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Premedication with Dexmedetomidine versus Midazolam for Prevention of Emergence Delirium in Children

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ABSTRACT

***Objective*:** To determine the effects of premedication with Dexmedetomidine vs. Midazolam to prevent the emergence of delirium in children operated at our hospital.

Study Design: Quasi-experimental study.

***Place and Duration of Study*:** Anaesthesia and Pain Medicine Department, Combined Military Hospital, Okara Pakistan, from Apr 2021 to May 2022.

***Methodology*:** Children who operated in the main operation theatre of our hospital without any complications during the study period were recruited for this comparison of two medications to prevent the emergence of delirium. Study participants were allocated to two groups: Group-A received premedication with Dexmedetomidine, and Group-B received Midazolam in standard doses. An independent assessor assessed post-operative delirium using the Pediatric Anesthesia Emergence Delirium Scale.

Results: A total of 130 children were included in the study, and they met the inclusion/exclusion criteria**.** The mean age of the children in the study was 5.66±3.55 years. 80(61.5%) patients were male, while 50(38.5%) were female. 29(22.3%) children showed the presence of emergence delirium, while 101(77.7%) did not show the presence of emergence delirium on the Pediatric Anesthesia Emergence Delirium Scale. It was revealed that children in Group-A had significantly fewer chances of having emergency delirium as compared to children in Group-B (p-value <0.001).

***Conclusion*:** Emergence delirium was not uncommon in children undergoing surgeries under general anaesthesia at our unit. Children in which Dexmedetomidine was used as a premedication agent had less chance of having emergency delirium as compared to those who were pre-medicated with Midazolam.

Keywords: Delirium**,** Dexmedetomidine, General anesthesia, Midazolam.

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INTRODUCTION

Surgical procedures are carried along well with the help of anaesthesia expertise in all major or even minor procedures. Surgeries involving patients with extremes of ages usually carry more risk than usual and need specifically tailored management from both surgery and anaesthesia points of view.[1,2] Complications of any procedure can increase manifold if the proper pre-anaesthetic assessment or premedication with standardised and non-anaesthetic needs to be done adequately.[3]

No procedure can be completely complication-free. Even minor procedures or those with minimum risk factors can cause complications during the course of surgery or in the early post-operative period.[4] Early onset confusion after the surgery is a separate entity encountered by surgeons, critical care experts and anaesthetists in routine.[5] Patients of all age groups, despite baseline cognitive functioning, are prone to develop delirium or cognitive deficits for some time after the surgical procedure.[6]

Multiple trials have been done to look for a pre-anaesthetic agent that could reduce the risk of post-operative emergence delirium in children undergoing various types of surgeries. Wang *et al*. in 2021 did a study. They revealed that the use of Midazolam or anti-emetics may be helpful in the prevention of emergence delirium among patients undergoing various surgical procedures.[7] Sun *et al*. targeted children undergoing cardiac surgeries for the role of Dexmedetomidine in the prevention of emergency delirium. They concluded that if this agent is continuously infused in a controlled setting, it reduces the requirement of anaesthesia and thus reduces the chances of emergence of delirium and post-operative agitation and confusion.[8] Cho *et al*. targeted children from Korea and published an RCT revealing that Dexmedetomidine had better analgesic effects after the

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surgery. However, with regard to the prevention of emergency delirium, both medications were equally effective.[9] Still, no guidelines restrict anaesthesia doctors from using any one type of medication for the prevention of emergency delirium, and much work is still being done to find the best option for this purpose.

Managing peri and post-operative complications is usually shared between surgeons, anaesthetists, and critical care physicians. Pediatric surgery is an evolving speciality in our part of the world. Still, local authorities are in the phase of doing training and practising guidelines, which include the availability of pediatric anaesthesia experts as well.[10] Limited local data has been available regarding the use of various pharmacological agents as pre-anaesthesia medications in order to reduce the chances of emergence delirium in children. Therefore, we planned this study to determine the effects of premedication with Dexmedetomidine Vs Midazolam for preventing the emergence of delirium in children operated on at our unit.

METHODOLOGY

The Quasi-experimental study was conducted at the Anaesthesia and Pain Medicine Department, Combined Military Hospital, Okara Pakistan, from April 2021 to May 2022. Permission from the Hospital Ethics Committee (letter number IERC/Anaes/ 2021/04) was sought prior to the commencement of the study. The sample size was calculated using the WHO sample size calculator and keeping the population proportion of emergence delirium in children at 6.6%.[11] The non-probability consecutive sampling technique was used to gather the required sample size for this study, and then the lottery method was used to randomly divide the patients into two groups.

Inclusion Criteria: Children aged 1 to 12 who underwent a surgical procedure under general anaesthesia lasting less than 90 minutes in our general and paediatric surgery unit were included.

Exclusion Criteria: Children who underwent surgeries under local or regional anaesthesia or those who underwent cardiothoracic, head, neck or brain surgeries were excluded. Children whose surgery time lasted for more than 90 minutes or those who required blood transfusion during or soon after the surgery were excluded as well. Children with recent head trauma or having any neuro-degenerative, developmental, or congenital disorders were part of the exclusion criteria. Children with known drug allergies to medications used in the study were also not included.

Informed consent was obtained from primary caregivers (in most cases, one of the parents) before surgery after they had been given a detailed study description. Children were divided into two groups randomly via a lottery method. Group-A received Dexmedetomidine in addition to other routine pre-anaesthetic medications, while Group-B just received Midazolam in addition to the routine pre-anaesthetic medications (Figure).

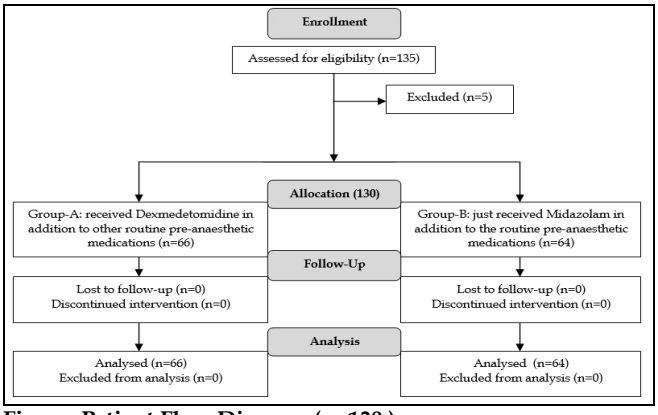

Figure: Patient Flow Diagram (n=130)

Dexmedetomidine was given in standard dose as an infusion (4 µg/kg)[12] preoperatively just before the induction of anaesthesia by an anaesthetist in Group-A, while Midazolam to Group-B was given as a bolus at a dose of 0.5 mg/kg.[13] A consultant anaesthetist assessed delirium using the Pediatric Anesthesia Emergence Delirium Scale (PAEDS) 24 hours after the procedure. The assessing consultant was blinded regarding the use of medications among the study participants. PAEDS includes various parameters like making eye contact, restlessness, purposeful actions, and awareness of surroundings. A cut score of 10 was used to classify children as having emergency delirium.[14]

The team used Statistical Package for the Social Sciences (SPSS) version 23.00 to analyse data. Mean and standard deviation were calculated for the age of the patients included in the study. Descriptive statistics were calculated for quantitative variables, including n(%). The Pearson chi-square test was used to see the statistical difference in the presence of various post-operative outcome parameters, including emergence delirium, between the two groups studied in the analysis. The *p*-value less than or equal to 0.05 was considered significant for this study.

RESULTS

A total of one hundred and thirty children were included in the study, meeting the inclusion/exclusion criteria**.** The mean age of the children in the study was 5.66±3.55 years. Table-I shows the general characteristics of children included in the study. 80(61.5%) patients were male, while 50(38.5%) were female. 29(22.3%) children showed the presence of emergence delirium, while 101(77.7%) did not show the presence of emergence delirium on the Pediatric Anesthesia Emergence Delirium Scale. 66(50.7%) patients were given Dexmedetomidine, while 64(49.3%) were given Midazolam. Abdominal surgery patients were the most common, 35(26.9%) in our study, followed by patients having ENT surgeries 31(23.8%). Table-II shows the results of the statistical analysis. It was revealed that children in group A had significantly fewer chances of having emergency delirium as compared to children in group-B (*p*-value <0.001). A fall in blood pressure was also seen significantly more in children administered Midazolam than in those administered Dexmedetomidine (*p*-value 0.001). Drop in SpO2 and complaints of nausea/vomiting were not statistically significantly different in both groups (*p*-values 0.348 and 0.891, respectively).

Table-I: Characteristics of Children Included in the Study n=(130)

Study Parameters	n(%)
Age (years)	
Mean+SD	5.66±3.55 years
Range (min-max)	1year - 12 years
Gender	
Male	80(61.5%)
Female	50(38.5%)
Emergence delirium	
No	29(22.3%)
Yes	101(77.7%)
Medication used	
Dexmedetomidine	66(50.7%)
Midazolam	64(49.3%)
Types of Surgeries	
Abdominal	35(26.9%)
Ear, nose and throat	31(23.8%)
Plastic	23(17.6%)
Genitourinary	20(15.3%)
Bones, muscles, joints	19(14.6%)
Others	02(1.5%)

DISCUSSION

Children are a vulnerable group of the population who are more prone to develop adverse effects of medications or complications after surgical procedures. Sub-specialities according to the needs of this group have been developed. We in Pakistan lack facilities for pediatric anaesthesia, and usually, this burden is managed by adult anaesthetists. Emergence delirium is not an uncommon finding in children after the surgery. Multiple risk factors may be responsible for this finding. Few pre-anesthetic medications may be protective against this phenomenon. Therefore, we conducted this study with the rationale of determining the effects of premedication with Dexmedetomidine Vs Midazolam for preventing the emergence of delirium in children operated on at our unit.

Table-II: Difference among two Groups Regarding Various Post-Operative Variables Including Emergence Delirium (n=130)

Parameters	Group A (n=66)	Group B (n=64)	*p*-value
Emergence delirium			
No	60(90.9%)	41(64.1%)	<0.001
Yes	06(9.1%)	23(35.9%)	
Drop in pulse/blood pressure			
No	61(92.4%)	45(70.3%)	0.001
Yes	05(7.6%)	19(29.7%)	
Drop in sPO2			
No	61(92.4%)	56(87.5%)	0.348
Yes	05(7.6%)	08(12.5%)	
Post-operative nausea/vomiting			
No	53(80.3%)	52(81.25%)	0.891
Yes	13(19.7%)	12(18.75%)	

Pasin *et al*., in 2015, published a meta-analysis of randomised controlled trials regarding Dexmedetomidine vs Midazolam as pre-anaesthetic medication in children. They came up with the conclusion that post-operative analgesia, anxiety, and agitation were better in children who were pre-medicated with Dexmedetomidine as compared to those who were pre-medicated with Midazolam.[15] results were not significantly different as patients who were given Dexmedetomidine had less chance of emergence delirium and a drop in pulse and blood pressure after the surgery. Yao *et al*. published an RCT on children undergoing surgery for strabismus regarding the difference in the incidence of emergency delirium in children getting Dexmedetomidine or Midazolam during anaesthesia.[16] They revealed that Dexmedetomidine was better than Midazolam in preventing emergence delirium in pediatric patients included in their study. We used Dexmedetomidine infusion instead of the nasal route, but the results were not significantly different, and Dexmedetomidine was better in preventing emergency delirium.

A systematic review published by FitzSimons *et al*. concluded that there was no statistically significant

difference between Dexmedetomidine and Midazolam in preventing the emergence of delirium in patients undergoing different types of surgeries under general anaesthesia.[17] Our results were contrary to those generated by FitzSimons *et al*., as in our study, children in which Dexmedetomidine was used as a premedication agent had less chance of having emergency delirium than those who were pre-medicated with Midazolam. Prabhu *et al*., in the Indian population, compared different agents to look for their role in the prevention of post-operative agitation and anxiety secondary to the anaesthetic agent used. They came up with the findings that emergency anxiety and analgesia were better in patients who got Dexmedetomidine as compared to those who got Midazolam.[18] Overall induction and recovery were also smooth in the Dexmedetomidine group. We found similar results with Dexmedetomidine infusion, and the emergence of delirium and a fall in pulse/blood pressure was seen less in the Dexmedetomidine group than in the midazolam group.

LIMITATION OF STUDY

Inclusion/exclusion criteria was strict for the study but still number of confounding factors may be responsible for emergence delirium in study participants therefore with this study design we cannot conclude regarding delirium as consequence of any medication or any medication having any protective role against emergence delirium.

CONCLUSION

Emergence delirium was not uncommon in children undergoing surgeries under general anaesthesia at our hospital. Children in which Dexmedetomidine was used as a premedication agent had less chance of having emergency delirium as compared to those who were pre-medicated with Midazolam.

Conflict of Interest: None.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

WA & MUK: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

BY & MS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

WT & FHF: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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