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Research article

Dexmedetomidine with magnesium sulphate as adjuvants in caudal block to augment anaesthesia and analgesia in paediatric lower abdominal surgeries

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ABSTRACT

Purpose: To investigate the implication of dexmedetomidine and magnesium sulphate addition to bupivacaine in caudal anesthesia in paediatric lower abdominal surgeries.
Study design: Randomized controlled trial.
Setting: Paediatric University Hospital.
Subjects: 120 children undergoing surgeries in the lower half of the body under general anaesthesia with a supplementary caudal block using 1 ml/kg bupivacaine 0.25%.
Methods: Participants were randomly allocated into four groups; group C (saline as an additive to bupivacaine), group MG (50 mg magnesium sulphate added to bupivacaine), group D (1 μg/kg dexmedetomidine added to bupivacaine), and group MGD (the same doses of both dexmedetomidine and magnesium sulphate were added to bupivacaine). Time to first analgesia request (1ry outcome), and pain assessment by The Face, Legs, Activity, Cry, Consolability (FLACC) score just after recovery, then every 30 min in the early two hours, then at the 4th, 6th, 12th,18th, and 24th hours were compared between the groups.
Results: Time to first analgesia request was significantly longer in the three study groups compared to group C with $p < 0.001$ (median values of 5, 14.5, 13.5, and 20.47 h in groups C, D, MG, and MGD in consequence). FLACC scores were significantly higher in group C in comparison to the other study groups by the early 2nd, 4th, and 6th postoperative hours. The group MGD has significantly lowest FLACC at the 6th postoperative hour.
Conclusion: The combination of dexmedetomidine and magnesium sulphate with bupivacaine caudal block can prolong the time to first analgesia request.

1. Introduction

Postoperative pain in children is difficult to be assessed and associated with a strong emotional component. Caudal epidural anaesthesia is a common technique which can provide both intra and postoperative analgesia in paediatric surgeries [1]. Prolongation of caudal analgesia can be achieved by the addition of various adjuvants such as opioids, ketamine, α_2-adrenoceptors agonists, and opioids [2–4]. Opioids carry the risk of postoperative respiratory depression, while ketamine has the potential of neurotoxicity if inadvertently injected intrathecally [4]. As a result, effective and safe anaesthetic-sparing agents that carry neuroprotective effect have been widely studied. Dexmedetomidine as a selective α_2-adrenoceptor agonist has gained the attention of researchers because of its cardiac, renal, and neuroprotective properties in preclinical studies [5]. It appears to be less neurotoxic than other existing agents and has the potential to be neuroprotective in the neonatal and paediatric settings [6]. Its selectivity for α_2-adrenoceptor makes it much more effective sedative and analgesic agent than clonidine [7]. This selectivity is mainly responsible for the proposed neuroprotective effects of dexmedetomidine [8]. α_2-adrenoceptors agonists have relevant physiological properties which induce sedation and analgesia, plasma catecholamine reduction, attenuation of surgery induced stress responses, and shivering prevention via the α_2-adrenoceptors in the central nervous system [9]. Dexmedetomidine promotes sedation in a manner similar to physiological sleep (cooperative sedation) due to its regulation of wakefulness through its action on the ventrolateral preoptic nucleus (VLOP) neuronal circuity [10,11]. It is also evident that perineural dexmedetomidine when added to local

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anaesthetic can prolong the duration of analgesia through blocking of the hyperpolarization-activated cation current [12].

Regarding to magnesium, the interest to study its analgesic effects is increasing. Magnesium antinociceptive effects are primarily based upon the regulation of calcium influx into the cell. It is a physiological calcium antagonist and blocks N-methyl D-aspartate (NMDA) receptor, and such antagonism prevents the central sensitization from nociceptive stimulation. Many studies have suggested that epidurally administered magnesium as an adjuvant could reduce the postoperative pain in adults. But few studies are available regarding its use as an adjuvant in the caudal block for postoperative analgesia in paediatrics [13–17].

2. Aim

We designed this study to evaluate the implication of adding dexmedetomidine, magnesium sulphate, or their combination with isobaric bupivacaine 0.25% caudal anaesthesia in paediatric patients undergoing lower abdominal surgeries upon the time to first analgesia request (Primary outcome). Sedation, motor recovery, and hemodynamic stability are investigated as well (Secondary outcome).

3. Patient and methods

This is a randomized clinical trial, performed in Paediatric hospital of Assiut University. It was approved by our local institutional ethics committee and registered in Clinical trials (NCT02487355). The study adhered to Good Clinical Practice, the Declaration of Helsinki [18], and conducted in accordance with the Consort checklist in the period between August 2015 to December 2016. Written parental informed consent was obtained from 120 participants of ASA classification I or II children undergoing elective lower abdominal surgeries under general anaesthesia with caudal block supplementation. Study exclusion criteria included; parental refusal, allergy to local anesthetics, coagulation disorders, infection or anatomic abnormalities at the site of caudal injection, the current use of calcium channel blockers or medication that may affect the neurologic system, an intensive need for preoperative sedation or analgesia, and or prolonged surgery (> 90 min.). Randomization was done through computer-generated random number tables, and placed in an opaque sealed envelope which was opened in the morning of surgery by the anesthesiologist who was going to give the caudal block.

According to randomization, 120 participants were equally and randomly allocated into one of the four groups. The principal component of the mixture which was injected caudally was bupivacaine 0.25% in a dose of 1 ml/kg in all participants. The adjuvants were added as following: **Group (C):**1 ml of normal saline as placebo. **Group MG**: magnesium sulphate (50 mg), and 0.5 ml normal saline. **Group D**: dexmedetomidine1 μg/kg (Precedex 100 μg/mL; Hospira, Inc., Lake Forest, IL USA) in 1 ml normal saline. **Group MGD**: dexmedetomidine (1 μg/kg), and magnesium sulphate (50 mg) in 1 ml saline. Maximum total volume to be injected was 30 ml in all patients.

The caudal block medications were prepared by anaesthesia technician (high nurse) under complete aseptic conditions. Parents or guardians and the postoperative follow-up anesthesiologist were kept blind to grouping.

Induction of anaesthesia was done under basic anaesthesia monitoring (ECG, non-invasive blood pressure, SPO2, and Capnography after intubation) through the face mask with sevoflurane (concentration of 8% in oxygen). An intravenous cannula (22–24 gauge) was placed and secured in the dorsum of the hand. Tracheal intubation was facilitated with cisatracurium (0.1 mg/kg), then the endotracheal tube was secured. The patient was placed in the lateral decubitus position, and a single dose caudal block (standard loss of resistance technique) was performed through a 23-gauge needle, then the child was turned supine, and anaesthesia was maintained with isoflurane (concentration of 1:1.5% corrected for age) in air oxygen mixture (ratio of 1:1).

HR was continuously monitored, and the MAP was measured every 5 min during the whole anaesthesia process. Values of both HR and MAP were selectively collected pre and after induction, then at the 15th minute following administration of caudal block (with the skin incision), 30th minute, by the end of surgery, at recovery, then by the end of 1st, and 2nd postoperative hours.

During surgery, the adequacy of analgesia was observed through stable hemodynamics, and any increase by ≥20% in HR or systolic blood pressure (SBP) above the pre-incision values, the child was withdrawn from the study and received intravenous 1 μg/kg Fentanyl. Bradycardia (≥20% decrease in HR) was treated with iv. atropine (0.01 mg/kg), while hypotension (≥20% decrease in SBP) was treated with iv fluids or ephedrine (0.5 mg/kg) as appropriate.

Intravenous fluids were administered at a flow rate of 3–5 ml/kg/hr. No extra analgesics or sedatives were administered. The surgical incision was allowed at least 15 min after the injection. At the end of surgery, muscle relaxation was reversed by neostigmine (50 μg/kg) and atropine (10 μg/kg), then the patient was extubated and transferred to post-anaesthesia care unit (PACU). Postoperative adverse events such as nausea, vomiting, hypotension, bradycardia, and respiratory depression (defined by bradypnea and decreased SPO2 of less than 95%), and residual muscle weakness were noted and treated.

3.1. Data collection

The time to first analgesia request was recorded. Analgesia was monitored though The Face, Legs, Activity, Cry, Consolability (FLACC) pain score immediately with recover, and every 30 min until the 2nd hour, then at the 4th, 6th, 12th,18th, and 24th hours [19]. Intravenous paracetamol (15 mg/kg) was given when the FLACC score was ≥3. Postoperative sedation was assessed by Ramsay's sedation scale [20] at the same time points of FLACC assessment. Motor power scale [21] was used to assess the regaining of motor strength at the 1st, 2nd, 3rd, 4th, 6th, 8th, 12th, 18th, and 24th hours postoperatively. A complete loss of muscle motor tone when the limb is moved passively was considered flaccidity, whereas partial return of muscle tone (hypotonia), and contraction with partial ability to move the limb was considered partial recovery. Full ability to move the limb against gravity without any support was considered as normal (full) recovery.

3.2. Statistical analysis

Based upon previous study [9], and a calculated sample size of 28 would have an 80% power to detect a difference of 20% in time to first analgesic requirement with type I error of $\alpha = 0.05$ using a confidence interval of 95%. Thirty patients were enrolled in each group to compensate for any dropouts during the study. Data were expressed as numbers, ratios, mean ± standard deviation (SD), standard error (SE), median, and range as appropriate. Categorical variables (gender, ASA classification, frequency of paracetamol administration) were compared using chi-square (χ^2) test while continuous parametric data variables (HR, MAP, time to first analgesia request) by one-way ANOVA test. Continuous non-parametric data variables (FLACC score, sedation, and motor scales) were compared by Kruskal Wallis test. A two-tailed p-value < 0.05 was considered statistically significant. Statistical analysis was done using the computer program IBM, SPSS (Statistical Package for Social Sciences), Version 23, 2016.

4. Results

A total number of 120 patients were enrolled equally into the four groups as shown in CONSORT flow chart (Fig. 1). There were insignificant differences between groups with regards to age, gender, weight, ASA Status, and operative procedure as shown in (Table 1).

Time to the first request of analgesia request showed a significant

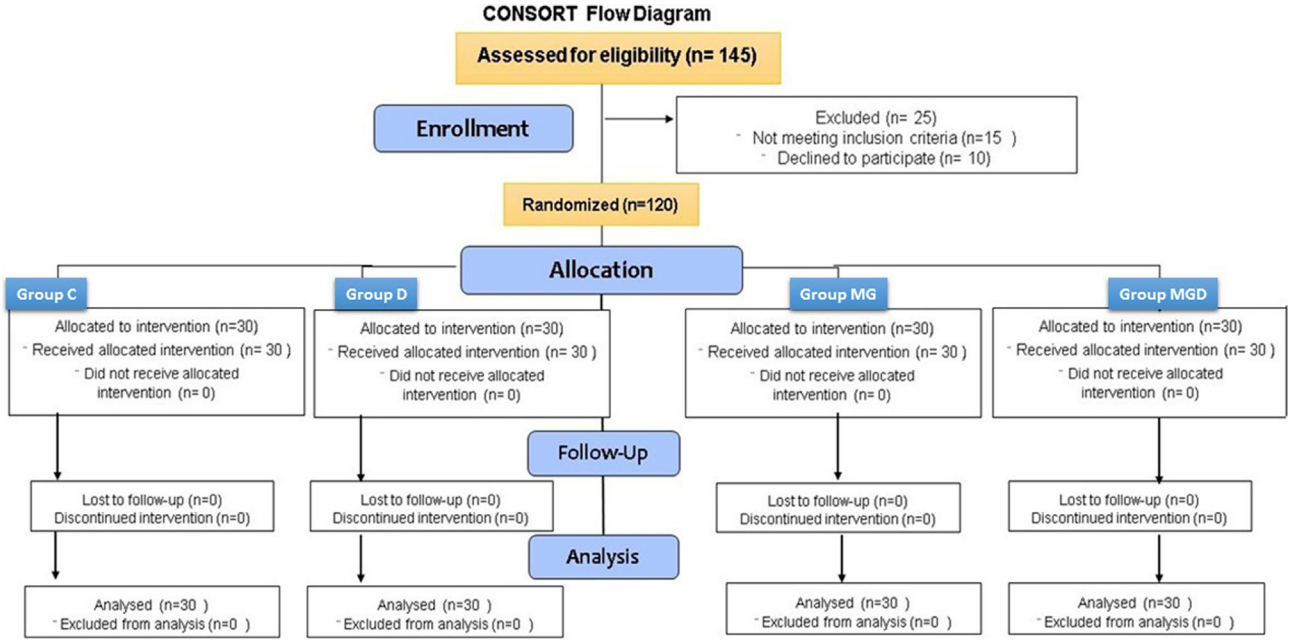

Fig. 1. CONSORT flow chart.

difference between the four groups ($p < 0.001$), and the times were significantly longer in the three study groups compared to control group. The group MGD has significantly the longest duration of analgesia up to 20.47 h when compared to the other three groups (Fig. 2).

Total paracetamol consumption over 24 h showed significant differences between all groups with $p < 0.001$. Both groups D and Mg showed significantly lower total paracetamol consumption when compared to group C. Group MGD total paracetamol consumption was nil; hence, showed significant differences in comparison to the other three groups. There were significant differences between the four groups with regards to the frequency of paracetamol administrations. Group MGD patients haven't required paracetamol during the study period; while, group C patients showed the highest frequency of paracetamol administrations (see Table 2).

Postoperative FLACC scores (Table 3) have shown significant differences between the four groups during the early six postoperative hours. FLACC scores were significantly higher in the group C in comparison to D, MG, and MGD groups by the 2nd, and 4th hours, while by the 6th hour, group C score was significantly higher than in scores in MG, and MGD groups. The group MGD showed significantly lowest FLACC score than the other groups at the 6th hour.

Postoperative Ramsey sedation scale showed significant differences between study groups during the whole first postoperative hour. Up to the time of 90 min, patients in group MGD showed significantly highest scale than those in other groups, while group C showed significantly the lowest scale (Fig. 3).

Table 1
Demographic and clinical data.

Variables	C n = 30	D n = 30	MG n = 30	MGD n = 30	P value
Gender (male/female)	13/17	14/16	16/14	15/15	0.88
Age (years)	3.4 ± 1.71	3.24 ± 1.68	3.89 ± 1.37	4.03 ± 1.58	0.78
Weight (kg)	14.64 ± 3.72	14.57 ± 3.98	15.8 ± 4.48	17.1 ± 3.98	0.44
ASA I/II	30/0	30/0	30/0	30/0	–
Operative details					
Operative time (min.)	37.67 ± 14.74	34.33 ± 12.08	48.33 ± 19.43	40.33 ± 12.88	0.08
Operative type (number of patients)					
Ambigious Genitalia	0	2	0	0	–
Appendicectomy	0	0	0	4	–
Colostomy closure	0	2	0	0	–
Congenital hernia	8	8	4	4	–
Congenital megacolon	2	0	2	0	–
Encysted hydrocele	4	0	0	0	–
Excisional biopsy	0	2	0	0	–
Hernia of canal of Nuck	2	4	2	4	–
Hypospadius	8	2	18	6	–
Incisional hernia	2	0	0	2	–
Inguinal hernia	0	2	2	2	–
Obstructed hernia	0	0	0	2	–
Umbilical hernia	0	0	2	0	–
Undescended testis	4	8	0	6	–

Data are expressed as ratios, mean ± SD, or numbers. Group C; control group, Group D; dexmedetomidine group, Group MG magnesium group, Group MGD dexmedetomidine and magnesium group. *P* value < 0.05 is considered statistically significant.

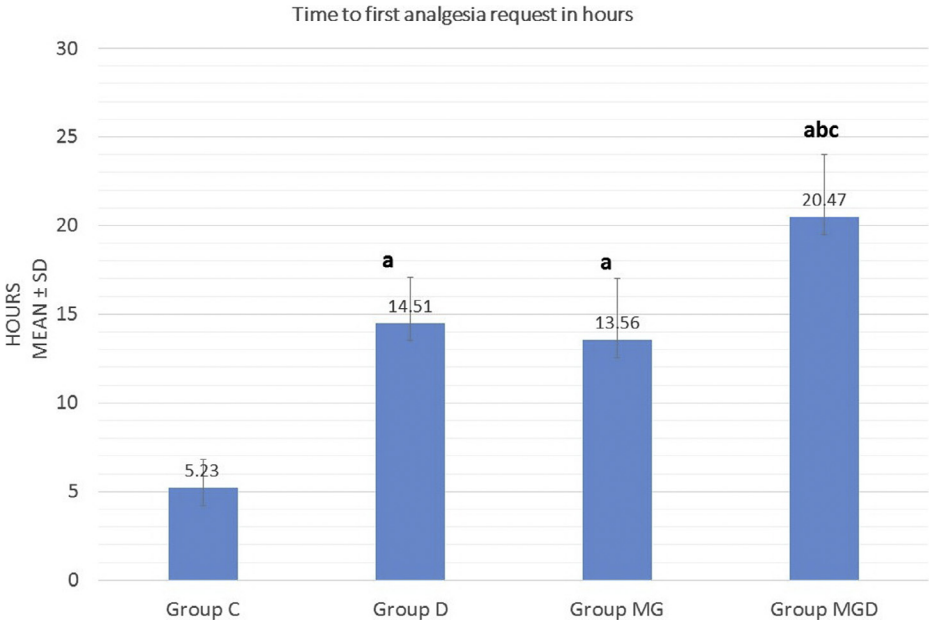

Fig. 2. Time to first analgesia request. Data are presented mean ± SD. Group C; control group, Group D; dexmedetomidine group, Group MG magnesium group, Group MGD dexmedetomidine and magnesium group. (a) Statistically significant difference in comparison with group C, (b) Statistically significant difference in comparison with group D, (c) Statistically significant difference in comparison with group Mg. P value < 0.05 is considered statistically significant.

Table 2
Paracetamol consumption.

Item	C n = 30	D n = 30	MG n = 30	MGD n = 30	*P value*
Frequency of paracetamol (15 mg/kg/dose)					
No paracetamol	0(0%)	0 (0%)	8(26.67%)	30(100%)	< 0.001*
One time	10 (33.33%)	11 (36.67%)	18(60.0%)	0(0%)	
Two times	6 (20.0%)	5(16.67%)	3(10.0%)	0 (0%)	
Three times	14 (46.67%)	14 (46.67%)	1 (3.33%)	0 (0%)	
Total consumption in mg	515.6 ± 41.23	228.3 ± 17.42[a]	306.2 ± 34.25[a]	0 ± 0[a,b,c]	< 0.001*

Data are expressed as numbers of the patients with ratio, or mean ± SD. Group C; control group, Group D; dexmedetomidine group, Group MG magnesium group, Group MGD dexmedetomidine and magnesium group. *Statistically significant difference between the four groups, [a]Statistically significant difference in comparison with group C, [b]Statistically significant difference in comparison with group D, [c]Statistically significant difference in comparison with group Mg. *P* value < 0.05 is considered statistically significant.

Table 3
Postoperative FLACC score mean ± SE (min-max).

FLACC	C n = 30	D n = 30	MG n = 30	MGD n = 30	P Value (between the 4 groups)
30 min	0.67 ± 0.18 1(0.0–2.0)	0.27 ± 0.15 0(0.0–2.0)	0.50 ± 0.19 0(0.0–2.0)	0.20 ± 0.14 0(0.0–2.0)	0.013*
60 min	0.60 ± 0.19 0(0.0–2.0)	0.47 ± 0.19 0(0.0–2.0)	0.60 ± 0.19 0(0.0–2.0)	0.20 ± 0.10 0(0.0–1.0)	0.326*
90 min	0.93 ± 0.18 1(0.0–3.0)	0.73 ± 0.15 1(0.0–2.0)	0.80 ± 0.17 1(0.0–2.0)	0.40 ± 0.16 0(0.0–2.0)	0.155*
2 h	2.0 ± 0.25 2(2.0–4.0)	0.80 ± 0.22[a] 1(0.0–2.0)	0.53 ± 0.23[a] 0(0.0–3.0)	0.27 ± 0.15[a] 0(0.0–2.0)	< 0.001*
4 h	3.20 ± 0.20 3(2.0–4.0)	0.87 ± 0.23[a] 1(0.0–2.0)	0.53 ± 0.23[a] 0(0.0–3.0)	0.67 ± 0.21[a] 0(0.0–2.0)	< 0.001*
6 h	2.93 ± 1.33 4(1.0–4.0)	2.33 ± 0.36 2(0.0–4.0)	2.27 ± 0.37[a] 1(0.0–4.0)	1.53 ± 0.32[a,b,c] 0(0.0–2.0)	< 0.001*
12 h	1.53 ± 0.16 1(1.0–3.0)	1.33 ± 0.21 2(0.0–3.0)	1.13 ± 0.16 2(0.0–2.0)	0.73 ± 0.11 0(0.0–1.0)	0.17
18 h	1.533 ± 0.17 1(1.0–3.0)	1.33 ± 0.21 1(0.0–3.0)	1.13 ± 0.16 1(0.0–2.0)	1.03 ± 0.12 1(0.0–2.0)	0.24
24 h	1.33 ± 0.23 1(1.0–4.0)	1.20 ± 0.20 1(1.0–4.0)	1.60 ± 0.32 1(1.0–4.0)	1.13 ± 0.13 1(1.0–2.0)	0.502

Data are expressed as mean ± SE, median and range. Group C; control group, Group D; dexmedetomidine group, Group MG magnesium group, Group MGD dexmedetomidine and magnesium group. *Statistically significant difference between the four groups, [a]Statistically significant difference in comparison with group C, [b]Statistically significant difference in comparison with group D, [c]Statistically significant difference in comparison with group Mg. *P* value < 0.05 is considered statistically significant.

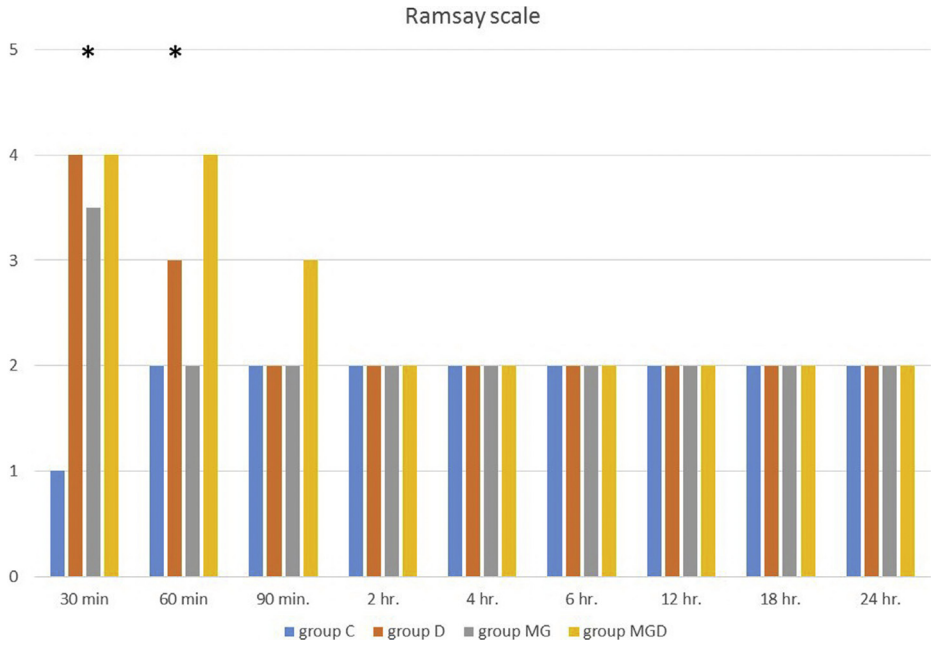

Fig. 3. Ramsay Scale. Data are expressed as median values. Group C; control group, Group D; dexmedetomidine group, Group MG magnesium group, Group MGD dexmedetomidine and magnesium group. (*) Significant differences between groups. *P* value < 0.05 is considered statistically significant.

Fig. 4. Motor power scale. Data are expressed as median values. Group C; control group, Group D; dexmedetomidine group, Group MG magnesium group, Group MGD dexmedetomidine and magnesium group. (*) Significant differences between groups. *P* value < 0.05 is considered statistically significant.

Postoperative motor power scale showed significant differences between all groups at the 1st and 2nd hours, with group C patients have significantly the highest motor scale than the other groups at the same period. All participants have demonstrated full recovery of their motor power strength (scale = 10) by the 3rd hour as shown in Fig. 4.

Perioperative changes in the MAP (Fig. 5) showed a significant decrease in group D patients after the caudal block by the 15th min compared to patients in groups C and MG. By the 30th min., there was significant sustained MAP decrease in group D compared to group MG patients. At the end of surgery, MAP values were significantly lower in the groups which received dexmedetomidine (D, and MGD) compared to group C. Patients in group D have a significantly lower MAP than those in group MG immediately after recovery, and patients in the control group have significantly higher MAP than the other three study groups during at the first postoperative hour. Heart rate changes (Fig. 6) showed that group C patients have significantly the highest values after recovery and up to the 1st postoperative. By the 2nd postoperative hour, HR values were significantly low in group MGD in comparison to the other study groups. Observed hemodynamic changes were within clinically accepted ranges.

No respiratory depression, circulatory instability, neurologic deficit (weakness), or urinary retention was noted in our study participants.

5. Discussion

To our knowledge, this is the only study which utilized dexmedetomidine, magnesium, and bupivacaine in combination for the caudal block in paediatrics. The key finding of our study is that such combination has provided the longer time to first analgesia request and better pain alleviation. Consumptions of paracetamol were reduced in

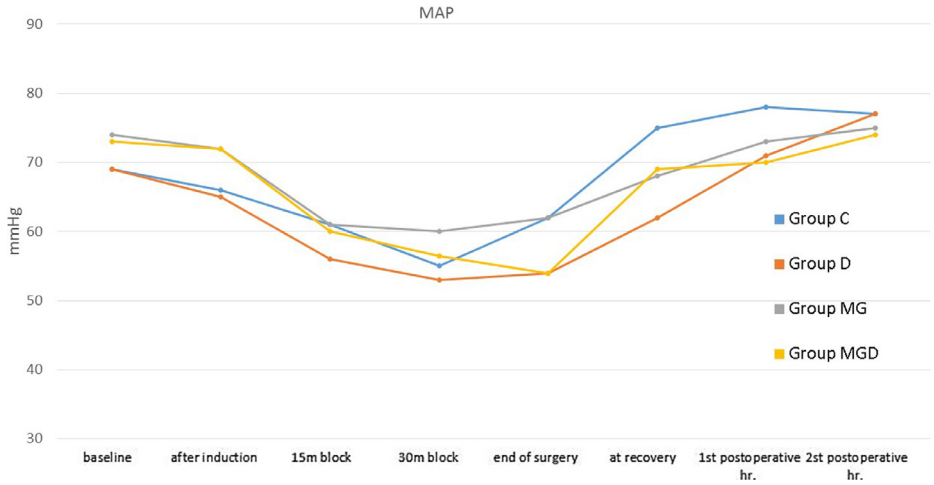

Fig. 5. Perioperative MAP changes. Data are presented as mean. Group C; control group, Group D; dexmedetomidine group, Group MG magnesium group, Group MGD dexmedetomidine and magnesium group. *P* value < 0.05 is considered statistically significant.

dexmedetomidine, and magnesium groups. There was no need for paracetamol for pain alleviation in the mixed group (Magnesium and dexmedetomidine) during the study period.

This is in agreement with Makhni et al who recruited 50 adult patients underwent infra-umbilical surgeries under spinal anaesthesia and were randomized equally into two groups. Group D patients received an intrathecal injection of ropivacaine with 10 μg dexmedetomidine, versus group M which received intrathecal ropivacaine with 10 μg dexmedetomidine, and 57 mg magnesium sulphate. They found significantly longer time to the first rescue analgesia in group M [22].

Each adjuvant in our study is well-known to be unique in its mechanism of action, safe, and can prolong the pain-free period. It is evident that neuraxial dexmedetomidine exerts analgesia by inhibiting spinal microglial and astrocytes activation, depressing the release of nociceptive substances, interrupting spinal neuro-glial cross action; hence, regulating the nociceptive transmission [1–4]. These antinociceptive effects of intrathecal dexmedetomidine are dose-dependent [5,6]. Its selective agonistic effect upon α2- adrenoceptors in the dorsal horn of the spinal cord can inhibit the release of neurotransmitters, preventing prolongation of neural activity which makes it as an effective sedative and analgesic agent [9].

The prolongation of analgesia in dexmedetomidine group is in agreement with Goyal et al who studied postoperative analgesia duration in 100 children who underwent infra-umbilical surgeries, and found that the analgesia duration was significantly prolonged in the group received dexmedetomidine added to bupivacaine through the caudal approach in comparison to those who received bupivacaine only [23]. Saadway and Xiang studies have compared local anaesthetic (ropivacaine and bupivacaine) with, and without dexmedetomidine for caudal analgesia, and confirmed that the duration of analgesia was significantly longer whenever dexmedetomidine was administrated [24,25].

Magnesium sulphate is a noncompetitive N-methyl D-aspartate (NMDA) antagonist with its analgesic action is based mainly upon the regulation of calcium influx into the cells [13]. Studies have demonstrated that magnesium sulphate administration for paediatric caudal analgesia in a single 50 mg bolus dose can prevent intraoperative discomfort, and delay the onset of postoperative pain [13,26]. In our study the mean duration of analgesia was significantly longer in the study groups compared to the control group; however, the combined group has shown the longest duration of analgesia. Our findings agree with Yousef et al who compared either magnesium or dexamethasone as additive to ropivacaine caudal analgesia in children who underwent inguinal hernia repair. They found a significant prolongation of analgesia duration in the magnesium group [13].

FLACC score which is a well-known validated score for pain

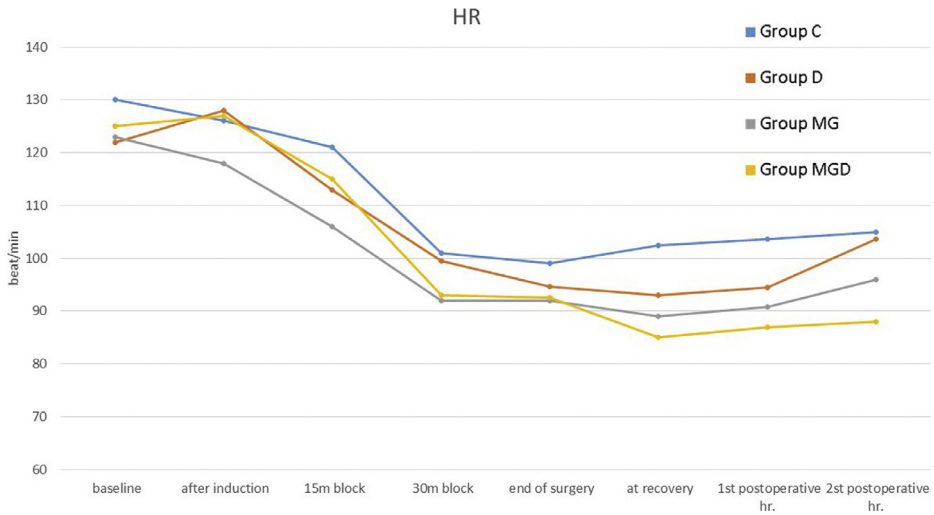

Fig. 6. Perioperative HR changes. Data are presented as mean. Group C; control group, Group D; dexmedetomidine group, Group MG magnesium group, Group MGD dexmedetomidine and magnesium group. *P* value < 0.05 is considered statistically significant.

alleviation in paediatric, showed significant reductions in the study groups (MG, D, and MGD) at the 2nd, and 4th postoperative hours in comparison to corresponding scores in group C patients. The validity of FLACC score was discussed in previous studies and it was comparable with other pain assessment score in paediatrics e.g. COMFORT behavioral scale, and Checklist of Nonverbal Pain Indicators [27,28].

Our FLACC score results are supported by Anand et al study which randomized 60 children into two groups receiving ropivacaine with dexmedetomidine (group RD) or ropivacaine alone (group R). FLACC pain score reflected that the duration of postoperative analgesia was significantly longer in group RD [29]. The same was shown by Wu et al study, which confirmed that neuraxial dexmedetomidine as a local anaesthetic adjuvant, significantly decreased postoperative pain intensity and prolonged the analgesic duration [30].

Also, we found a significant reduction of FLACC pain score and analgesia consumption in the magnesium group, which agrees with Kim et al who used ropivacaine alone, or with magnesium (50 mg) through caudal block in 80 children undergoing inguinal herniorrhaphy. They found significantly lower postoperative pain scores and analgesia consumption when magnesium was added. They also found that the time to return of normal functional activity was shorter with no difference in the incidence of adverse effects [31].

Giving our concern for a possible neurotoxicity from neuraxial dexmedetomidine, we selected a dose of 1 μg/kg similar to the study done by Hou et al, which suggested that low doses of intrathecal dexmedetomidine (0.75:1.50 μg/kg) can relieve pain without the risk of neurotoxicity [7]. Al-Zabenetal also mentioned that caudal dexmedetomidine in a dose of 1 μg/kg was comparable to the dose of 2 μg/kg regarding to the prolongation of postoperative analgesia, with shorter duration of postoperative sedation, lower incidence of side effects, and devoid of neurotoxicity [8]. We monitored the return of motor function as an indicator of the return of neuro-conduction, in addition to sedation score. The return of motor strength showed significant differences between control group and all other study groups at the 1st and 2nd postoperative hours; however, full motor recovery was established by the 3rd hour in all patients.

We have found higher Ramsay sedation scales in study groups which received dexmedetomidine compared to group C. Interestingly, the sedative effect of dexmedetomidine was easily reversed with verbal or physical stimuli with the child returning to sleep when not stimulated. This is in concordance with the reports which denoted that neuraxial dexmedetomidine was associated with beneficial alteration in the postoperative sedation scores in the form of better quality of sleep and a prolonged duration of sedation [9,24,29,32]. Dexmedetomidine has hypnotic and supraspinal analgesic effects attributed to the suppressed release of inhibitory control trigger neurotransmitters, which can decrease histamine release, and the net result is hypnosis resembling normal sleep without ventilatory suppression [10]. Delirium which is a common drawback form the other sedatives is not an issue with dexmedetomidine as it does not act though gamma-aminobutyric acid system [33].

The statistical differences in hemodynamics between groups were of no clinical significance and all values were within accepted ranges. This is in accordance with Fares et al study upon a group of children who received caudal block, where they found a statistical difference between caudal bupivacaine group and dexmedetomidine plus bupivacaine group, which was clinically insignificant, and this has augmented the concept that bradycardia and the possible hypotensive effects of α2-adrenoceptors agonists appear to be less pronounced in children than in adults [32]. Saadawy et al also have found a non-statistically significant difference regarding hemodynamics when utilizing dexmedetomidine with bupivacaine versus bupivacaine alone through the caudal block in 60 children who underwent infraumbilical surgeries under general anaesthesia [24]. However, a meta-analysis done by Wu et al concluded that the risk of bradycardia, but not the hypotension is increased with the use of neuraxial dexmedetomidine [30]. Xiang et al have also revealed that supplementation of caudal bupivacaine with dexmedetomidine (1 μg/kg) attenuated the hemodynamic response to hernial sac traction in paediatric patients undergoing repair of an inguinal hernia [25].

No episodes of SPO2 desaturation nor respiratory depression have been noticed in our trial. This is augmented by Ramsay and his colleague who mentioned that α2-agonists have no respiratory depressant effect [34].

6. Limitations

The early use of FLACC can be considered as a weak point for postoperative pain evaluation in the presence of differences in motor and sedation scales between groups during first four postoperative hours.

7. Conclusion

The combination of dexmedetomidine (1μg/kg), and magnesium sulphate (50 mg) with 0.25% bupivacaine caudal block prolongs the duration of the pain-free period in paediatric patients undergoing lower abdominal surgeries compared to bupivacaine only, or bupivacaine with each one of them alone. The combination carries a safe profile on motor, respiratory, and cardiovascular functions.

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Conflict of interest

The authors declared that there is no conflict of interest.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.egja.2018.06.001.

References

[1] Bailey B, Trottier ED. Managing pediatric pain in the emergency department. Paediatr Drugs 2016;18:287–301.
[2] Abdel-Ghaffar HS, Moeen SM, Moeen AM. Topical versus caudal ketamine/bupivacaine combination for postoperative analgesia in children undergoing inguinal herniotomy. Saudi J Anaesth 2017;11(1):41–8.
[3] Kalappa S, Sridhara RB, Kumaraswamy S. Dexmedetomidine as an adjuvant to preemptive caudal epidural ropivacaine for lumbosacral spine surgeries. J Clin Diagn Res 2016;10:UC22–4.
[4] Singhal NR, Jones J, Semenova J, Williamson A, McCollum K, Tong D, Jerman J, Notrica DM, Nguyen H. Multimodal anesthesia with the addition of methadone is superior to epidural analgesia: a retrospective comparison of intraoperative anesthetic techniques and pain management for 124 pediatric patients undergoing the Nuss procedure. J Pediatr Surg 2016;51(4):612–6.
[5] Fisher B, Zornow MH, Yaksh TL, Peterson BM. Antinociceptive properties of intrathecal dexmedetomidine in rats. Eur J Pharmacol 1991;192(2):221–5.
[6] Alam A, Suen KC, Hana Z, Sanders RD, Maze M, Ma D. Neuroprotection and neurotoxicity in the developing brain: an update on the effects of dexmedetomidine and xenon. Neurotoxicol Teratol 2017;60:102–16.
[7] Jarineshin H, Fekrat F, Kargar Kermanshah A. Treatment of postoperative pain in pediatric operations: comparing the efficiency of bupivacaine, bupivacaine-dexmedetomidine and bupivacaine-fentanyl for caudal block. Anesth Pain Med 2016;6(5):e39495.
[8] Ma D, Hossain M, Rajakumaraswamy N, Arshad M, Sanders RD, Franks NP, Maze M. Dexmedetomidine produces its neuroprotective effect via the alpha 2A-adrenoceptor subtype. Eur J Pharmacol 2004;502(1–2):87–97.
[9] Kamal M, Mohammed S, Meena S, Singariya G, Kumar R, Chauhan DS. Efficacy of dexmedetomidine as an adjuvant to ropivacaine in pediatric caudal epidural block. Saudi J Anaesth 2016;10:384–9.
[10] Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M. The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. Anesthesiology 2003;98(2):428–36.

[11] Fernandes ML, do Carmo Santos M, Gomez RS. Sedation with dexmedetomidine forconducting electroencephalogram in a patient with Angelman syndrome: a case report. Braz J Anesthesiol 2016;66(2):212–4.
[12] Brummett CM, Hong EK, Janda AM, Amodeo FS, Lydic R. Perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolongs the duration of analgesia by blocking the hyperpolarization-activated cation current. Anesthesiology 2011;115(4):836–43.
[13] Yousef GT, Ibrahim TH, Khder A, Ibrahim M. Enhancement of ropivacaine caudal analgesia using dexamethasone or magnesium in children undergoing inguinal hernia repair. Anesth Essays Res 2014;8(1):13–9.
[14] Farouk S. Pre-incisional epidural magnesium provides pre-emptive and preventive analgesia in patients undergoing abdominal hysterectomy. Br J Anaesth 2008;101:694–9.
[15] Kim SM, Cho SH, Kim SH, Lee DG, Chae WS, Jin HC. The effects of epidural magnesium on postoperative pain management in patients with patient-controlled epidural analgesia after a thoracotomy. Korean J Anesthesiol 2009;57:466–71.
[16] Bilir A, Gulec S, Erkan A, Ozcelik A. Epidural magnesium reduces postoperative analgesic requirement. Br J Anaesth 2007;98:519–23.
[17] Birbicer H, Doruk N, Cinel I, et al. Could adding magnesium as adjuvant to ropivacaine in caudal anaesthesia improve postoperative pain control? Pediatr Surg Int 2007;23:195–8.
[18] World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310(20):2191–4.
[19] Merkel SI, Voeoel-Lewus T, Shayevitz JR, Malviya S. The FLACC: a behavioral scale, for scoring postoperative pain in young children. Pediatr Nurs 1997;23:293–7.
[20] Ramsay MA, Kuterman DL. Dexmedetomidine as a total intravenous anesthetic agent. Anesthesiology 2004;101:787–90.
[21] Kumar M, Gupta KK, Kataria AP. Comparison of caudal ropivacaine 0.2% with bupivacaine 0.2% in pediatric patients – a randomized controlled trial. Anesth Pain Intensive Care 2015;18:141–6.
[22] Makhni R, Attri JP, Jain P, Chatrath V. Comparison of dexmedetomidine and magnesium sulfate as adjuvants with ropivacaine for spinal anesthesia in infra-umbilical surgeries and postoperative analgesia. Anesth Essays Res 2017;11(1):206–10.
[23] Goyal V, Kubre J, Radhakrishnan K. Dexmedetomidine as an adjuvant to bupivacaine in caudal analgesia in children. Anesth Essays Res 2016;10(2):227–32.
[24] Saadawy I, Boker A, Elshahawy MA, Almazrooa A, Melibary S, Abdellatif AA, Afifi W. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in pediatrics. Acta Anaesthesiol Scand 2009;53(2):251–6.
[25] Xiang Q, Huang DY, Zhao YL, Anand GH, Liu YX, Zhong L, Luo T. Caudal dexmedetomidine combined with bupivacaine inhibit the response to hernial sac traction in children undergoing inguinal hernia repair. Br J Anaesth 2013;110(3):420–4.
[26] Albrecht E, Kirkham KR, Liu SS, Brull R. The analgesic efficacy and safety of neuraxial magnesium sulphate: a quantitative review. Anaesthesia 2013;68(2):190–202.
[27] Bai J, Hsu L, Tang Y, van Dijk M. Validation of the COMFORT Behavior scale and the FLACC scale for pain assessment in Chinese children after cardiac surgery. PainManag Nurs 2012;13(1):18–26.
[28] Voepel-Lewis T, Zanotti J, Dammeyer JA, Merkel S. Reliability and validity of the face, legs, activity, cry, consolability behavioral tool in assessing acute pain in critically ill patients. Am J Crit Care 2010;19(1):55–61.
[29] Anand VG, Kannan M, Thavamani A, Bridgit MJ. Effects of dexmedetomidine added to caudal ropivacaine in paediatric lower abdominal surgeries. Indian J Anaesth 2011;55:340–6.
[30] Wu HH, Wang HT, Jin JJ, Cui GB, Zhou KC, Chen Y, Chen GZ, Dong YL, Wang W. Does dexmedetomidine as a neuraxial adjuvant facilitate better anesthesia and analgesia? A systematic review and meta-analysis. PLoS One 2014;9(3):e93114.
[31] Kim EM, Kim MS, Han SJ, Moon BK, Choi EM, Kim EH, Lee JR. Magnesium as an adjuvant for caudal analgesia in children. Paediatr Anaesth 2014;24(12):1231–8.
[32] Fares KM, Othman AH, Alieldin NH. Efficacy and safety of dexmedetomidine added to caudal bupivacaine in pediatric major abdominal cancer surgery. Pain Physician 2014;17(5):393–400.
[33] Martin E, Ramsay G, Mantz J, Sum-Ping ST. The role of the alpha2-adrenoceptor agonist dexmedetomidine in postsurgical sedation in the intensive care unit. J Intensive Care Med 2003;18(1):29–41.
[34] Ramsay MA, Luterman DL. Dexmedetomidine as a total intravenous anesthetic agent. Anesthesiology 2004;101(3):787–90.