Original Article

PRE-EMPTIVE ANALGESIA FOR POSTOPERATIVE PAIN RELIEF IN CHILDREN – ROLE OF PARACETAMOL

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SUMMARY:

This prospective clinical study was carried out in the Dept. of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU, Dhaka, during the period of May 2003 to July 2003. The study was done to emphasize the importance of giving analgesics pre-emptively instead of waiting for the child to complain of pain and to produce smooth recovery after surgery by decreasing immediate post-operative pain in children by a simple, safe acceptable drug. The children scheduled for tonsillectomy under general anaesthesia were recruited in this study. The analgesic efficiency of rectal paracetamol in two doses, 25 mg/kg bodywt.(Gr-P_{25}) and 50 mg/kg. bodywt. (Gr-P_{50}) were compared with Diclofenac Sodium suppository 1mg/ kg body weight (Gr-D) given half an hour before induction of anaesthesia. Pain scoring was done by TPPPS (Toddler Pre-schooler postoperative pain scale). Heart rate and blood pressure were stable in Gr-P_{50} and Gr-D. Time of first demand of analgesic was delayed in Gr-P_{50} and Gr-D. Total paracetamol consumption in 24 hours was less in Gr-P_{50}(181±14.25) and Gr-D (212±25) than Gr-P_{25}(318± 26.39). Total duration of analgesia in Gr- P_{50} (657±9.94) mins. and in Gr-D(502±10.63) mins. and in Gr-P_{25}(288±23.17) mins. Pre-emptive high dose rectal paracetamol appears to be more effective than diclofenac sodium suppository for postoperative analgesia in children undergoing tonsillectomy.

INTRODUCTION:

Pain is not just a sensory modality but also an experience. The IASP defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. Pre-emptive analgesia, an evolving clinical concept, involves the introduction of an analgesic regimen before the onset of noxious stimuli, to prevent sensitization of the nervous system to subsequent stimuli that could amplify pain.[2] Pre-emptive analgesia would be directed at central neurons by using NSAIDs, paracetamol, ketamine, local anaesthetics and opioids either alone or in combination.[3] In this study, pre-empt rectal paracetamol and diclofenac sodium has been included.

As post operative pain in children is intense and short lasting, children with mild and moderate pain need analgesia only for 24 hrs. and can be managed by simple medication[4]. Paracetamol is commonly used in children for mild to moderate pain. It is well tolerated and relatively free of side-effects in clinical doses[5]. On the other hand diclofenac sodium is an excellent analgesic, but it has the side effects like gastro-intestinal bleeding, depression of platelet function, increased bleeding time, decreased renal and splanchnic perfusion[6,7]. Diclofenac sodium therefore have greater risks in tonsillectonmy where bleeding from tonsil bed is likely to be large[8]. Thus, in the present study, role of pre-emptive paracetamol in controlling pain in children has been studied. Different doses of paracetamol are used to see the range of analgesia in terms of quality and compared with diclofenac sodium, a commonly used NSAID.

MATERIALS AND METHODS:

This prospective study was carried out in the department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandu Sheikh Mujib Medical University, Dhaka during the period of May 2003 to July 2003. The children aged between 6-12 years with ASA grade I & II and scheduled for tonsillectomy under general

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anaesthesia were recruited in this study. Children with known allergy to study drugs, hypovolaemia, hepatic and renal diseases, hemorrhagic diathesis and bronchial asthma were excluded form this study.

After recruitment children were randomly divided into three groups by card sampling, twenty in each group. The group P_{25} received paracetamol 25mg kg body weight per rectum, Group P_{50} received paracetamol 50mg/kg body weight per rectum and Group D received diclofenac sodium 1 mg/kg body weight per rectum –half an hour before induction of anaesthesia. The administered dose was maintained close to the calculated dose. Patients data were collected in prescribed forms containing patients particulars, preoperative baseline (Pulse, blood pressure, temperature) parameters, per and postoperative parameters.

After pre-oxygenation for 3 mins with 100%oxygen, induction of anaesthesia was done with thiopentone sodium 4-5 mg/kg IV and tracheal intubation was done after giving Inj. Suxamethonium 1.5 mg/kg IV. Maintenance of anaesthesia with N_2O 70%, O_2 30% and halothane – 0.5% with long acting muscle relaxant atracurium besylate 0.5 mg/kg body weight. Residual effect of neuromuscular blocking drug was reversed by Inj. neostigmine 40 ìg/kg with atropine 20 ìg/kg and tracheal extubation performed. Peroperative analgesia maintained by Inj. Fentanyl 1µg/kg at the time of induction and $D_5$0.225 NS fluid was used by IV drip at a rate of 6 ml/kg/hr.

Children were assessed both preoperatively and at 15mins, 1 hour, 4 hours, 8 hours in the post-operative ward. Study parameters included TPPPS (Toddler Pre-schooler post operative pain scale) for measuring pain intensity at 15 minutes afterward, 1 hour afterward, 4 hours afterward and 8 hours afterward, Variables of TPPPS were verbal complaint/cry/groan/moan/grunt, facial expression motor behavior, rub/touch painful area.

If TPPPS >3/10 then injection pethidine 0.5mg/kg IV, was administered, Time of first demand of analgesia, heart hate, blood pressure, temperature, complications like nausea, vomiting, sedation, bleeding, recovery were observed.

Statistical Analysis:

All results were expressed as mean ± SEM calculated for each of the variable at all observation time of all children in each group. The data were compiled and analyzed with the help of chi-square and one-way ANOVA test. Values were expressed as significant if $p<0.05$ (Confidence limit-95%)

RESULTS

Observation of the present study was analyzed in the light of comparison among each subject groups. Each group having n=20. All results were expressed as mean ± SEM or in frequencies as applicable. The studied groups became statistically matched for age (P=0.51), weight (P=0.49), baseline pulse rate (P=0.55) as well as baseline mean blood pressure (P=0.91).

Heart rate (beats/min) of the studied groups are displayed in Table-II, Figure-1. Baseline heart rate were not different significantly (P=0.55) in all three groups but varied significantly at induction (P=0.05), at 5 mins after induction (P=0.01), at 15 mins after induction (P=0.00), at extubation (P=0.01), 15 mins, after extubation (P=0.05), 4 hrs after extubation (P=0.01), 8 hrs, after extubation (P=0.01). Heart rate was not significant (P=0.59) at 1 hr. after extubation. There are significant interaction between groups time (0.00, 0.00 and 0.00) in three groups.

Table-I

Demography

Groups / parameters	Gr-P_{25}	Gr-P_{50}	Gr-D	F value	P value
Age in years (ranged)	8.7±0.37(7-12)	8.9±0.36(7-12)	8.6±o.41(6-12)	0.81	0.51
SexMaleFemale	11(55%)9 (45%)	13 (65%)7 (35%)	9 (45%)11 (55%)		
Body weight in kg	28.8±1.44	27.05±1.15	26.10±1.56	0.43	0.49

Values are expressed as mean±SEM or in frequencies. Within parenthesis are ranged of age distribution or percentage over column total. Between group analyses were done by one way ANOVA. Values are expressed as significant if $p<0.05$ (CI-95%).

Table-II

Changes of mean heart rate (beats/min) at different time period of the studied groups.

Group S/ time	Base line	At induction	5 min after induction	15 min after induction	At extubation	15 min after extubation	1 hr after extubation	4 hr after extubation	8 hr after extubation	F value	P value
Group	94±1.4	113±1.5	110±1.5	103±1.49	112±0.9	107±1.6	100±1.8	105±1.8	102±1.63	5.46	0.00
-P_{25}	5	8	2		0	6	9	3			
Group	92±0.8	110±0.4	105±0.6	105±0.63	109±0.5	105±0.8	98±1.11	94±1.14	97.50±1.	3.48	0.00
-P50	1	8	4	8	0	6		3	39		
Group	92±0.9	114±0.9	111±1.0	107±0.99	115±0.8	110±1.0	101±1.7	94±1.39	101±1.46	2.99	0.00
-D	8	8	2		1	1	5				
F	0.63	1.79	2.98	3.55	2.53	0.97	0.53	1.33	2.49		
P	0.55	0.05	0.01	0.00	0.01	0.05	0.59	0.01	0.01		

Values are expressed as mean±SEM. Between group analyses were done by one way ANOVA. Values are expressed as significant if p<0.05 (CI-95%). - (0.00, 0.00 and 0.00) in three groups.

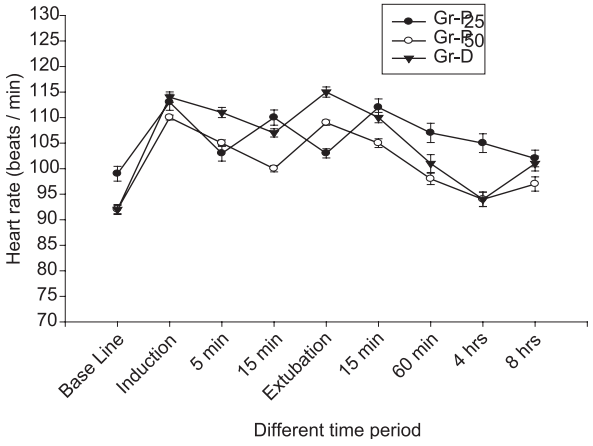

Fig:-1: *Changes of heart rate in different time period*

Mean blood pressure (mm of Hg) three studied groups are displayed in Table-III, Figure-2. Baseline mean blood pressure were not significantly different (P=0.91) in all three groups but varied significantly 15 mins after induction (P=0.00), at extubation (P=0.00) 15 mins, after extubation (P=0.02), 1 hr. after extubation (P=0.00), 4 hr after extubation (P=0.00), 8 hr. after extubation (P=0.00). There are significant interaction between groups x time (P=0.00, P=0.00 and P=0.01).

Changes of temperature (^{o}F) at different time period of three studied groups are displayed in Table-IV, Figure-3. Baseline changes of temperature were not significantly different (P=0.631) in all three groups but varied significantly 5 mins after induction (P=0.05), at 15 mins after induction (P=0.00), at

Table-III

Changes of mean blood pressure (mm of Hg) at different time period of the studied groups.

Group s/ time	Base line	At induction	5 min after induction	15 min after induction	At extubation	15 min after extubation	1 hr after extubation	4 hr after extubation	8 hr after extubation	F value	P value
Group	7611.8	8411.9	8411.5	88±L2	85±1.25	82±1.55	80±1.24	82±1.29	80f1.21	6.5	0.0
-P_{25}	35	22	64	26	8	2	3	5	5	8	0
Group	75±1.2	83±1.3	80±1.2	78±1.2	82±0.82	78±0.68	76±0.78	75±0.95	75f0.79	5.7	0.0
-P50	63	32	12	05	0	0	9	0	9	8	0
Group	76±0.9	84	8311.3	80±1.0	85±1.36	82±1.14	79±0.95	75±0.87	79±1.03	2.9	0.0
-D	57	±2.045	78	75	5	5	7	2	8	6	1
F	0.01	0.07	0.12	2.53	4.33	3.99	5.64	3.44	4.11		
P	0.91	0.10	0.34	0.00	0.00	0.02	0.00	0.00	0.00		

Values are expressed as mean±SEM. Between group analysis were done by one way ANOVA. Values are expressed as significant if p<0.05 (CI-95%).

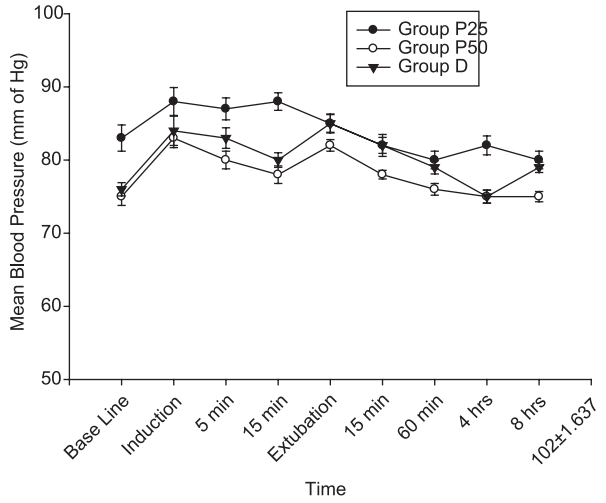

Fig.-2: Chages in blood pressure (mmHg) at different time period of the studied group)

Table-IV

Changes of temperature (0^c) at different time period of the studied groups.

Groups / time	Base line	At induction	5 min after induction	15 min after induction	At extubation	15 min after extubation	1 hr after extubation	4 hr after extubation	8 hr after extubation	F value	P value
Group P25	98.39±0 .089	98.43±0 .077	98..35f0. 086	98.08±0 .103	97.78±0 .100	97.63±0 .120	97.13±0 .121	98.22±0 .086	99.01±0 .062	1.1 1	0.0 5
Group Pso	98.38±0 .073	98.36±0 .076	97.89±0. 082*	97.51±0 .063	97.15±0 .075	96.92±0 .078	96.96±0 .691	97.88±0 .111	98.74±0 .096	3.4	0.0 0
Group D	98.34±0 .045	98.24± 0.046*	98.10±0. 051	97.90±0 .034	97.76f0 .08	97.84±0 .07	97.81t0 .685	98.51±0 .060	98.88±0 .033	2.9 9	0.0 0
F	0.31	0.09	1.1	2.1	1.30	2.40	3.49	4.10	2.19		
P	0.631	0.10	0.05	0.00	0.05	0.00	0.00	0.00	0.01		

Values are expressed as mean±SEM. Between group analysis were done by one way ANOVA. Values are expressed as significant if p<0.05 (CI-95%).

extubation (P=0.05), 15 mins after extubation (P=0.00), 1 hr. after extubation (P=0.00), 4 hrs after extubation (P=0.00), 8 hrs after extubation (P=0.01). There were significant interaction between groups in time (P=0.05, P=0.00 and P=0.00).

Pain intensity of three studied groups was assessed by TPPPS. TPPPS of three studied groups are displayed in Table-V, Figure-4. TPPS varied significantly 15 minuets after extubation (0.00), at 1 hr after extubation (P=0.00), at 4 hrs. after extubation (P=0.00), at 8 hrs. after extubation (P=0.00). There are significant interaction between groups X time (P=0.01, P=0.00 and P=0.01).

Total analgesic requirements of three studied groups are displayed in Table-VI, Figure-5 and 6. Time of first demand of analgesic in all three groups were significant (P=0.001). Total paracetamol consumed in all three groups were also significant (P=0.00)

RECOVERY STATUS

The recovery status of the patients in this study was assessed. The rates of recovery were evaluated by using "Modified Steward Coma Scale" at 5 and 10 minutes after extubation. In Gr-P_{25} out of 20 patients 2 obtained score 7 after 5 minutes and 18 obtained score 7 or more after 10 minutes. In Group-P_{50} out of 20 patient's 14 obtained score 7 or more after 5 minutes and 6 obtained score 7 or more after 10 minutes of extubation. In Group-D out of 20 patient's 14 obtained score 7 or more after 5 minutes and 6 obtained score 7 or more after 10 minutes of extubation (Table-VII).

Values are expressed in frequency, within parenthesis percentage over column total. Between group analysis were done by c2 test. Values are expressed as significant if p<0.05 (CI-95%)

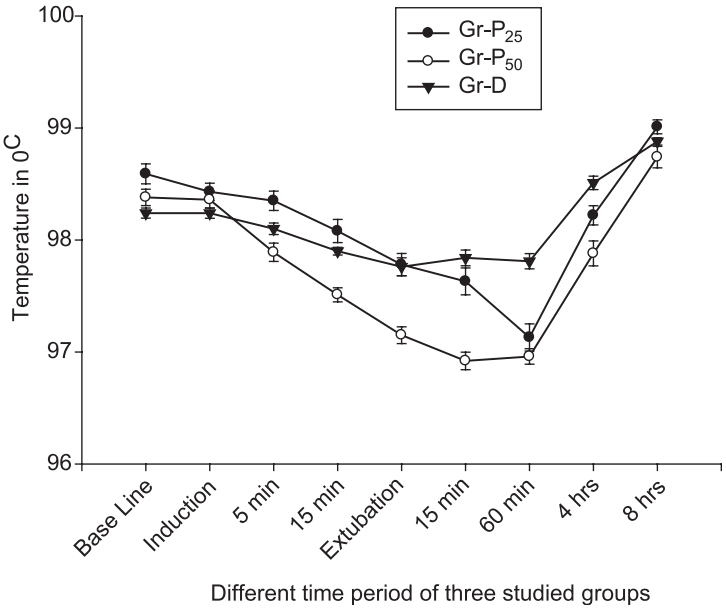

Fig.-3: *Changes of temperature in the studied groups*

Table-V

TPPPS score of three studied groups

Groups/ score	15 min after extubation	1 hr after extubation	4 hr after extubation	8 hr after extubation	F value	P value
Gr-P_{25}	0.70±0.27	0.25±0.12	2.00±0.19	1.75±0.19	2.10	0.01
Gr-P_{50}	0.10±0.10	0.05±0.01	0.04±0.01	0.05±0.01	4.20	0.00
Gr-D	0.95±0.11	0.05±0.05	0.025±0.013	2.0±0.22	1.89	0.01
F	4.32	3.44	9.33	8.93		
P	0.00	0.00	0.00	0.00		

Values are expressed as mean±SEM. Between group analysis were done by one way ANOVA. Values are expressed as significant if $p<0.05$ (CI-95%).

Table-VI

Total Analgesics requirement in mg.

Groups / parameters	Gr-P25	Gr-P50	Gr-D	F value	P value
Time of first analgesic demand in minutes	288±23.17	657±9.94	502±10.63	9.34	0.00
Total Paracetamol consumed in mg	318±26.39	181±14.25	212±25	7.32	0.00

Values are expressed as mean±SEM. Between group analysis were done by one way ANOVA. Values are expressed as significant if $p<0.05$ (CI-95%).

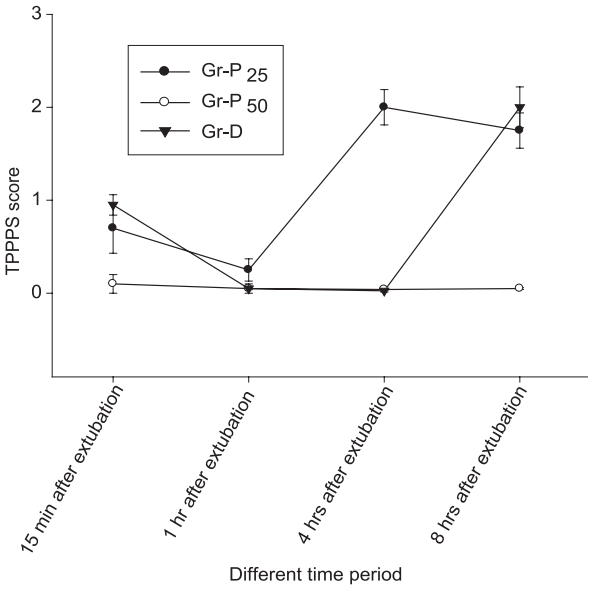

Fig-4: *TPPPS of three studied groups*

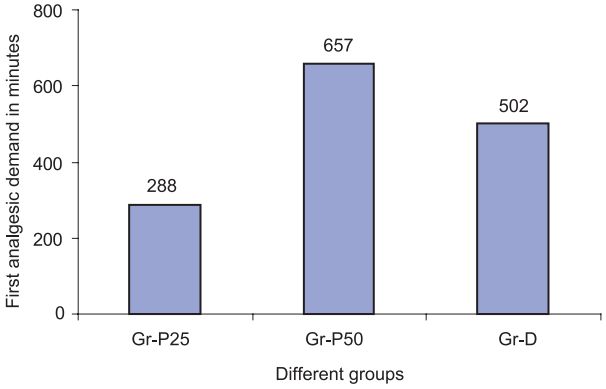

Fig-5: *Time of first analgesic demand in minute*

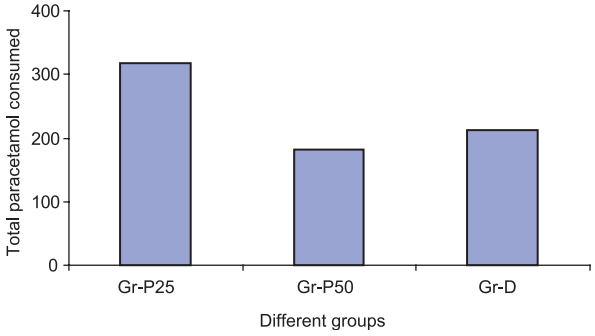

Fig-6: *Total paracetamol in 24 hours*

Table-VII

Recovery status

Group/Time	*Group-P 25*	*Group-P 50*	*Group-D*	*P value*
5 minutes after extubatione"7	2 (10)	14 (70)	14 (70)	0.0001
10 minutes after extubatione"7	18 (90)	6 (30)	6 (30)	0.0001

Values are expressed in frequency, with in paranthesis percentage over colum total. Between groups analysis were done by X^2 test. values are e xpressed as significant if :M<0.05 (CI-95%)

DISCUSSION:

Pre-emptive analgesia is an antinociceptive treatment that prevent establishment of altered central processing of afferent input from sites of injury.[9] The most important condition for establishment of effective pre-emptive analgesia are the establishment of an effective level of antinociception before injury and the continuation of this effective analgesia level into the post injury period to prevent central sensitization during the inflammatory phase. The concept of pre-emptive analgesia was formulated by Crile at the beginning of previous century on the basis of clinical observation [10].

The recommended daily dose for paracetamol in children in 90mg/kg given 4 to 6 hourly [11 12]. Although the optimum paediatric dose for antipyresis is 20mg/kg[12 13 14]: this dose should only be used as a loading dose if repeated administration is envisaged with range of 10-15

mg/kg[13]. Concern about hepatoxicity has result in cautious preoperative dosing regimes, but both pharmacokinetic and pharmacodynamic data have shown these to be inadequate[9] . While there is increasing evidence that a single rectal loading dose of 35-45 mg/kg results in more desirable plasma paracetamol concentrations[15] .In our present study, we have used 25mg/kg and 50mg/kg body weight of paracetamol per rectum which were within the recommended dose suggested by Brian Anderson, Frank & Coulthard, Temple and Wilcon et al[11,12,13,15].

In the present study, we have also used Diclofenac sodium, a dose of 1 mg/kg body weight per rectum. Though diclofenac sodium is an excellent analgesic but it has the side effects like gastro-intestinal bleeding, depression of platelet function, increase in bleeding time, hepatotoxicity, decreased renal and splanchnic perfusion [6,7]. Diclofenac sodium therefore have greater risks in tonsillectomy where bleeding from tonsil bed is likely to be large[8] .

In our study, we have used paracetamol in two doses Gr. P_{25}-25mg/kg body weight per rectum Gr.P_{50}-50mg/kg body weight per rectum and Diclofenac sodium 1mg.kg body weight per rectum It was found that, Gr.P_{50} patients has duration of analgesia(657±9.94) minutes on the other hand GrP_{25} patients had duration of analgesia (288±23.17) minutes and Gr.D patients had duration of analgesia(502±10.63)minutes.

Again, in our study, we have managed postoperative pain by Inj. Pethidine o.5mg/kg IV. as rescue analgesic. Only 2 children of group P_{25} received Inj. Pethidine 0.5mg/kg IV. as rescue analgesic. Twenty four hrs. paracetamol consumption was significantly lower in Group P_{50} (181± 14.25) than Group P_{25}(318±26.39) and Gr.D (212±25).

Post operative pain scoring was done by TPPPS. (Toddler preschooler postoperative pain scale). It is an observation scale for measuring postoperative pain in children. In adults, pain assessment can be done by the visual analogue scale(VAS). But this is not applicable on children. So in TPPPS multiple variables like verbal complaint, cry, groan, moan, grunt, facial expression, restless motor behavior, rub/ touch painful area are used and scored accordingly. TPPPS varied significantly in 15 mins after extubation (P=0.00), at 1hr after extubation (P=0.0), at 4 hr after extubation(P=0.00) and at 8 hr after extubation(P=0.00) in Group.P50.

Paracetamol is an effective antipyretic at plasma concentration of 0.066-0.130mmol/L[15,16,17]. In our study, body temperature of children also had decreased significantly in Gr. P_{50} & Gr.D. This may be due to paracetamol or diclofenac used, general anaesthesia [18], cold ambient temp. in the operating room, use of large amount of unwarned intravenous fluid [19]Although the patients body temperature had been reduced but not to the extent of hypothermia, even of mild variety.

Acute pain results in sympathetic over activity which is manifested by increase in heart rate, blood pressure, peripheral resistance and cardiac output[20]. In this present study, heart rate and blood pressure remained stable throughout the study period in Gr. P_{50} and Gr.D.

CONCLUSION

In the present study, we found that time of first demand of analgesic was delayed in Gr- P50 than Gr-D and Gr-P25. Total duration of analgesic was also greater in Gr-P50 than Gr-D and Gr-P25. So, it can be concluded that, pre-emptive high dose rectal paracetamol (50mg/kg body weight) appears to be more effective than diclofenac sodium suppository for controlling post operative pain in children undergoing tonsillectomy.

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