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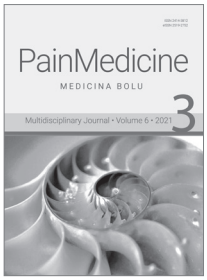

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A comparative study of caudal anesthesia with bupivacaine v/s bupivacaine with dexmedetomidine in lower abdominal surgeries in pediatric age group

Running title: Caudal anesthesia and postoperative pain in children

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Abstract

Background: *caudal anaesthesia has short-term effect. Alpha-2 adenoreceptors when used as adjuvant to local anaesthetic in children prolongs analgesic duration. The study is aimed to assess the efficacy of addition of dexmedetomidine with Bupivacaine in caudal block for extending postoperative analgesia and its safety profile in pediatric infra-umbilical surgeries.*

Method: *the prospective interventional longitudinal double blinded study was conducted on 60 patients randomly divided into two groups by simple lottery method: group B who received (0.25%) bupivacaine 1 ml/kg plus 1 ml normal saline (NS), and those in group BD who received (0.25%) bupivacaine 1 ml/kg plus 0.5 μg/kg dexmedetomidine in 1 ml NS. Post-surgery, both groups were compared in R studio v1.2.5001. Association between the adverse effect and other variables (age, gender, type of surgery, groups) were assessed by Multiple linear regression.*

Results: *in group BD, duration of analgesia prolonged significantly ($P < 0.05$). In group BD, FLACC score at initial four hours and at 12th hour was significantly less ($P < 0.05$). Group B was more likely to receive high number of rescue analgesia ($P = 0.0005$; OR = 11.769). No significant difference was observed concerning hemodynamics, respiratory parameters and adverse effect between both groups ($P > 0.05$).*

Conclusion: *in children, dexmedetomidine when used along with bupivacaine prolongs postoperative analgesia duration, without any significant side effects.*

Key words*: bupivacaine, dexmedetomidine, hemodynamics, postoperative pain*

Introduction

Post-operative pain is strongly associated with emotional component and is difficult to assess specially in the paediatric age group [1]. Several techniques have emerged for pain relief in this group inclusive of both regional and systematic analgesia [2]. Caudal epidural anaesthesia, either in form of continuous infusion or bolus is the commonest regional technique that provides analgesia both peri and post-operation in children [3]. Although it has huge advantages such as early extubation, low risk of infection and ambulation, its use is limited due to short term effect of analgesia [2]. Ad-

juvants such as alpha-2 adrenoceptors agonists, ketamine and opioids are used for prolongation of anaesthesia [4–6]. However, use of ketamine and opioids are rather limited due to post-operative complications [6]. Therefore, adjuvants having a neuroprotective effect are widely studied.

Alpha-2 adrenoceptors agonists are well known to have physiological properties that induce sedation and analgesia, reduce plasma catecholamine, attenuates stress responses and shivering induced by surgery [7]. Dexmedetomidine is a potent alpha-2 adrenoceptor agonist with renal, cardiac and neuroprotective properties [8]. Its alpha-2 adrenoceptor selection makes it an optimum sedative and analgesic agent compared to other alpha-2 adrenoceptor agonist [9]. Since dexmedetomidine acts on the ventrolateral preoptic nucleus (VLOP) in regulating wakefulness, it promotes sedation similar to cooperative sedation [10, 11]. Previous studies have reported that dexmedetomidine if added to local anaesthesia prolongs analgesic duration by blocking the hyperpolarization-activated cation current [12].

However, the study was conducted to assess the efficacy of addition of dexmedetomidine with Bupivacaine in caudal block for extending postoperative analgesia and its safety profile in pediatric infra-umbilical surgeries.

Materials and Methods

The prospective interventional longitudinal double blinded study conducted in department of anesthesiology at tertiary care hospital. The minimum sample size was calculated (n=~ 49) considering 80 % power with 95 % level of significance in R studio (v1.2.5001) software using appropriate R code (pwr. chisq. test (w, n, sig, level, power)). A total of 60 patients undergoing elective infra-umbilical surgeries aged 2–10 years and belonging to American standard association (ASA) status I and II were included and II were included and written consent was obtained prior to the study. Patients were randomly divided into Group B (n = 30) and Group BD (n = 30). Randomization was done by simple lottery method. Each patient was assigned a number and every alternate number obtained from lottery draw was added in same group. Patients with delayed milestones, allergy to proposed drugs, bleeding and clotting disorders, congenital malformations of the back and pre-existing neurological or spinal disease, congenital heart disease and history of infection at the back or proposed region of anesthesia, were excluded from the study. All medications were prepared by the anaesthesiologist who were not participating in the study. All healthcare personnel, the patients and the parents of children were blinded to the medications administered caudally.

Pre-anesthetic check-up was carried out a day prior. Patients were kept fasting as described in ASA guidelines [13]. All patients were premedicated with mixture of Inj. Ketamine 5 mg/kg + Inj. Glycopyrrolate 0.004 mg/kg + Inj. Midazolam 0.05 mg/kg IM. On arrival to operation theater (OT), Electrocardiogram, Pulse oximetry (SpO_2), Heart Rate (HR) and Noninvasive Blood Pressure (NIBP) were monitored. Patients were preoxygenated (100 %) for 3 minutes (Jackson-Ree's circuit) and lignocaine (2 %) 1 mg/kg was given prior to the induction.

Adequate size laryngeal mask airway (LMA) was introduced, and anesthesia was maintained using O_2 (50 %) + N_2O (50 %) + sevoflurane 0.5–1.5 %. After induction, caudal block was performed under aseptic precautions. Patients in group B received (0.25 %) Bupivacaine 1 ml/kg plus 1 ml normal saline. Whereas the patients in group BD received (0.25 %) Bupivacaine 1 ml/kg + 0.5μg/kg Dexmedetomidine in 1 ml normal saline. Heart Rate (HR), Blood Pressure (BP), Respiratory Rate (RR), and O_2 saturation were recorded immediately after and every 10 min thereafter till the patient was shifted to the ward. Post-operation, duration of analgesia and pain by face, legs, activity, cry, consolability scale (FLACC)were assessed as described by Goyal *et. al* [2]. Rescue analgesic paracetamol 30 mg/kg suppository was given to maintain the low pain score. The total number of analgesic doses received in 24 hours and the adverse effect were noted in both the groups.

Statistical analysis

All the data collected were organized in Microsoft EXCEL 2016. The Statistical Software R studio 1.2.5001 was used. Both the groups were compared using Mann-Whitney test (duration of analgesia), chi-square test (FLACC score and number of rescue analgesia) and independent t-test (hemodynamic and respiratory parameters). Multiple linear regression was used to analyze the association between the adverse effect and other variables (age, gender, type of surgery, groups). P value (< 0.05) was considered statistically significant.

Results

The male: female ratios of groups B and BD were 29 : 1 and 14 : 1, respectively. Demographic and clinical data of the sample is given in Table 1.

Duration of analgesia was noted as the time from injection of caudal anesthesia with bupivacaine or bupivacaine with dexmedetomidine, to the first dose of rescue analgesia. The mean duration of analgesia in group B and BD were 288.1 minutes and 541 minutes respectively. Mann Whitney test showed that duration of analgesia was significantly prolonged when dexmedetomidine was used along with bupivacaine ($P < 0.001$).

Multiple linear regression showed that demographic variables (age, gender, weight) did not have significant ef-

Table 1. Demographic and clinical distribution of the sample size (n = 60)

Variables	Frequency (n = 60)
Mean age (months)	59.12 ± 27.032
Mean weight (kilograms)	14.07 ± 3.799
Surgical type	
• Herniotomy	22
• Orchidopexy	15
• Circumcision	11
• Herniotomy + Circumcision	05
• Hypospadias Repair	04
• Implant Removal	01
• Open Appendectomy	01
• Second Toe Amputation With Wide Excision	01

fect on analgesia duration (P > 0.05). Neither did duration of the surgery. Surgical type such as open appendectomy and orchidopexy + circumcision significantly affected the duration of analgesia (P = 0.041; P = 0.011 respectively).

During initial four hours FLACC score was significantly high in group B (P < 0.05). At the 8th hour, there was increase in FLACC score in group BD. However, the difference between both groups was insignificant (P = 0.059). At the 12th hour, FLACC score decreased significantly in group BD whereas it increased in group B (P = 0.0001). No significant difference in FLACC score was observed after the 12th hour between both groups.

Number of rescue analgesics used have been given in Table 2. Minimum number of rescue analgesics required in group B was two compared to one in group BD. Maximum number of rescue analgesics required in group B was four compared to three in group BD. Group B was more likely to receive high number of rescue analgesia compared to group BD (P = 0.0005; OR 11.769).

Minimal complications of hypotension, bradycardia and vomiting were observed in four cases of both groups. Mann Whitney test showed that the hemodynamic and respiratory parameters of children in both groups did not change significantly with time (P > 0.05). There was no significant association observed between the demographic variables, type of surgery and adverse effect (P > 0.05) in both the groups. Chi-square test further confirmed that the adverse effects were not significantly associated with the groups (P > 0.05). This indicates that dexmedetomidine is safe to use in children.

Discussion

Dexmedetomidine is a potent alpha-2 adrenoceptor agonist. It enters the central nervous system (CNS) through

Table 2. Number of rescue analgesics used

	Number of children	
No. of doses of rescue analgesics	**Group B**	**Group BD**
1	–	9
2	13	18
3	15	3
4	2	–

diffusion into cerebrospinal fluid (CSF) or by absorption and reaches α-2 receptors present in the spinal cord, brain and brainstem [14, 15]. On stimulating the alpha-2 receptors calcium entry into nerve terminals is decreased. This facilitates analgesia. In the present study, it was found that when dexmedetomidine was used as an adjuvant with bupivacaine, duration of analgesia increased significantly, and number of rescue analgesics required reduced. All this occurred without any significant adverse effects.

Demographic data is comparable to similar studies by Kurrapiah *et al.* and Hassan *et al.* [16, 17]. However, Kurrapiah et al conducted their study specifically on patients undergoing surgery for hypospadias.

Duration of analgesia was prolonged significantly when dexmedetomidine was used along with bupivacaine compared to bupivacaine alone. This finding concurs with the findings of previous studies [2, 16, 18]. Duration of analgesia was not significantly affected by any of the demographic variables (P > 0.05). Surgery type such as open appendectomy and orchidopexy + circumcision significantly affected the duration of analgesia (P = 0.041; P = 0.011 respectively) [19]. FLACC score during initial four hours and 12th hours of post-surgery was significantly low in group BD (P < 0.05). This illustrates an enhancement of analgesia when dexmedetomidine was used as an adjuvant with bupivacaine. However, the significantly lesser number of rescue analgesics required post-surgery in the group with dexmedetomidine is obvious due to the lower FLACC score. In the bupivacaine group, all the patients required ≥2 rescue analgesics. Previous studies have also reported that dexmedetomidine when used along with bupivacaine lowers the FLACC score and the required number of rescue analgesics [2, 20]. This can be attributed to the mechanism of action of dexmedetomidine.

Minimal complications of vomiting, bradycardia and hypotension were seen. The incidence of complications was statistically insignificant. This is similar to the findings of Goyal V *et al.* [2]. However, Goyal V *et al.* evaluated only the incidence of nausea and vomiting and reported that the incidence of nausea and vomiting were higher in the group injected with bupivacaine alone. Interestingly, this difference was not observed in the study conducted.

There were no significant changes observed in the hemodynamic and respiratory parameters of both the groups. This concurs with the findings of previous study [16]. This depicts that dexmedetomidine is safe to use in children irrespective of demographic variables.

However, the present study was performed on a small population hence degree of generalization on the effect of dexmedetomidine on patients could not be made. A similar study with large sample size and with different dosage of dexmedetomidine would provide better insights on the efficacy and safety profile of dexmedetomidine in paediatric group.

Conclusion

In paediatric group, dexmedetomidine when used along with bupivacaine prolongs the duration of postoperative analgesia when compared to bupivacaine alone, without any significant side effects.

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Порівняльне дослідження каудальної анестезії за допомогою бупівакаїну проти бупівакаїну з дексмедетомідином при операціях на нижній частині живота у віковій групі дітей

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Резюме

Передумови: *каудальна анестезія має короткочасну дію. При використанні в якості ад'юванту до місцевого анестетику у дітей альфа-2-адренорецептори продовжують тривалість знеболення. Дослідження мало на меті оцінити ефективність додавання дексмедетомідину з бупівакаїном у каудальну блокаду для розширення післяопераційної аналгезії та її профіль безпеки при педіатричних інтрапупкових операціях.*

Методи: *Проспективне інтервенційне поздовжнє подвійне сліпе дослідження було проведено на 60 пацієнтах, випадковим чином поділених на дві групи простим методом лотереї. Група B отримала (0,25%) бупівакаїну по 1 мл/кг плюс 1 мл звичайного фізіологічного розчину (НС), а ті, хто в групі BD, отримали (0,25%) бупівакаїну 1 мл/кг плюс 0,5 мкг/кг дексмедетомідину в 1 мл НС. Після операції обидві групи порівнювали в R studio v1.2.5001. Асоціацію між побічним ефектом та іншими змінними (вік, стать, тип операції, групи) оцінювали за допомогою множинної лінійної регресії.*

Результати: *у групі BD тривалість аналгезії значно подовжилася (P < 0,05). У групі BD показник FLACC на початкових чотирьох годинах і на 12-й годині був значно меншим (P < 0,05). Група B частіше отримувала велику кількість рятувальних аналгезій (P = 0,0005; OP = 11,769). Не було виявлено суттєвої різниці щодо гемодинаміки, параметрів дихання та побічних ефектів між обома групами (P > 0,05).*

Висновок: *у дітей дексмедетомідин при одночасному застосуванні з бупівакаїном подовжує тривалість післяопераційного знеболення без значних побічних ефектів.*

Ключові слова: *бупівакаїн, дексмедетомідин, гемодинаміка, післяопераційний біль*

Сравнительное исследование каудальной анестезии бупивакаином по сравнению с бупивакаином с дексмедетомидином при операциях на нижних отделах брюшной полости в детской возрастной группе

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Резюме

Предпосылки: *каудальная анестезия имеет кратковременный эффект. Аденорецепторы альфа-2 при использовании в качестве адъюванта к местному анестетику у детей продлевают действие анальгетика. Исследование было направлено на оценку эффективности добавления дексмедетомидина с бупивакаином в каудальном блоке для продления послеоперационной анальгезии и его профиля безопасности при педиатрических инфрапупочных операциях.*

Методы: *проспективное интервенционное продольное двойное слепое исследование было проведено с участием 60 пациентов, случайным образом разделенных на две группы с помощью метода простой лотереи. Группа B, получавшая (0,25%) бупивакаин 1 мл/кг плюс 1 мл физиологического раствора (NS), и пациенты в группе BD, которые получали (0,25%) бупивакаин 1 мл/кг плюс 0,5 мкг/кг дексмедетомидина в 1 мл NS. После операции обе группы сравнивались в R studio v1.2.5001 Связь между побочным эффектом и другими переменными (возраст, пол, тип операции, группы) оценивалась с помощью множественной линейной регрессии.*

Результаты: *в группе BD продолжительность обезболивания значительно увеличилась (P < 0,05). В группе BD оценка FLACC в первые четыре часа и через 12 часов была значительно меньше (P < 0,05). Группа B с большей вероятностью получала большое количество экстренной анальгезии (P = 0,0005; OR = 11,769). Не наблюдалось значительных различий в отношении гемодинамики, респираторных параметров и побочных эффектов между обеими группами (P > 0,05).*

Заключение: *у детей дексмедетомидин при одновременном применении с бупивакаином продлевает продолжительность послеоперационного обезболивания без каких-либо значительных побочных эффектов.*

Ключевые слова: *бупивакаин, дексмедетомидин, гемодинамика, послеоперационная боль*