-value<0.001.
S: Significant; HS: Highly Significant; NS: Not Significant.

Table 7: Intergroup comparison of oxygen saturation (%) at various intervals after giving premedication.

minutes. It further decreased to 4.38 ± 0.59 at 20 minutes and finally 4.08 ± 0.66 at 30 minutes after the study drug was given (Table 3).

In group 3, sedation score showed a minimal change from baseline value of 5 ± 0 to at 5 ± 0, 4.97 ± 0.15, 4.92 ± 0.26, 4.90 ± 0.30 at 5, 10, 20 and 30 minutes respectively (Table 3).

On intergroup comparison, it was found that the sedation score at 10 and 20 minutes was significantly lower in group 1 & 2 as compared to group 3.

At 30 minutes, the sedation score came out to be significantly lower in groups 1 than that of group 2 and 3 (Table 3). Therefore, children in group 1 were found to be more sedated than those in group 2 and 3 at 30 minutes after giving premedication.

Haemodynamic parameters after giving premedication

There was no statistically significant difference in heart rate, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and SpO_2 amongst the three groups before administration of the study drugs (Table 2).

In group 1, the mean heart rate decreased from 114.27 ± 17.04 to 94.75 ± 8.92 at 5 minutes and it continued to decrease at 10, 20 and 30 minutes to 93.13 ± 8.75, 90.55 ± 7.36 and 88.68 ± 6.12 respectively from the baseline (Tables 3 and 4).

The mean values for Systolic Blood Pressure decreased from baseline value of 119 ± 11.54 to 118.50 ± 8.54 at 5 minutes, 117.30 ± 9.14 at 10 minutes, 114.90 ± 8.05 20 minutes and 114.30 ± 9.4 at 30 minutes. However, the mean values of systolic blood pressure were higher as compared to those of group 2 (Tables 3 and 5).

DBP also decreased from baseline value of 79.67 ± 6.76 to 67.55 ± 7.70 at 5 minutes, 66.25 ± 7.38 at 10 minutes, 63.50± 6.91 at 20 minutes, 62.98 ± 6.98 at 30 minutes (Tables 3 and 6).

Oxygen saturation showed minimal changes. No case of desaturation was reported (Table 7). In Group 2, the mean HR decreased from 115.40 ± 10.84 to 107 ± 13.90 at 5 minutes and it continued to decrease at 10, 20 and 30 minutes to 106 ± 13.70, 105 ± 13.90 and 105 ± 13.60 respectively from the baseline (Table 4).

The mean values for SBP decreased from baseline value of 116.87 ± 11.84 to 104 ± 10.80 at 5 minutes, 103 ± 10.80 at 10 minutes, 104 ± 10.30 20 minutes and 104 ± 10.50 at 30 minutes (Table 5).

DBP also decreased from baseline value of 75.67 ± 7.20 to 62.70 ± 4.54 at 5 minutes, 62.20 ± 4.38 at 10 minutes, 62.20 ± 4.26 at 20 minutes, 61.90 ± 4.3 at 30 minutes. SpO_2 showed minimal changes. No case of desaturation was reported (Tables 6 and 7).

In group 3, HR values were 119.93 ± 9.13 and showed a decline at 5

Group	Reaction to Intravenous Cannulation Mean ± SD (Score)
1	3.6 ± 0.48
2	2.45 ± 0.6
3	1.67 ± 0.47

p- value<0.001

Table 8: Reaction to intravenous cannulation.

Reaction to Intravenous Cannulation		
Group	**p-value**	**Remarks**
1 versus 2	<0.001	HS
1 versus 3	<0.001	HS
2 versus 3	<0.001	HS

Table 9: Intergroup comparison of reaction to intravenous cannulation.

Group	Mask Acceptance by the child Mean ± SD (Score)
1	1.13 ± 0.33
2	2.58 ± 0.81
3	3.37 ± 0.62
	p-value<0.001

The mean difference is significant at p-value <0.05 and highly significant at p-value<0.001.

Table 10: Mask acceptance by the child.

minutes (107 ± 10.46) and was almost unchanged at 10 minutes (106.50 ± 11.19), 20 minutes (106.50 ± 12.24) and 30 minutes (106.90 ± 13.04) (Table 4).

The mean values of SBP was almost unchanged at 5, 10, 20 and 30 minutes (105.50 ± 7.07, 105 ± 7.62, 104.70 ± 8.22, 105.50 ± 9.95 respectively) which was less than the baseline mean value (115.93 ± 16.21) (Table 5).

The mean DBP decreased from the baseline value of 76.67 ± 7.65 to 67.18 ± 5.64 at 5 minutes, 67 ± 6.67 at 10 minutes, 67.20 ± 6.69 at 20 minutes and 66.78 ± 7.58 at 30 minutes (Table 6).

The mean SpO_2 changed from the baseline value of 99.87 ± 0.34 to 99.20 ± 0.82, 98.90 ± 0.84, 98.93 ± 0.79, 98.98 ± 0.62 at 5, 10, 20 and 30 minutes respectively. No case of desaturation was reported (Table 7).

Reaction to intravenous cannulation: [Score 1=Fight without success; 2=Fight with success; 3=Minor resistance; and 4=No reaction]

The score of reaction to i.v. cannulation was 3.6 ± 0.48 in group 1 which was higher than group 2 (2.45 ± 0.6); it was still higher than group 3 (1.67 ± 0.47). Reaction to i.v. cannulation was best in group 1 (Tables 8 and 9).

Mask acceptance by the child: [Score 1=cooperative, no coaxing; 2=mildly resistant, wears mask with minimal coaxing; 3=moderately resistant, objects placement of mask even with coaxing; 4=markedly resistant, unable to place mask on patient's face despite coaxing

The score was 1.13 ± 0.33 in group 1, it was more in group 2 at 2.58 ± 0.81, still higher in group 3 at 3.37 ± 0.62. Mask acceptance was better with the study drugs when compared to the control group (Table 10).

Intraoperative vitals

Group 1: Gradual decrease in HR was observed. It decreased from 92.2 ± 6.83 at 10 minutes to 86.4 ± 12.3, 86 ± 12.5, 84.2 ± 11.7, 84 ± 11.7 and 84 ± 11.5 at 20, 30, 40, 50 and 60 minutes. SBP decreased from 93.3 ± 7.15 at 10 minutes to 91.9 ± 5.51, 91. 10 ± 6.2, 90 ± 7.49, 89.2 ± 8.09 at 20, 30, 40 and 50 minutes. It increased to 92 ± 7.50 at 60 minutes. DBP showed decline from 10 to 60 minutes (mean values: 59.9 ± 4.78, 60 ± 5.43, 59.4 ± 5.09, 59.3 ± 5.57, 59.1 ± 5.41, 58 ± 5.57) SpO_2 remained stable with mean values of 99.10 ± 0.78, 98.90 ± 0.89, 98.70 ± 0.88, 98.80 ± 0.82, 98.60 ± 0.62 and 98 ± 0.50at 10 to 60 minutes intraoperatively.

Group 2: HR was almost invariable throughout intraoperative period. It was observed to be 109 ± 14.3, 108 ± 12.7, 108 ± 12.9, 109 ± 12, 109 ± 12.5 and 108 ± 12.5 at 10, 20, 30, 40, 50 and 60 minutes. SBP remained stable at 10, 20 and 30 minutes (mean values**:** 108 ± 9.72, 108 ± 9.21**,** 108 ± 10). It was 107 ± 10.9, 110 ± 12 and 110 ± 11 at 40, 50 and 60 minutes. DBP was stabilised throughout intraoperative period (mean values from 10 minutes to 60 minutes: 65.8 ± 4.67, 65.2 ± 5.14, 65.1 ± 5.26, 65.5 ± 5.49, 65.9 ± 6.25, 66 ± 6.60). $SpO_2$was stable with mean values of99.70 ± 0.48, 99.50 ± 0.68, 99.80 ± 0.41, 99.50 ± 0.69, 99.30 ± 0.69 and 99.20 ± 0.55at 10 to 60 minutes intraoperatively.

GROUP 3: HR increased from101.7 ± 12.03 at 10 minutes to 106.9 ± 10.54 at 20 minutes. It was 107.6 ± 11.53, 106.3 ± 11.58, 107.8 ± 12.86 and 108 ± 12.6 at 30, 40, 50 and 60 minutes. SBP was recorded to be 108.7 ± 9.77, 108.2 ± 10.55, 109.1 ± 10.15, 108.4 ± 10.22, 110.4 ± 9.30 and 110.5 ± 10 at 10, 20, 30, 40, 50 and 60 minutes. DBP increased gradually from 10 to 60 minutes intraoperatively (mean values65.80 ± 4.76, 67.43 ± 5.53, 67.38 ± 4.57, 67.86 ± 5.03, 67.48 ± 6.41, 69 ± 6.5) SpO_2 was stable at mean values of 99.70 ± 0.56, 99.80 ± 0.46, 99.64 ± 0.54, 99.72 ± 0.45, 99.68 ± 0.55 and 99.20 ± 0.55 at 10 to 60 minutes intraoperatively.

Emergence score: [1=Excellent (quiet); 2=Good (occasional crying); 3=Fair (crying, but able to be quieted); 4=Poor (thrashing, unable to be quieted]

Emergence score was found to be lowest (1.65 ± 0.62) in group 1 as compared to the other two groups (group 2-2.20 ± 0.85 and group 2-3.35 ± 0.62). Emergence score was found best in group 1. All the groups had significant difference in the emergence score (Tables 11 and 12).

Postoperative sedation: [1=Asleep; not readily arousable; 2=Asleep; responds slowly to verbal commands; 3=Drowsy; readily responds to verbal commands; 4=Awake; calm and quiet; 5=Awake and active]

Group 1, 2 and 3 showed minimal sedation in postoperative period. However, children in group 1 were far more comfortable and calm as compared to the other two groups.

Group 1 Mean ± SD	Group 2 Mean ± SD	Group 3 Mean ± SD
1.65 ± 0.62	2.20 ± 0.85	3.35 ± 0.62

p-value<0.001.

Table 11: Emergence score after surgery (postoperatively).

Emergence Scores postoperatively		
Group	**p-value**	**Remarks**
1 versus 2	<0.001	HS
1 versus 3	<0.001	HS
2 versus 3	<0.001	HS

Table 12: Intergroup comparison of emergence scores postoperatively.

Side effects

No side effects were noted with any of the study drugs. There was no pain or local irritation; no patient complained of any smell or taste with any of the drugs. There was no episode of severe bradycardia or hypotension and no episodes of respiratory depression or apnoea with any of the drugs.

Discussion

Oral transmucosal fentanyl is absorbed in mucosal tissues of mouth in sufficient quantities during and after dissolution to produce sedation and analgesia. The bioavailability of oral transmucosal fentanyl citrate in children is 0.33 to 0.38**.** Another advantage of oral transmucosal administration of fentanyl is that the sustained therapeutic blood levels achieved may offer analgesia for painful procedures that last an hour or more. This contrasts with the short duration of analgesia (minutes) with single low doses of intravenous fentanyl. The main attraction of OTFC is its easy use by a non-invasive route, which makes it highly acceptable to paediatric patients. Also, the good quality clinical effect doubles the charm of this formulation. Oral Transmucosal Fentanyl Citrate is safe and effective as an analgesic and premedicant in the setting of monitored outpatient wound care in children and OTFC offers the advantage of improved palatability. OTFC is available in the form of lozenge which has the active drug mounted on its holder stick. Lozenge is pleasant in taste and easy to suck. Also it does not leave any bitter aftertaste. Saliva dissolves the lozenge, releasing the drug for absorption across the oral mucosa.

Midazolam belongs to imidazobenzodiazepine group. It is utilized not only as a premedicant but also as a sedative and an induction agent. It is the most commonly used premedicant in children in the present scenario of medical practice. It has been shown to be more effective than presence of parents or placebo in reducing anxiety and improving compliance at induction of anaesthesia.

In our study, it was found that significant preoperative sedation was provided by fentanyl via oral route and midazolam via the intranasal route. Preoperative sedation was better with fentanyl (mean sedation score at 30 minutes of drug administration 3.70 ± 0.56) as compared to midazolam (4.08 ± 0.66) and control group (4.90 ± 0.30). The effects on hemodynamics were modest and did not require any pharmacological intervention.

Our results were similar to the study conducted by Sneha P et al. which evaluated the efficacy of intranasal midazolam spray in dose of 0.2 mg/kg in children before surgery**.** It produces effective sedation and anxiolysis in children [4,5]. Transient nasal irritation is an undesirable side effect observed with intranasal route. Similarly Erden et al. [6] showed that intranasal midazolam premedication provided efficacious sedation and analgesia during ESWL in children.

All patients in fentanyl group were more co-operative at the time of intravenous cannulation (mean score, 3.6 ± 0.48; Table 8) as compared to those in midazolam (2.45 ± 0.6) and control group (1.67 ± 0.47). Also, supported by work of Servicio et al. who found favourable results in OTFC group as far as the way of accepting a venous puncture was concerned as compared to oral midazolam group [4]. Reduction of distress and struggle of a child at the time of induction (especially painful procedures like venipuncture) could lead to avoidance of traumatic experiences (both physical and mental). A smooth induction generally follows an uneventful intraoperative course and an improved immediate post-operative period.

The mask acceptance was excellent in fentanyl group (mean score, 1.13 ± 0.33; Table 10) when compared to midazolam (2.58 ± 0.81) and control group (3.37 ± 0.62). This is in accordance to the work of Tarek which compared Midazolam Syrup versus Midazolam syrup plus fentanyl lozenge and proved midazolam plus fentanyl lozenge to be superior in reducing apprehension at i/v cannulation and improving mask acceptance.

The level of agitation at emergence in our study was significantly lower in fentanyl group (mean emergence score, 1.65 ± 0.62; Table 11) as compared to midazolam (2.20 ± 0.85) and control group (3.35 ± 0.62). Majority of the children who were given fentayl lollipop were calm and pain free at the time of extubation. They followed verbal commands and responded well to the questions asked.

In our study, there was no case of sneezing or nasal irritation after transnasal midazolam spray was reported. There were no intraoperation complications and no case was noted to have adverse drug reactions (nausea, vomiting, pruritis, oxygen desaturation, abdominal pain, dizziness, urinary retention or apnea).

Our study reported no case of desaturation, however, Klein et al. noticed a brief oxygen saturation below 93% on room air in three patients out of 28 in the oral midazolam plus oral transmucosal fentanyl group as compared with oral midazolam plus placebo group [7].

Conclusion

Premedication is an essential component of anaesthetic management especially in paediatric age group. Children suffer from severe anxiety and apprehension when separated from their parents for the induction of anaesthesia. Preoperative anxiety can affect the smoothness of induction, emergence from anaesthesia and the psychological state of the child. Although preoperative visit by the anaesthesiologist to establish rapport with the child can help to minimize the child's anxiety; pharmacological agents are very helpful to provide sedation and aid in smooth induction.

Premedicant drugs can be administered by several routes each having its own merits and demerits. The intranasal route for administration of these drugs is useful as it provides quick and virtually complete absorption, avoids the gastrointestinal tract and the hepatic first pass metabolism, allows attainment of rapid brain levels of the drug and avoids exposure of children to needles. It is painless and does not require a sterile technique.

Present study was conducted to compare and evaluate the efficacy of oral transmucosal fentanyl citrate and nasal transmucosal midazolam spray as premedicants in children undergoing elective surgery.

It was concluded that oral transmucosal fentanyl citrate in the dose of 15 μg/kg is better than nasal transmucosal midazolam spray (0.2 mg/kg) in providing good preoperative sedation, decreasing anxiety at the time of placement of anaesthesia mask and intravenous cannulation and minimising the level of agitation at emergence.

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