Zagazig University Medical Journal
www.zumj.journals.ekb.eg

Manuscript ID ZUMJ-1907-1316 (R1)

DOI 10.21608/zumj.2019.14564.1316

ORIGINAL ARTICLE

Effect Of each Of Dexmedetomidine and Clonidine as adjuvant to bupivacaine caudal block on the severity of Stress Response and Postoperative Pain in Pediatric undergoing Inguinal Hernia repair Surgery.

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Submit Date	2019-07-11
Revise Date	2019-08-01
Accept Date	2019-08-10

ABSTRACT

Background: Caudal block is considered a safe anesthetic technique in pediatrics. Various additives were studied to improve the quality of caudal block. This study was conducted to evaluate the effects of caudal dexmedetomidine versus clonidine on postoperative pain and stress response when used as adjuvant to bupivacaine.

Patients and methods: Randomized double blinded trial included fourty eight ASA physical status class I and II patients aged 1-6 years who were scheduled for unilateral inguinal hernia repair. After induction of propofol sedation, caudal block was established. Patients allocated randomly into three groups with 16 patients in each. **Group A** patients received 1ml/kg of 0.25%bupivacaine plus 1ml normal saline. **Group D** patients received 1ml/kg of 0.25%bupivacaine plus dexmedetomidine 1µg/kg that was mixed with normal saline up to 1ml. **Group C** patients received 1ml/kg of 0.25%bupivacaine plus clonidine 1µg/kg that was mixed with normal saline up to 1ml. Hemodynamic parameters and serum cortisol levels were recorded. Postoperative analgesia duration, total analgesic requirements and side effects were recorded.

Results: Postoperative duration of analgesia in dexmedetomidine and clonidine groups was significantly prolonged than in bupivacaine group only, while in dexmedetomidine group was more prolonged than in clonidine group. Serum cortisol level was significantly lower in dexmedetomidine and clonidine groups compared to bupivacaine group. There were neither significant hemodynamic changes nor side effects detected.

Conclusion: Addition of 1µg/kg of either dexmedetomidine or clonidine to bupivacaine in caudal anesthesia led to prolongation of the duration of postoperative analgesia and attenuation of the stress response without postoperative complications.

Keywords: Dexmedetomidine, Clonidine, Stress response, Pediatric, Caudal anesthesia

INTRODUCTION

Pain following surgeries is one of the popular untreated medical problems especially in children. Various methods had been studied for postoperative pain control in pediatric patients to provide better quality and prolongation of the analgesia duration.[1] Caudal block is a safe technique performed for pediatric anesthesia. However, the main disadvantage of caudal block is the limited duration of analgesia following single injection.[2] Various potentiating agents were

used with local anesthetics such as morphine, ketamine, clonidine, neostigmine and dexmedetomidine.[3,4,5,6] Dexmedetomidine was proved to be potent analgesic agent used in various anesthetic techniques because of its high selectivity to alpha 2 adrenergic receptors.[7] Clonidine is also selective alpha 2 adrenoreceptor agonist drug which is effective in caudal anesthesia and improves the quality of analgesia with less postoperative analgesic requirement and side effects.[8]

Aim of the study: The study aim was to evaluate the effects of adding either clonidine or dexmedetomidine to caudal bupivacaine on the severity of neuroendocrine stress response and postoperative pain in pediatrics undergoing inguinal hernia repair surgery.

Patients and methods:

This prospective randomized double blinded controlled clinical trial was carried out at Zagazig University Hospitals from **January2017** till **January2019**. Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. Fourty eight ASA physical status class I and II pediatric patients of both sexes aged between 1-6 years old and weighting ranged from 10 to 20kg scheduled for inguinal hernia repair surgery at one side only were included. Patients with history of delayed development, mental retardation, any factor affecting cortisol level including endocrinal, neuronal disease and steroids administration and those with any contraindication to regional anesthesia including coagulation disorder, infection at puncture site and history of allergy to the study drugs were excluded from the study. Patients were evaluated preoperatively, all routine and specific investigations were noted and patients fasting (2hours for clear fluids and 6hours for semisolid and solid food) was confirmed. All operations were scheduled as the first case in the operation room to equalize the circadian changes in stress hormone levels. Patients were premedicated with 0.01mg /kg atropine and 0.1mg/kg midazolam after insertion of IV line. On arrival in the operating room, routine monitors were applied for recording heart rate (HR), mean arterial pressure (MAP) and oxygen saturation (SPO2) and intravenous lactated ringer infusion at rate of 6ml/kg/h was given. Patients were allocated randomly by sealed envelope into 3 equal groups, 16 patients in each and the anesthesiologist was blinded to each solution. Group A received 1ml/kg of 0.25%bupivacaine plus 1ml normal saline. Group D received 1ml/kg of 0.25% bupivacaine plus dexmedetomidine 1μg/kg that was mixed with normal saline up to 1ml. Group C received 1ml/kg 0.25% bupivacaine plus Clonidine 1μg/kg that was mixed with normal saline up to 1ml. After preoxygenation by simple mask ventilation, all patients received sedation with 2mg/kg propofol and then continuous infusion of 100μg/kg/min. Sedation was considered adequate, when the patient was unconscious and arousable only purposefully following repeated or painful stimulation, [9] laryngeal mask inserted and spontaneous respiration was maintained then he was turned to left lateral position for establishment of caudal block. Under complete antiseptic condition, the sacral hiatus was located, having as landmark the posterior superior iliac spines and the spinal processes of the sacral vertebrae. The puncture was performed with a 23 gauge needle and the correct needle position was checked by using the loss of resistance technique followed by injecting 3ml of saline then underlying skin was palpated for presence of swelling and if no swelling was present and the injection was heard by stethoscope over lumber spine (swoosh test), the needle was in correct position. After negative aspiration for blood or cerebrospinal fluid, the prepared drugs were injected into caudal space then patient was turned supine immediately after the injection. Surgeons started the surgery at the onset of caudal analgesia which occurred within 15

minutes after local anesthetic injection. The block was considered successful if there were absence of gross movement of limbs and hemodynamic instability by absence of increase in HR and MAP >20% compared to base line in response to painful stimuli with no analgesic given by any route intra-operatively. Intraoperative adverse effects like Bradycardia was defined as decrease in heart rate below the normal range for age i.e. <80 bpm for toddlers and <70 bpm for young children and was treated with atropine 0.01mg/kg. Hypotension was defined as decrease in MAP>30% from basal value [10] and was treated with IV fluids administration. Any response to painful stimuli was considered as failure of the block and the patient received general anesthesia with isoflurane, muscle relaxant and endotracheal tube insertion and the patient was excluded from the study. Toward the end of the surgery propofol infusion was stopped then patients were extubated and transferred to post anesthesia care unit (PACU). MAP and HR were recorded preoperatively (basal), immediately after induction of anesthesia, immediately after caudal block, every 10 minutes till the end of the surgery, immediately postoperatively(0 H) and then every 2 hour for 6 hours. Serum cortisol levels were recorded before induction of anesthesia (baseline), immediately after skin incision and postoperatively when patients achieved modified aldrete score [11]of 10**.**For serum cortisol measurement, 2ml of blood were delivered into sterile plain vacutainer tubes with stopper left to clot at 37c for 10 minutes then centrifuged at 3000(rpm) for 10 minutes. The serum was used for cortisol measurement by using ELISA"cobas 8000-e601" supplied by Roche diagnostics. Postoperative pain assessment by using face, legs, activity, cry, consolability score (FLACC) [12] **(table1)** was done at 30minutes from extubation and then every 2 hour till time of rescue analgesia then suppository10mg/kg of paracetamol was given. After that pain was assessed at every time analgesics were requested by resident and if pain score was equal or more than 4 analgesic was given. Total number of analgesic doses for postoperative pain relief in 1st24 hours and postoperative analgesia duration (the time interval between administration of the caudal block and the first requirement of analgesia postoperatively and when FLACC was 4 or more) were recorded. Also, postoperative complications e.g. vomiting, hypotension, bradycardia were recorded.

Study Outcome measures: The primary outcome of this study was to evaluate the effects of caudal dexmedetomine and clonidine on the duration of postoperative analgesia when added to bupivacaine and the secondary outcome was to evaluate their effects on stress response and hemodynamic parameters.

Statistical analysis:

Sample size: Assuming that postoperative analgesia duration in dexmedetomidine group is 14.16±3.65 hours, in clonidine group is 11.24±2.48 hours, confidence level 95% and power 80% in previous study[13] so total sample size is 48cases divided into 16cases in controlled group (group A), 16 cases in group D and 16 patients in group C calculated by (EPI). Data were collected throughout history, basic clinical examinations, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. Qualitative data were represented as number and percentage while quantitative data were represented as mean± SD. The following tests were used to test for significant difference and association of qualitative variable by Chi square test(X2).Differences between quantitative independent groups by t test, multiple by ANOVA. P value was set at <0.05 for significant and <0.001 for high significant difference.

RESULTS

Statistically, there were no significant differences between the demographic data of the three studied groups (P value>0.05). (Table

2)

Regarding MAP and HR levels (Fig. 1&2) Statistically, MAP and HR basal levels and other levels at various times of measurements of the three groups showed no significant differences (p value>0.05).

Statistically, there were no significant differences between the basal serum cortisol level of the three groups (P value>0.05). After skin incision, serum cortisol level increased in all groups but in group A it was 27.11±3.98 µg /dl which was significantly higher than that in group C and D (p value<0.05) and also it was higher in group C than D but the difference was not statistically significant (P value>0.05). Postoperatively, serum cortisol decreased toward the baseline in all groups but still was significantly higher in group A than the other two groups (p value< 0.05) and in group C its level was slightly higher than group D but the difference was not statistically significant (P value>0.05). (Table3)

Regarding pain severity levels at 0 hour, FLACC pain score was 0 in the 3 groups. At 2hours, the FLACC pain scores in the three groups were below 4 and statistically they were comparable (P value>0.05). At 4 hours, FLACC pain scores in the three groups were below 4. The score in group A (3.57±0.61) was significantly higher than those in group in group C (2.11±0.47) and group D (1.93±0.25). At 6 hours, only FLACC pain score in Group A was higher than 4. Statistically, FLACC pain score in group A (4.68±0.87) was significantly higher than those in group C (2.93±0.57) and group D (2.5±0.51). FLACC score in Group C was higher than that in D but the difference between them was not significant till 6 & 8hours and the score remains below 4 (P value>0.05).

At 10 and 12 hours, the corresponding FLACC scores in group C (4.25 ±0.68 and 5.0±0.51respectively) were above 4 and significantly higher than those in group D (3.19 ±0.54 and 3.88±0.95 respectively) (P value<0.001). At 14 hours, FLACC score reached >4 in Group D and was (4.75 ±1.1). (Fig. 3)

Statistically, the time to the 1st rescue analgesia was significantly shorter in group A than that in group C and D (p value <0.001). Also it was shorter in group C than that in group D, but the difference was not significant (P value>0.05).Also statistically, the amount of the consumed of analgesic during the 1st 24 hours postoperatively in group A was highly significant higher than that in group C and D (P value<0.001), also in group D it was significantly lower than that in group C (P value<0.05) (Table 4).

Postoperative complications were not detected in the three studied groups

Table (1): FLACC pain scale: [12]

	0	1	2
Face	**No particular expression or smile**	**Occasional grimace or frown, withdrawn, disinterested**	**Frequent to constant frown, quivering chin ,clenched jaw**
Legs	**Normal position or relaxed**	**Un easy, restless, tense**	**Kicking or leg drawn up**
Activity	**Lying quietly , normal position ,moves easily**	**Squirming, shifting back and froths, tense**	**Arched ,rigid, drawn up**
Cry	**No cry (awake or asleep)**	**Moans or whimpers**	**Crying steadily, screams or sobs , frequent complaints**
Consolability	**Content, relaxed**	**Reassured by occasional touching, hugging or being talked to distract**	**Difficult to console or comfort**

Table (2): Patient demographic data of the three studied groups

Demographic data			Group A (n=16)	Group B (n=16)	Group C (n=16)	F (ANOVA)	P
Age(years)			2.87±1.1	3.12±1.02	3.46±1.2	0.629	0.538
Weight(kg)			13.75±3.25	14.18±2.97	14.68±2.93	0.376	0.688
Gender	Female	N	2	2	1	0.44	0.8
		%	12.5%	12.5%	6.2%		
	Male	N	14	14	15		
		%	87.5%	87.5%	93.8%		
ASA Ps classes	I	N	15	16	14	2.13	0.34
		%	93.8%	100.0%	87.5%		
	II	N	1	0	2		
		%	6.2%	0.0%	12.5%		

Data were presented as mean± SD.
N= number of male, female and patients with ASA Ps class I and II in each group, ASA Ps classes: American society of anesthesiologists physical status classes
n= total number of patients in each group, ANOVA f test: analysis of variance.
P value >0.05 is statistically insignificant.

Table (3): Serum cortisol levels at various times of measurements in the three studied groups

Serum cortisol level (µg/dl)	Group A (n=16)	Group C (n=16)	Group D (n=16)	F (ANOVA)	P
Basal	16.98±4.69	17.07±4.24	16.46±3.89	0.095	0.909
After skin incision	27.11±3.98	23.86±2.6	22.8±3.52	6.902	0.002*
postoperative	23.66±3.52	21.34±3.22	20.69±2.52	4.000	0.025*

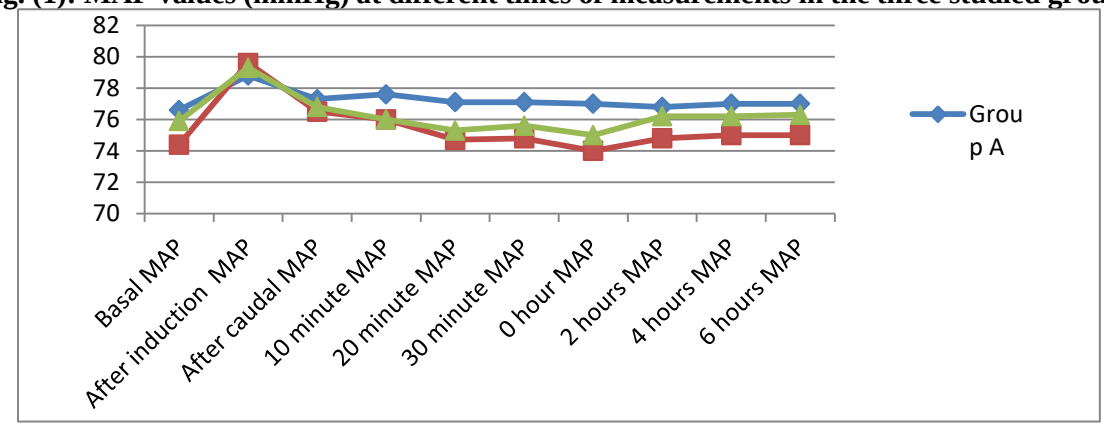
Data were presented as mean± SD.
n= total number of patients in each group, ANOVA f test: analysis of variance.
***p value <0.05 was statistically significant.**

Table(4):The time to the 1st rescue analgesia and the amount of the consumed of analgesic during the the 1st 24 hours postoperatively.

	Group A (n=16)	Group C (n=16)	Group D (n=16)	F (ANOVA)	P
Mean analgesic duration (per hour)	5.06±0.87	9.75±1.39	13.37±1.5	168.56	0.00**
Number of analgesic doses at 1st 24 hour	2.43±0.51	1.68±0.47	1.12±0.38	28.062	0.00**

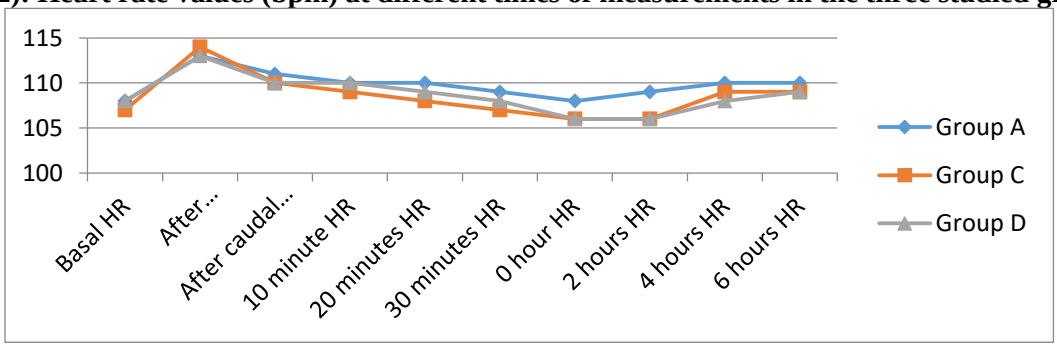
Data were presented as mean± SD.
n= total number of patients in each group, ANOVA f test: analysis of variance.
****P value < 0.001 was statistically high significant.**

Fig. (1): MAP values (mmHg) at different times of measurements in the three studied groups.



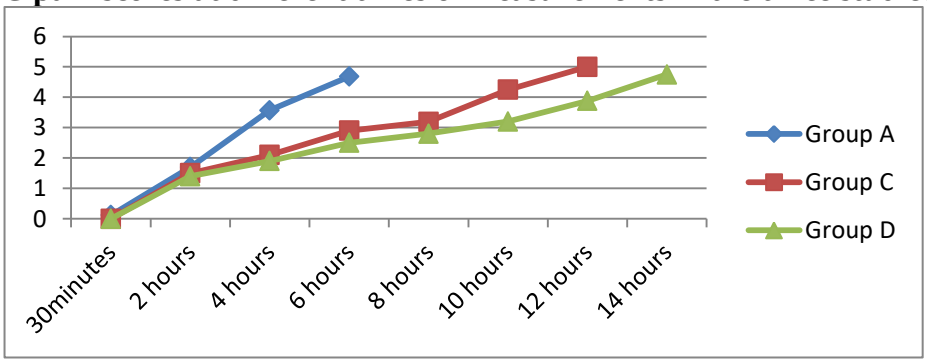
0 hour: immediate postoperative
Before 0 hour; pre and intra-operative, while after 0 hour; post-operative.
Data were presented as mean ±SD.
MAP: mean arterial pressure.
ANOVA F test: analysis of variance.

Fig. (2): Heart rate values (bpm) at different times of measurements in the three studied groups.



0 hour: immediate postoperative
Before 0 hour; pre and intra-operative, while after 0 hour; post-operative.
Data were presented as mean ±SD.
HR: Heart rate.
ANOVA F test: analysis of variance.

Fig. (3): FLACC pain scores at different times of measurements in the three studied groups.



Data were expressed as mean ±SD.
FLACC: face, legs, activity, cry, consolability.
ANOVA F test: analysis of variance.

DISCUSSION

The analgesic effect of dexmedetomidine and clonidine comes from being α-2 adrenergic receptor agonist with binding to either central or peripheral α-2 adrenergic receptor responsible for this action. The higher selectivity of dexmedetomidine to α-2 adrenergic receptor than to α-1 adrenergic receptor makes it more analgesic than clonidine.[14]

El-Hennawy et al.[15]conducted a study on pediatric patients scheduled for lower abdominal surgeries and found that addition of 2μg/kg of either clonidine or dexmedetomidine to 0.25% bupivacaine prolonged the duration of postoperative analgesia compared to bupivacaine alone. Patients in bupivacaine group had significantly higher FLACC score at 4 hours after being discharged from the PACU compared with both dexmedetomidine and clonidine groups, where 30% of patients achieved a FLACC score of 4 compared with 0%and5% in dexmedetomidine and clonidine groups respectively. The number of patients with adequate analgesia in either dexmedetomidine or clonidine groups was significantly higher than that in bupivacaine group of patients. Also, **Neogi et al.**[16]in their study compared the effects of 1μg/kg clonidine and 1μg/kg dexmedetomidine as adjuncts to 0.25% ropivacaine for caudal analgesia in pediatric patients scheduled for lower abdominal surgeries and found that there was significant difference between ropivacaine group and both clonidine and dexmedetomidine groups with no significant advantage of clonidine over dexmedietomidine or the reverse. **Gupta&Pratap.**[17] compared the effects of clonidine 1μg/kg and dexmedetomidine 1μg/kg as adjuncts to ropivacaine0.25% for caudal analgesia in pediatric patients undergoing lower abdominal surgeries and found that the duration of analgesia was significantly prolonged in dexmedetomidine group than either clonidine or ropivacaine groups, also the total analgesic requirements postoperatively was significantly lower in dexmedetomidine when compared with clonidine and bupivacaine groups**. Jinjil et al.**[18]carried out a study on pediatric patients (2-8 years old)scheduled for lower abdominal surgeries and found that addition of 1μg/kg of either clonidine or dexmedetomidine to 0.25%bupivacaine in caudal block prolonged the duration of postoperative analgesia with more prolongation with dexmedetomidine compared to clonidine group of patients. **Mavuri et al.**[19]in a previous study carried out on pediatrics scheduled for lower abdominal surgeries, found that the duration of postoperative analgesia in dexmedetomidine group reached up to 14 hours and in clonidine group was about 11 hours, also the total number of analgesic doses required in the 1st 24 hours was significantly higher in ropivacaine group than either clonidine or dexmedetomidine groups. However, **Joshi et al.** [20]ruled out the effects of caudal clonidine. They explained that by using lower bupivacaine concentration (0.125%) than other previous studies that used bupivacaine (0.25%).

Dexmedetomidine and clonidine induce sympatholysis by stimulation of the pre-junctional inhibitory alpha-II receptors with subsequent decrease of norepinephrine release.[21] Results of this study showed that there were neither significant differences in hemodynamics nor side effects between the three groups of patients and this was in agreement with previous studies. **Parameswari et al.**[22]found that addition of 1μg/kg of clonidine to caudal bupivacaine increased the duration of caudal analgesia compared with bupivacaine only without side effects reported in a study carried out on pediatric patients(1-3years old) scheduled for infra umbilical surgeries. **Goswami et al.**[23] carried out a study on pediatric patients aged (2-7 years old) scheduled for elective infra umbilical surgeries and found that addition of dexmedetomidine 2 μg/kg to bupivacaine (0.25%) increased the duration of analgesia without side effects. They explained the absence of significant changes in hemodynamic parameters by the relatively

smaller dose of either clonidine or dexmedetomidine (1μg/kg). However, **Bonisson et al.**[24] carried out a study on pediatric patients (1-10years old) scheduled for surgical repair of hypospadias and found that addition of 3μg/kg of caudal clonidine to bupivacaine caused significant postoperative decrease in HR with more sedation without an effect on the duration of analgesia.

The primary mechanism responsible for cortisol release in response to stress is mediated by the afferent nerve signals generated from the surgical site, which in turn activate the hypothalamus to produce corticotropin-releasing hormone and arginine vasopressin.[25] The effects of dexmedetomidine or clonidine on decreasing cortisol level may be explained by their extra analgesic effects mediated by binding to central or spinal α-2 adrenergic receptor when administrated by various routes.[26] The results of this study were in agreement with **Ahuja et al.**[27]study carried out on pediatric patients scheduled for lower abdominal surgeries under general plus caudal anesthesia either with bupivacaine alone or with clonidine or fentanyl and they found that postoperative cortisol level was lower in clonidine group compared to the fentanyl and bupivacaine groups. Also, **Nasr &Abdelhamid**[28]carried out a study to evaluate the effects of caudal dexmedetomidine on stress response in pediatric patients aged 1-3years old scheduled for elective cardiac surgeries who received general anesthesia with caudal block and they found that patients who received2.5 mg/kg of 0.25%bupivacaine plus 0.5μg/kg of dexmedetomidine in caudal block had a significant lower values of serum cortisol level when compared to patients who received 2.5mg/kg of 0.25% bupivacaine plus 1μg/kg of fentanyl.

Limitations of the present study: The present study was limited to patients scheduled to unilateral inguinal hernia repair surgery only. The stress response actually includes metabolic, hormonal, and immunological responses, but we studied only a part of this response in the form of serum cortisol level.

CONCLUSION

Addition of 1μg/kg of either dexmedetomidine or clonidine to bupivacaine in caudal anesthesia led to prolongation of the duration of postoperative analgesia and attenuation of the stress response without postoperative complications.

Conflict of Interest: None.

Financial Disclosures: Nothing to declare.

REFERENCES

1. **Elfawal S.M., Abdelaal WA, Hosny MR.** Comparative study of dexmedetomidine and fentanyl as adjuvants to levobupivacaine for caudal analgesia in children undergoing lower limb orthopedic surgery. Saudi J Anaesth. 2016; 10(4):423–27.
2. **Tsui B.C. and Berde C.B.** Caudal analgesia and anesthesia techniques in children. Curr Opin Anaesthesiol 2005;18(3):283–88
3. **Hager H., Marhofer P., Sitzwohl C., Adler L., Kettner S., & Semsroth M.** Caudal clonidine prolongs analgesia from caudal S (+)-ketamine in children. Anesth Analg.2002; 94(5):1169–72
4. **Engelman E. &Marsala C. Bayesian.** Enhanced meta-analysis of post-operative analgesic efficacy of additives for caudal analgesia in children. Acta Anaesthesiol Scand 2012;56(7):817–32
5. **Chertin B., Zeldin A., Kocherov S., Loscovic A., Ostrovsky I.A. &Gozal Y.** Use of caudal analgesia supplemented with low dose of morphine in children who undergo renal surgery. Curr Urol, 2016; 9(3):132–37.
6. **Jain K., Sethi S. K., Yadav S. L., Mathur V., Thada B. & Garg D.** Dexmedetomidine enhances the efficacy of 0.25% ropivacaine for postoperative analgesia in pediatric caudal epidurals. Anesthesia,Pain &Intensive Care 2018;22(2):199-206.
7. **Carollo DS, Nossaman BD, Ramadhyani U.** Dexmedetomidine: A review of clinical applications.Curr. Opin. Anesthesiol, 2008; 21(4):457–61
8. **Priolkar S. &D'Souza S. A**. Efficacy and safety of clonidine as an adjuvant to bupivacaine for caudal analgesia in pediatric infra-umbilical surgeries. Journal of clinical and diagnostic research: JCDR, 2016; 10(9):13-6.
9. **American Society of Anesthesiologists.** Continuum of depth of sedation: definition of general anesthesia and levels of sedation/analgesia. Approved by ASA House of Delegates on October 13, 1999, and last amended on October 15, 2014.
10. **Shaikh S. I. & Atlapure B. B.** Clonidine as an adjuvant for bupivacaine in caudal analgesia for sub-umbilical surgery: A prospective randomized double blind study.Anaesthesia, Pain & Intensive Care, 2019; 19(3)240-46.

11. **Aldrete J.A.and Kroulik D.A.** The post anesthesia recovery score.Anesth.Analg.1970; 49(6):924-34.
12. **Merkel S.I., Voepel-Lewis T., Shayevitz J.R., Malviya S**. The FLACC.A behavioral scale for scoring postoperative pain in young children. Pediatr Nurse 1997; 23(3):293-7.
13. **Ganeshnavar A., Joshi C. and Shilpa Masur S. Y.** Comparison of dexmedetomidine and clonidine as adjuvants to 0.25% bupivacaine in paediatric caudal block for infraumbilical surgeries Intl J Clin. Diag. Res.2015; 3(4): 11- 21.
14. **Coursin D.B. and Maccioli G.A**. Dexmedetomidine. Curr Opin Crit Care 2001; 7(4):221–6.
15. **El-Hennawy A.M., Abd-Elwahab A.M., Abd-Elmaksoud A.M., El-Ozairy H.S. &Boulis S.R**. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children.Br. J. Anaesth.2009; 103(2):268-74.
16. **Neogi M., Bhattacharjee D.P., Dawn S. &Chatterjee N.A**. Comparative study between clonidine and dexmedetomidine used as adjuncts to ropivacaine for caudal analgesia in pediatric patients. Journal of Anesthesiology Clinical Pharmacology.2010; 26(2):149-52.
17. **Gupta S.&Pratap V.** Addition of Clonidine or Dexmedetomidine to Ropivacaine prolongs caudal analgesia in children. Indian Journal of Pain, 2014; 28(1):36-41.
18. **Jinjil K., Ganguly S., Bhatnagar V., Dwivedi D. &Gupta M**. A comparative study of post-operative pain relief with dexmedetomidine versus clonidine as adjuvants in 0.2% ropivacine for caudal epidural block in children undergoing lower abdominal surgeries. Indian J Basic Appl Med Res, 2016; 5(4):499-508.
19. **Mavuri G., Jain P., Chakraborty S., Mucherla S. K. &Jadon A.** A randomized double-blinded comparison between dexmedetomidine and clonidine as an adjuvant to caudal ropivacaine in children for below umbilical surgery. Journal of Clinical Sciences, 2017; 14(4):157.
20. **Joshi W., Connelly N. R., Freeman K. & Reuben S. S.** Analgesic effect of clonidine added to bupivacaine 0.125% in pediatric caudal blockade. Pediatric Anesthesia, 2004; 14(6):483-48.
21. **Moss J. and Glick D.** The Autonomic Nervous System. In: Miller RD, editor. Miller's Anesthesia. 6th Ed. Philadelphia: Elsevier Churchill Livingstone, 2005; pp.617–77.
22. **Parameswari A., Dhev A. M. & Vakamudi M.** Efficacy of clonidine as an adjuvant to bupivacaine for caudal analgesia in children undergoing sub-umbilical surgery. Indian journal of anesthesia, 2010; 54(5):458-63.
23. **Goswami D., Hazra A.& Kundu, K.** Comparative study between caudal bupivacaine (0.25%) and caudal bupivacaine (0.25%) with dexmedetomidine in children undergoing elective infra-umbilical surgeries. J Anesth Clin Res, 2015; 6(11):583-7.
24. **Bonisson A. C. M., Fernandes M. L., Araujo G. F., Vieira F. E., Noronha L. M. &Gomez R. S.** Combination of clonidine-bupivacaine in caudal epidural anesthesia for hypospadias surgery in children: prospective, randomized, blind study. Revista brasileira de anestesiologia, 2019; 69(1):27-34.
25. **Desborough J.P.** The stress response to trauma and surgery. J Anaesth.2000;85(1):109-17
26. **Maze M., Virtanen R., Daunt D., Banks S. J., Stover E. P. &Feldman D.** Effects of dexmedetomidine, a novel imidazole sedative-anesthetic agent, on adrenal steroidogenesis: in vivo and in vitro studies. Anesthesia and analgesia, 1991; 73(2):204-8.
27. **Ahuja S., Aggarwal M., Joshi N., Chaudhry S., &Madhu S. V.** Efficacy of caudal clonidine and fentanyl on analgesia, neuroendocrine stress response and emergence agitation in children undergoing lower abdominal surgeries under general anesthesia with sevoflurane. Journal of clinical and diag, 2015;9(9):UC01-5
28. **Nasr D. A. &Abdelhamid H. M.** The efficacy of caudal dexmedetomidine on stress response and postoperative pain in pediatric cardiac surgery. Annals of cardiac anesthesia, 2013; 16(2):109-14.

HOW TO CITE

Al maghawry, E., gaafar, T., El sawy, A., mohammed, R. Effect of each of Dexmedetomidine and Clonidine as adjuvant to bupivacaine caudal block on the severity of stress response and postoperative pain in pediatric undergoing inguinal hernia repair surgery.. *Zagazig University Medical Journal*, 2021; 2(279-287): -. doi: 10.21608/zumj.2019.14564.1316