DEXMEDETOMIDINE IN ANESTHESIA OF CHILDREN SUBMITTED TO VIDEOLAPAROSCOPIC APPENDECTOMY: A DOUBLE-BLIND, RANDOMIZED AND PLACEBO-CONTROLLED STUDY

MARIA CRISTINA SMANIA*, JEFFERSON PEDRO PIVA, PEDRO CELINY R GARCIA

Work carried out by the Division of Anesthesia of Hospital São Lucas, Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS) and Department of Pediatrics. School of Medicine of PUCRS, Porto Alegre, RS

SUMMARY

OBJECTIVES. To evaluate the hemodynamic responses to nociceptive stimuli in children submitted to videolaparoscopic appendectomy under balanced anesthesia with isoflurane and dexmedetomidine.

METHODS. Randomized, double-blind and placebo-controlled study involving 26 children submitted to videolaparoscopic appendectomy carried out at Hospital São Lucas (PUCRS) between May 2004 and February 2005. Patients were assigned to two groups: (a) Dexmedetomidine group (n=13): infusion of 1μg/kg over 10 minutes and maintenance dose of 0.5μg/kg/h) as an adjuvant to inhaled isoflurane anesthesia; (b) Control group (n=13): normal saline infusion at a similar rate and volume of the dexmedetomidine infusion. During the different surgical and anesthetic periods, groups were compared regarding heart rate, systolic and diastolic arterial blood pressures as well as need of supplemental fentanyl infusion. Student's t test, ANOVA, and Finner's procedure were used for statistical analysis.

RESULTS. During the strongest nociceptive stimuli (airway access and abdominal catheter placement), the heart rate and systolic blood pressure increased significantly (p < 0.001) in the control group compared to the dexmedetomidine group. Compared to baseline levels, the hemodynamic responses to nociceptive stimuli were more stable when dexmedetomidine was used in combination with inhaled isoflurane anesthesia. The need for supplemental doses of fentanyl and the hemodynamic parameters were similar for both groups.

CONCLUSION. Dexmedetomidine combined with inhaled isoflurane for anesthesia of children submitted to videolaparoscopic appendectomy, efficiently blocks the hemodynamic responses to nociceptive stimuli. When compared to placebo, the use of dexmedetomidine did not change the need for supplemental doses of fentanyl for maintenance of hemodynamic parameters during the intraoperative period.

KEY WORDS: Dexmedetomidine. Alpha adrenoceptor agonist. Laparoscopy. Pediatric anesthesia. Appendectomy.

*Correspondence:

Rua São Vicente, 117 apto 301 Porto Alegre - RS CEP: 90630-180 mcsmania.ez@terra.com.br

Introduction

Technological advances and improved experience with videolaparoscopy have allowed this surgical technique to be increasingly used in pediatric surgical patients. Currently, videolaparoscopy has become more widespread for treatment of acute appendicitis in children. Balanced anesthesia with inhaled agents in combination with different opioids has been the method of choice for this procedure.

Dexmedetomidine is a selective and potent α_2 -adrenoceptor agonist, with hypnotic, analgesic and sympatholytic properties.^{2,3,4} In surgical patients, it reduces the use of other anesthetics,^{5,6,7} minimizes sympathetic response to nociceptive stimuli^{6,8} and improves intraoperative hemodynamic stability.⁶

Clinical trials addressing the use of dexmedetomidine in children are still scarce. Most publications concerning pediatric patients are case reports disclosing the intraoperative use of dexmedetomidine, to its use

as an adjuvant in assisted ventilation in the Intensive Care Unit (ICU);¹¹ and in the management of opioid dependency.¹²

This study aimed to assess hemodynamic responses to nociceptive stimuli when dexmedetomidine is used as an adjuvant anesthetic to isoflurane in pediatric patients submitted to videolaparoscopic appendectomy. The need of supplemental fentanyl doses to maintain hemodynamic parameters stable during surgery was also evaluated.

METHOD!

Between May 2004 and February 2005 a randomized, double-blind and placebo-controlled study was conducted with children (2 to 14 years of age), admitted to Hospital São Lucas (PUCRS), with acute appendicitis, scheduled for videolaparoscopic appendectomy. Decision for the surgical approach (laparotomy or videolaparoscopy) was taken solely by the assistant surgeon, with no interference from the researchers.

Only patients graded as American Society of Anesthesiologists (ASA) I and II were included in the study. The study protocol was submitted to and approved by the Research Ethics Committee of Hospital São Lucas (PUCRS). Parents or legal surrogates were informed of the study objectives and signed a consent form for inclusion of their children in the research. Children with a history of allergy to midazolam, fentanyl, propofol, atracurium, isoflurane, or dexmedetomidine were excluded.

On admission to the surgical ward, patients were assigned to the following groups: (a) Dexmedetomidine group: use of dexmedetomidine as adjuvant to inhaled isoflurane anesthesia. Intravenous (IV) Dexmedetomidine (2 μ g/ml) was infused during IO minutes (I μ g/kg – rapid phase) followed by a maintenance infusion (0.5 μ g/kg/h) until the end of surgery; (b) Placebo - control group: normal saline solution (0.9%) infusion as adjuvant to inhaled isoflurane anesthesia, at the same rate and volume used for dexmedetomidine administration.

All children underwent a fasting period of at least six hours. Preoperative intravenous hydration and antibiotic coverage (gentamicin plus clindamycin) were prescribed by the on-duty emergency pediatrician and/or by the pediatric surgeon. Hydration with normal saline solution at 0.9% was maintained during surgery. The anesthesia stages were as follows:

- I) Preanesthetic medication: on admission to the surgical ward all patients received intravenous midazolam infusion (0.1 mg/kg; maximum of 5mg).
- **2) Anesthesia monitoring:** A Datascope Passport II- 5LXG monitor was used to control hemodynamic parameters (continuous ECG, phase II; noninvasive blood pressure monitoring; pulse oximetry) and anesthetic gas analysis. Assisted ventilation was provided by a Takaoka Monterey respirator with the tidal volume and/or respiratory frequency adjusted to maintain PaCO₂ at less than 45mmHg, with an oxygen flow of 2l/min.
- **3)** Induction and maintenance of anesthesia: Anesthetic induction was performed after 10 minutes of intravenous administration of dexmedetomidine or placebo. Concurrently, sevoflurane 1% was inhaled in order to blind the surgical team to the induction agent. Sevoflurane was interrupted after five minutes of IV dexmedetomidine or placebo administration. With this procedure the end-tidal concentration could be equivalent to 0% at the time of induction.

After 10 minutes, IV propofol (2.0 mg/kg) combined with lidocaine 1% (1/3 of its volume) (13); IV fentanyl (1.5 μ g/kg) and IV atracurium (0.5 mg/kg) were infused. Tracheal intubation was performed after two minutes. Anesthesia was maintained with isoflurane 1.2%, supplemented with IV fentanyl (1 μ g/kg) if the systolic blood pressure or heart rate was 20% higher than the baseline levels. For adequate surgical relaxation, subsequent doses of atracurium (1/3 of the initial dose) were given every 30 minutes during maintenance of the pneumoperitoneum.

4) Intraoperative maintenance of hemodynamic parameters: Adjustments were predefined to prevent hypotension and low cardiac output, as well as to provide adequate analgesia.

- a) If blood pressure decreased (equal to or greater than 20% of baseline levels) normal saline (according to the hourly baseline requirement^{14,15}) was infused for 5 minutes and repeated up to three times, if hypotension persisted;
- b) If systolic blood pressure decreased (equal to or greater than 30% of baseline levels) isoflurane concentration was reduced from 1.2% to 0.5% with a concomitant normal saline infusion (same as in the previous item). If the blood pressure still remained low, dexmedetomidine infusion was reduced by 50%. If blood pressure levels did not reach at least 20% of baseline levels, intravenous administration of dexmedetomidine was discontinued and the patient excluded from the study and considered a treatment failure;
- c) If the heart rate decreased more than 30% from baseline levels, a dose of 0.0 l mg/kg intravenous atropine was administered. It could be repeated within five minutes if the heart rate did not reach levels above the minimum acceptable value of a 30% reduction. Patients were excluded from the study if they did not respond to atropine infusion or if reduction in the heart rate resulted in hypotension and/or low cardiac output;
- d) If systolic blood pressure and/or heart rate increased more than 20% from baseline levels, fentanyl (I $\mu g/kg$) was given at five-minute intervals. The endpoint was a maximal acceptable increment of 20% from baseline levels.

Data were collected using a standardized protocol, which included demographic data, fluid infusion before and during surgery, infused drugs, length of surgery and isoflurane volume administered. The author defined heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) as major parameters to assess the hemodynamic response to nociceptive stimuli during the following periods:

Baseline (M0): after premedication (midazolam) and prior to anesthetic induction;

Moment 1 (M1): after the administration of the anesthetic drugs and prior to tracheal intubation;

Moment 2 (M2): after tracheal intubation. The highest HR recorded during tracheal intubation was considered. SBP and DBP were measured immediately after tracheal intubation;

Moment 3 (M3): HR, SBP and DBP measured immediately before surgical incision;

Moment 4 (M4): HR, SBP and DBP measured immediately after surgical incision and during videolaparoscopic transumbilical trocar placement;

Moment 5 (M5): HR, SBP and DBP measured at maximum pneumoperitoneum insufflation of I2mmHg of CO2;

Moments 6 and 7 (M6 and M7): HR, SBP and DBP measured during placement of the second and third videolaparoscopy trocars on the right and left abdominal sides, respectively;

All unexpected events which took place during the anesthetic induction and surgery time were recorded as adverse effects as well as the need for supplemental doses of fentanyl for maintenance of intraoperative hemodynamic parameters at a maximum 20% increase from baseline levels (M0).

For sample size calculation, researchers considered the systolic blood pressure in M4 as the major parameter. They presumed that in

order to obtain a significant difference between the two groups there should be a difference greater than 15% in systolic blood pressure, in addition to a standard deviation (SD) of 10 mmHg and a power of 90%. Therefore, at least 11 patients would be required per group. The comparison between the means (general characteristics) was made using Student's t test. Behavior between the groups regarding the continuous variables of the major parameter (M0 through M7) was assessed by the repeated ANOVA measures. The *post hoc* comparison using Finner's procedure (16) was used to compare specific moments (M2, M4, M6 and M7) between the two groups as well as behavior of the means between these moments and the baseline values (M0), within the same group. The SPSS 11.0 (Statistical Package for the Social Sciences) was used for statistical analysis.

RESULTS

Between May 2004 and February 2005, 35 videolaparoscopic pediatric appendectomies were performed at the Hospital São Lucas (PUCRS). Of these patients, 27 children were anesthetized by the main researcher (MCS) and one was not included in the study because parents refused to sign the consent form. Subsequently, 13 were allocated to the dexmedetomidine group and another 13 to the placebo group.

Both groups were homogeneous (Table 1) in terms of age, weight, gender and baseline hemodynamic parameters. The only exception was the length of preoperative fasting, which was longer (p=0.03) in the dexmedetomidine group. It should be highlighted that in both groups an extremely small volume (approximately $36\text{ml/m}^2/h$) of parenteral hydration was used preoperatively.

Results regarding systolic blood pressure, diastolic blood pressure and heart rate at the different moments of analysis are shown in Table 2 and Figure 1.

The behavior of hemodynamic parameters assessed during videolaparoscopic appendectomy in the dexmedetomidine and placebo-control groups is next described.

Systolic blood pressure (SBP): There was a remarkable increase in systolic blood pressure in the control group when compared to the dexmedetomidine group (p=0.009). (Figure 1). Comparing both groups at the different moments, significant differences in SBP levels at M2, M4, M6 and M7 (p=0.03;<0.01;<0.01 and <0.01, respectively) were found; the mean values at these moments were higher in the control group than in the dexmedetomidine group.

Diastolic blood pressure (DBP): No statistically significant differences were observed between the groups regarding DBP levels, in the comparison between groups (p=0.32), or in the assessment of specific moments M2, M4, M6 and M7 (p=0.20; 0.07; 0.15 and 0.12, respectively) (Figure 1).

Heart rate: The mean heart rate values were higher in the control group (p=0.001), as well as at moments M2, M4, M6 and M7 when compared to the dexmedetomidine group (p<0.01, at all moments) (Figure 1).

By comparing the moments of highest stimulation (M2, M4, M6 and M7) in relation to the baseline levels (M0) within the group, it was observed that:

| Table I - General characteristics of the patients | | | | |
|---|--------------------|--------------------|----------|--|
| Characteristic | DMD | PLACEBO | р | |
| | n=13 | n=13 | | |
| Age (years) | 9.2± 1.6 | 9.2± 2.0 | p=0.93 | |
| Weight (kg) | 37.3 ± 11.2 | 38.8±13.9 | p=0.76 | |
| Gender F/M | 3/10 | 3/10 | p = 1.00 | |
| ASA I/II | 0/13 | 0/13 | p=1.00 | |
| SBP M0 (mmHg) | ± .4 | 115 ± 8.3 | p=0.30 | |
| DBP M0 (mmHg) | 62 ± 8.8 | 68 ± 8.6 | p=0.14 | |
| HR M0 (bpm) | 96 ± 14.5 | $ 0 \pm 4.6 $ | p=0.33 | |
| Length of surgery (min) | 101.5±27.1 | 84.1 ± 14.6 | p=0.05 | |
| Preoperative fasting (h) | 17.8±6.7 | 12.2±6.0 | p=0.03 | |
| Preoperative hydration (ml/m²/h) | 36.0 <u>+</u> 26.9 | 33.8 <u>+</u> 19.8 | p=0.80 | |
| Intraoperative hydration (ml/Kg/h) | 5.1 ± 1.8 | 5.3±1.9 | p=0.79 | |
| Use of analgesic in the last six hours | 4 | 3 | p=0.50 | |
| Vomiting in the last 24 hours | 5 | 4 | p=0.50 | |

DMD: Dexmedetomidine; ASA: American Society of Anesthesiology classes; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; M0: baseline measurements (admission to the surgical ward, after administration of midazolam).

Table 2- Hemodynamic parameters recorded during different surgical moments: dexmedetomidine (DMD) versus placebo groups

| | | DMD | PLACEBO | р |
|--------------------------|------------------|---|---|---------------------------|
| Baseline levels (MO) | SBP DBP HR | ± .4 62 ± 8.79 96 ± 4.49 | 115 ± 8.29 68 ± 8.60 101 ± 14.56 | |
| Pre-intubation (M1) | SBP DBP HR | 95 ± 18.67 53 ± 16.81 77 ± 12.89 | 96 ±9.03 54 ±12.50 90 ±13.89 | |
| Intubation (M2) | SBP DBP HR | 97 ± 21.23 57 ± 16.09 86 ± 13.58 | 13 ± 4. 0 65 ± 3.79 18 ± 23.8 | 0.03 l 0.20 < 0.0 l |
| Pre-incision (M3) | SBP DBP HR | 85 ± 11.17 40 ± 10.26 81 ± 13.78 | 95± 6.94 55±13.39 95±13.88 | |
| Umbilical trocar (M4) | SBP DBP HR | 93 ± 11.43 52 ± 11.58 89 ± 13.10 | 113 ± 12.61 66 ± 16.39 116 ± 21.60 | < 0.01 0.07 < 0.01 |
| Pneumoperitoneum (M5) | SBP DBP HR | 101 ± 9.22 57 ± 12.65 82 ± 10.47 | 118 ± 15.85 65 ± 15.23 107 ± 22.25 | |
| 2nd trocar (M6) | SBP DBP FC | 107± 13.98 58 ± 15.09 89 ± 15.70 | 126 ± 15.7 68 ± 15.15 121 ± 17.82 | < 0.01 0.15 < 0.01 |
| 3rd trocar (M7) | SBP DBP HR | 107 ± 14.79 59 ± 13.50 86 ± 16.10 | 126 ± 2.58 69 ± 2.26 120 ± 8.81 | < 0.01 0.12 < 0.01 |

SBP: systolic blood pressure (mmHg); DBP: diastolic blood pressure (mmHg); HR: heart rate (bpm); p= comparisons made using Finner's procedure

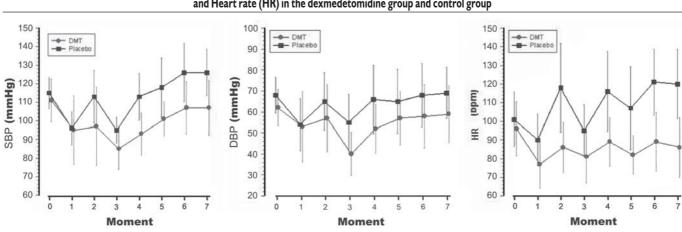


Figure 1- The mean values of Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Heart rate (HR) in the dexmedetomidine group and control group

Systolic blood pressure: Comparing to the baseline values (M0), a remarkable decrease in SBP levels in the dexmedetomidine group at M2 and M4 (p=0.01 and <0.01, respectively); and non-significant differences at M6 and M7 were observed.

However, the control group showed a significant increase in SBP at M6 and M7, when compared to the baseline levels (p=0.04 and 0.03, respectively), whereas no significant difference was observed at M2 and M4 (p=0.71 and 0.60, respectively).

Diastolic blood pressure: No significant differences were observed in the dexmedetomidine and control groups, when DBP was compared in M2, M4, M6 and M7 with the baseline levels (p=0.35; 0.06; 0.48 and 0.46 respectively, in the dexmedetomidine group; and, p=0.50; 0.75; 0.98 and 0.76, in the control group).

Heart rate: No significant heart rate increase was observed in the dexmedetomidine group at M2, M4 and M6 compared to the baseline levels (p= 0.07; 0.18, and 0.15, respectively). However, there was a remarkable decrease in heart rate at M7 (p=0.01) when compared to baseline levels. On the other hand, the control group showed a heart rate increase at M2, M4, M6 and M7 when compared to the baseline levels (p<0.01; =0.03; <0.01 and <0.01, respectively).

Use of fentanyl as isoflurane adjuvant in general anesthesia during the surgery corresponded to 2.6 \pm 1.1 $\mu g/kg$ in the control group and 1.9 \pm 0.5 $\mu g/kg$ in the dexmedetomidine group (p=0.053). No significant difference between the two groups was found in relation to Isoflurane consumption (Dexmedetomidine group=12.6 ± 3.4 ml versus 14.9 ± 3.3 ml in the control group; p=0.1) as well as in arterial saturation of oxygen during the time of surgery.

One patient in the dexmedetomidine group (at the end of the infusion of $I\mu g/Kg$ for 10 minutes) showed a decrease of more than 30% in heart rate in comparison to baseline levels. Bradycardia was treated prior to the end of anesthetic induction, with immediate response. Two other patients in the dexmedetomidine group had a decrease in systolic blood pressure below the 30% established for the intervention. The first patient regained a normal blood pressure after receiving normal saline infusion and the second required normal saline

infusion plus a 0.5% reduction of the isoflurane concentration until blood pressure levels returned to normal. In the control group, two patients presented agitation during sevoflurane inhalation. One patient reacted to tracheal intubation and another moved during abdominal closure, before isoflurane inhalation was discontinued.

DISCUSSION

In this clinical, randomized and double-blind study, in which dexmedetomidine was compared to a placebo as an adjuvant anesthetic to inhaled isoflurane in children submitted to videolaparoscopic appendectomy, it was observed that: a) the hemodynamic response to nociceptive stimuli was lower in the dexmedetomidine group when compared to the control group; b) hemodynamic changes were especially due to heart rate oscillations during nociceptive stimulation; c) diastolic blood pressure levels remained unchanged in both groups, without oscillation when compared to the baseline levels; d) supplemental doses of fentanyl for maintaining the hemodynamic parameters stable during surgery were not different between groups; and, e) the amount of preoperative hydration given to both groups was smaller than the recommended baseline requirements. ^{14,15}

Suppression of hemodynamic response to nociceptive stimuli, with concomitant reduction of hormone release, is one of the major goals of an adequate "anesthetic state." ¹⁹ Blood pressure and heart rate are the hemodynamic variables habitually used to assess the adequate block of the response to surgical stimulation ^{17,18}. Similarly to what happens in adult patients, it was observed that during tracheal intubation dexmedetomidine induces lower increases of blood pressure levels and of the heart rate when compared to the placebo. ^{6,8} The same result was noted during placement of the trocars for laparoscopy. However, the greater differences were related to the heart rate: in the control group, the heart rate showed a remarkable increase, whereas in the dexmedetomidine group, it remained below baseline values.

Dexmedetomidine is known to have a sedative, analgesic and sympatholytic action.^{2, 3, 4} Plasma concentration of 1.2 ng/ml, close to

the ones obtained with the infusion of $0.7\mu g/Kg/h$, reduced norepinephrine levels by up to $50\%^{20}$. These levels remained low even in the presence of nociceptive stimuli. Therefore, it is believed that the control over heart rate observed in this study during surgical stimulation is mainly due to the sympathetic blocking action, combined with an increase in the vagal activation caused by dexmedetomidine. The sympathetic blocking action, combined with an increase in the vagal activation caused by dexmedetomidine.

Systolic blood pressure, unlike the heart rate, remained stable in the control group during tracheal intubation and during the umbilical trocar placement, with values closer to those of the baseline. This finding might have been influenced by the hypotensive effect of propofol²¹ used for anesthetic induction, since behavior of the other stimuli was different and the variations between groups were greater. Use of dexmedetomidine did not disclose any difference in diastolic blood pressure between groups. However, other studies²² revealed a remarkable increment of diastolic blood pressure, mostly when isoflurane doses of 0.6% had been used.²² This effect, attributed to the high peripheral vascular resistance caused catecholamine release in response to the nociceptive stimulus, would be blocked with the infusion of dexmedetomidine.²²

In the current study, infusion of $0.5\,\mu g/kg/h$ of dexmedetomidine as isoflurane adjuvant at 1.2% allowed control of the hemodynamic response to stimuli with values equal to or less than those of the baselines, reflecting adequate control of the sympathetic stimulus. However, the need for supplemental fentanyl during surgery, for maintenance of the hemodynamic parameters, was not different between groups when isoflurane was used in constant concentrations of 1 MAC (minimum alveolar concentration). Some studies have described a remarkable decrease in the MAC of isoflurane, with lessening of consumption, when combined with the continuous infusion of dexmedetomidine, in plasma concentrations of 0.3 and 0.6ng/ml.

It should be underscored that inadequate analgesia is not the only factor interfering with hemodynamic parameters during laparoscopy. The increase in abdominal pressure during laparoscopy, automatically maintained at 10mmHg via $\rm CO_2$ insufflations, increases peripheral vascular resistance and decreases stroke volume. 23,24,25 In this case, increment of systolic blood pressure and of heart rate would not be suppressed with supplemental opioid doses. Unfortunately, with this sample size a correct alternative for this answer cannot be defined.

An occasional finding that merits special attention concerns preoperative hydration which was obtained using smaller amounts than the recommended baseline requirements (75ml/m²/h). ^{14,15} Additionally, patients with an abdominal infectious process have a greater water loss due to ileum, vomiting and fever. ²⁶ Nevertheless, only two patients who received dexmedetomidine showed a decrease in blood pressure during surgery, thus requiring additional hydration. An explanation may be that only patients with a good health status (ASA I and II)¹⁷, who were normovolemic ²⁶ and did not have severe water loss, were included in the study. Hypovolemia of hypovolemic children may be intensified due to the vasodilation caused by anesthesia. ²⁶ These children require less anesthesia, greater intravascular volume, or both, to ensure an adequate cardiac output. ²⁶ Blood volume losses, greater than 20% would be needed to cause sinus tachycardia and a decrease in blood pressure. ^{27,28}

A limitation of this study is that no specific equipment was used to monitor the depth of anesthesia (BIS), and also the possible correlation with the control of hemodynamic disorders caused by nociceptive stimuli (29-33).

Clinical trials involving use of dexmedetomidine in children are restricted to sedation for magnetic resonance imaging exams³⁴ and as preanesthetic to reduce the incidence of agitation caused by sevoflurane.³⁵ Other findings in literature are described in case reports, which show the intraoperative use of dexmedetomidine, its use as an adjuvant in assisted ventilation in the ICU, and in the treatment of opioid dependency. ^{10,11,12,36} The authors believe that presumably this is the first double-blind study to assess the use of dexmedetomidine in pediatric surgical patients in this setting.

The current study, showed that an initial dose of dexmedetomidine (I μ glkg) followed by a maintenance dose of 0.5 μ g/Kg/h, as an adjuvant to isoflurane anesthesia, in children submitted to videolaparoscopic appendectomy, kept the heart rate and blood pressure stable, also in periods of heightened surgical stimulation. On the other hand, the hemodynamic effects of decreased heart rate and blood pressure were not clinically relevant even when patients received less hydration than recommended.

Conflict of interest: none

RESUMO

Dexmedetomidina na anestesia de crianças submetidas à apendicectomia por videolaparoscopia: um estudo duplo cego randomizado e placebo-controlado

OBJETIVOS. Avaliar a resposta hemodinâmica aos estímulos nocicepticos em crianças submetidas à apendicectomia por videolaparoscopia sob anestesia balanceada com isoflorane e dexmedetomidina.

MÉTODOS. Estudo randomizado, duplo cego e placebo controlado envolvendo 26 crianças submetidas à apendicectomia por videolaparoscopia no Hospital São Lucas da PUCRS entre maio de 2004 a fevereiro 2005. Os pacientes foram alocados: a) Grupo Dexmedetomidina (n = 13), administrada $I\mu g/kg$ em I0 minutos e manutenção de $0,5\mu g/kg/h$ como coadjuvante à anestesia inalatória com isoforane; b) Grupo Controle (n = 13), que recebia solução fisiológica com volume e velocidade de infusão semelhante ao grupo anterior. Durante os diferentes tempos cirúrgicos e anestésicos os grupos foram comparados em relação à freqüência cardíaca, pressão arterial sistólica e diastólica, assim como necessidade de doses suplementares de fentanil. Os grupos foram comparados pelo teste T, Qui quadrado, a ANOVA e Finner.

RESULTADOS. Nos momentos de maior estímulo doloroso (entubação, colocação dos trocateres abdominais), a freqüência cardíaca e tensão arterial sistólica aumentaram significativamente (p<0,001) no grupo placebo em comparação ao grupo dexmedetomidina. Houve maior estabilidade hemodinâmica aos estímulos nociceptivos quando a dexmedetomidina foi empregada na complementação anestésica ao isoforane. A necessidade de doses adicionais de fentanil na manutenção dos parâmetros hemodinâmicos estáveis foi semelhante entre os dois grupos.

Conclusão. A dexmedetomidina, utilizada como coadjuvante ao isoforane na anestesia de crianças submetidas à apendicectomia por

videolaparoscopia, bloqueia de forma efetiva a resposta hemodinâmica aos estímulos nociceptivos. No entanto, quando comparada ao placebo a dexmedetomidina não modificou a necessidade de doses complementares de fentanil para manutenção de parâmetros hemodinâmicos estáveis, durante o periodo intraoperatório. [Rev Assoc Med Bras 2008; 54(4): 308-13]

UNITERMOS: Dexmedetomidine. Alpha agonista. Laparoscopia. Anestesia pediátrica. Apendicectomia.

REFERENCES

- 1. Tobias JD. Anaesthesia for minimally invasive surgery in children. Best Pract Res Clin Anaesthesiol. 2002;16:115-30.
- 2. Kamibayashi T, Maze M. Clinical uses of α_2 -adrenergic agonists. Anesthesiology. 2000;93:1345-9.
- 3. Scholz J, Tonner P. α_2 -adrenoceptor agonists in anaesthesia: a new paradigm. Curr Opin Anaesthesiol. 2000;13: 437-42
- Khan ZP, Ferguson CN, Jones, RM. Alpha-2 and imidazoline receptor agonists; their pharmacology and therapeutic role. Anaesthesia. 1999; 54:146-65.
- 5. Kagawa K, Mammoto T, Hayashi Y, Kamibayashi T, Mashimo T, Yoshiya I. The effects of imidazoline receptors and α_2 adrenoceptors on the anesthetic requirement (MAC) for halothane in rats. Anesthesiology. 1997;87:963-7.
- Aho M, Erkola O, Kallio A, Scheinin H, Korttila K. Dexmedetomidine infusion for maintenance of anesthesia in patients undergoing abdominal hysterectomy. Anesth Analg. 1992;75:940-6.
- Aantaa R, Jaakola ML, Kallio A, Kanto J. Reduction of the minimum alveolar concentration of isoflurane by dexmedetomidine. Anesthesiology. 1997:86:1055-60
- 8. Scheinin B, Lindgren L, Randell T, Scheinin H, Scheinin M. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and perioperative fentanyl. Br J Anaesth. 1992;68:126-31.
- 9. Serling S. Dexmedetomidine in pediatric: controlled studies needed. Paediatr Anesth 2004; 14: 532
- Ard J, Doyle W, Bekker. Awake craniotomy with dexmedetomidine in pediatric patients. J Neurosurg Anesthesiol. 2003;15:263-6.
- 11. Tobias JD, Berkenbosch JW. Initial experience with dexmedetomidine in paediatric-aged patients. Paediatr Anaesthes. 2002;12:171-5.
- Tobias JD, Berkenbosch JW, Russo P. Additional experience with dexmedetomidine in pediatric patients. South Med J. 2003;93:871-5.
- Tan LH, Hwang NC. The effect of mixing lidocaine with propofol on the dose of propofol required for induction of anesthesia. Anesth Analg. 2003;97:461-4
- Siker D. Pediatric fluids, electrolytes and nutrition. In: Gregory GA. Pediatric anesthesia. 3rd ed. Philadelphia: Churchill Livingstone; 1994. p.83-117.
- Bruno F, Santana JCB, Lago P. Distúrbios hidroeletrolíticos na criança. In: Piva JP, Garcia PCR. Piva & Celiny medicina intensiva em pediatria. Rio de Janeiro: Revinter; 2005. p.317-33.
- 16. Hochberg Y. A sharper Bonferroni procedure for multiple tests of significance. Biometrika. 1988;75:800 –2.
- 17. Stanski D. Monitoring depth of anesthesia. In: Miller RD. Anesthesia.4th ed. Philadelphia: Churchill Livingstone; 1994. p.1127-59.
- Kaul HL, Bharti N. Monitoring depth of anaesthesia. Indian J Anaesth. 2002;46:323-32.

- Prys-Roberts C. Anaesthesia: a practical or impractical construct? Br J Anaesth. 1987;59:1341-5.
- Ebert TJ, Hall JE, Barney JÁ, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology. 2000; 93:382-94.
- 21. Hannallah RS, Baker SB, Casey W, McGill WA, Broadman LM, Norden JM. Propofol: Effective dose and induction characteristics in unpremedicated children. Anesthesiology. 1991;74:217-9.
- Khan ZP; Munday IT; Jones RM, Thornton C, Mant TG, Amin D. Effects of dexmedetomidine on isoflurane requirements in healthy volunteers. I: Pharmacodynamic and pharmacokinetic interactions. Br J Anaesth. 1999; 83: 372-80
- 23. Gueugniaud PY, Abisseror M, Moussa M, Godard J, Foussat C, Petit P, Dodat H. The hemodynamic effects of pneumoperitoneum during laparoscopic surgery in healthy infants; assessment by continuous esophageal aortic blood flow echo-Doppler. Anesth Analg. 1998;86:290-3.
- 24. Joris JL, Noirot DP, Legrand MJ, Jacquet NJ, Lamy ML. Hemodynamic changes during laparoscopic cholecystectomy. Anesth Analg. 1993;76:1067-71.
- 25. Wedgewood J, Doyle E. Anaesthesia and laparoscopic surgery in children. Paediatr Anaesth. 2001;11:391-9.
- Holl JW. Anesthesia for abdominal surgery. In: Gregory GA. Pediatric anesthesia. 3rd ed. Philadelphia: Churchill Livingstone; 1994. p 637-708.
- 27. Cabral AS, Bouzas LF, Bruno F, Piva JP, Garcia PCR. Trauma. In: Piva & Celiny medicina intensiva em pediatria. Rio de Janeiro: Revinter; 2005. p.563-79.
- 28. Aladangady N, Aitchison TC, Beckett C. Is it possible to predict the blood volume of a sick preterm infant? Arch Dis Child Fetal Neonatal Ed. 2004;89:F344-7.
- 29. Vianna PTG. Monitor de profundidade da hipnose. A eletroencefalografia bispectral. Rev Bras Anestesiol. 2001;51:418-25.
- MorimotoY, Hagihira S, Koizumi Y, Ishida K, Matsumoto M, Sakabe T. The relationship between Bispectral Index and electroencephalographic parameters during isoflurane anesthesia. Anesth Analg. 2004; 98:1336-40.
- 31. İannuzzi M, Iannuzzi E, Rossi F, Berrino L, Chiefarim. Relationship between Bispectral Index, electroencephalographic state entropy and effect-site EC50 for propofol at different clinical endpoints. Br J Anaesth. 2005;94:492-5.
- 32. Whyte SD, Booker PD. Bispectral Index during isoflurane anesthesia in pediatric patients. Anesth Analg. 2004;98:1644-9.
- 33. Denman WT, Swanson EL, Rosow D, Ezbicki K, Connors PD, Rosow CE. Pediatric evaluation of the bispectral index (BIS) monitor and correlation of BIS with end-tidal sevoflurane concentration in infants and children. Anesth Analg. 2000;90:872-7.
- 34. Koroglu A, Demirbilek S, Teksan H, Sagir O, But AK, Ersoy MO. Sedative, haemodynamic and respiratory effects on dexmedetomidine in children undergoing magnetic resonance imaging examination: preliminary results. Br J Anaesth. 2005;94:821-4.
- Ibacache M, Muñoz HR, Brandes V. Single-dose dexmedetomidine reduces agitation after sevoflurane anesthesia in children. Anesth Analg. 2004;98: 60-3.
- 36. Tobias J. Dexmedetomidine: applications in pediatric critical care and pediatric anesthesiology. Pediatr Crit Care Med. 2007;8:115-30.

Artigo recebido: 09/05/07 Aceito para publicação: 01/04/08