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BRIEF REPORT

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The effect of neuromuscular blockers in patients with intra-abdominal hypertension

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Abstract *Objective:* The objective was to prospectively study the effect of neuromuscular blockers on intra-abdominal pressure (IAP) and a number of physiological variables in patients with increased IAP. *Design:* Prospective cohort study. *Setting:* Intensive care unit of the Ghent University Hospital. *Patients and participants:* Ten critically ill patients with intra-abdominal hypertension (IAH). *Interventions:* An intravenous bolus of cisatracurium at a dose of 0.15 mg/kg was administered, and IAP was measured just before administration and then at 15, 30, 60 and 120 min. The effect of cisatracurium on central venous pressure (CVP), mean arterial pressure (MAP), abdominal perfusion pressure (APP) and heart rate (HR) was also evaluated. Urinary output was recorded prior to administration and after 60 and 120 min. *Measurements and results:* The median age of the patients was 50 years (interquartile range 38–65); five of them were male. APACHE II score on admission was 29 (IQR 14–37). IAH was caused by massive fluid resuscitation without obvious abdominal problem in five patients, by abdominal trauma in three, and by burns and bowel distension in one patient each. Bolus administration of cisatracurium significantly decreased IAP from 18 mmHg (16–20) at baseline to 14 mmHg (12–16) at 15 min ($p = 0.01$) and to 14 mmHg (13–17) at 30 min ($p = 0.02$). MAP, APP, CVP and HR remained unchanged. No significant effect on urinary output was observed. In all patients, IAP returned to the baseline level after 2 h. *Conclusions:* Bolus administration of cisatracurium can be used to temporarily reduce IAP in patients with IAH.

Keywords Intra-abdominal pressure · Intra-abdominal hypertension · Abdominal compartment syndrome · Surgery · Trauma · Critically ill patients · Intensive care

Introduction

Intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) have been identified as independent risk factors for organ dysfunction and mortality in critically ill patients [1, 2]. The effect of decompressive laparotomy (DL) has been studied most extensively, and was found to have a beneficial effect on organ function in patients with established ACS [3]. Although long-term functional results after DL are acceptable, especially considering the high mortality of untreated ACS, DL is associated with longer hospital stay, planned reoperations and possible complications of open-abdomen treatment. For this reason, a number of non-operative treatment options, such as the use of neuromuscular blockers (NMB) to improve compliance of the abdominal wall, have been described [4, 5]. The objective was to prospectively study the effect of a single dose of cisatracurium on intra-abdominal pressure (IAP) and on other physiologic parameters in patients with IAH.

Patients and methods

Patients were recruited between November 2005 and July 2006 from the 22-bed surgical intensive care unit (ICU) of Ghent University Hospital, a tertiary referral center with a total of 56 ICU beds. All adult, sedated and mechanically ventilated patients with a sustained increase in IAP $\geq$ 12 mmHg and recently developed or worsening organ dysfunction were considered eligible for the study. The study protocol was submitted to and approved by the local ethics committee, and informed consent was obtained from the patients' relatives.

In ten patients in supine position, an intravenous bolus of cisatracurium at a dose of 0.15 mg/kg (Nimbex; GSK, Belgium) was administered. IAP was measured just before administration and at 15, 30, 60 and 120 min after administration. IAP was measured using a custom-made device (BBraun, Belgium), based on the transvesical technique described by Cheatham et al. [6]. Patients were sedated using midazolam and morphine to a Richmond Agitation and Sedation Score of –5. IAH and ACS were defined according to the consensus definitions of the World Society on Abdominal Compartment Syndrome (WSACS) [7].

The effect on central venous pressure (CVP), mean arterial pressure (MAP), abdominal perfusion pressure (APP, defined as MAP minus IAP) and heart rate (HR) was also evaluated. Urinary output prior to administration, and after 60 and 120 min respectively was recorded.

The values at the different time points were compared using the Friedman test, and when this showed a significant difference, the difference between T0–T15, T0–T30 and T0–T60 was studied using a Wilcoxon test. A p value of 0.05 or lower was considered statistically significant. Values are reported as median and interquartile range (IQR).

Results

The median age of the patients was 50 years (IQR 38–65); five of them were male. APACHE II score on admission was 29 (IQR 14–37). IAH was caused by massive fluid resuscitation without obvious abdominal problem in five patients, by abdominal trauma in three, and burns and bowel distension in one patient each.

The Friedman test demonstrated significant differences in IAP at the different time points. Bolus administration of cisatracurium significantly decreased IAP from 18 mmHg (IQR 16–20) at baseline to 14 mmHg (IQR 12–16) at 15 min ($p = 0.01$) and to 14 mmHg (IQR 13–17) at 30 min ($p = 0.02$) (Table 1). The difference between T0 and T60 was not significant. No changes in CVP, MAP, APP, HR, peak airway pressure or urinary output were observed.

In only one patient with an IAP of 25 mmHg was there no reduction of IAP after administration of cisatracurium. In all patients, IAP returned to the baseline level after 120 min.

Discussion

In this study we demonstrated a statistically significant reduction in IAP at 15 and 30 min after administration of a single dose of cisatracurium. CVP, MAP, APP, HR and ventilatory parameters were not significantly altered. At 120 min all parameters had returned to the baseline values, which can be explained by the short half-life of cisatracurium (25–30 min in patients with normal organ function).

Several non-operative management strategies have been proposed for the treatment of IAH and ACS, most of them aimed either at decreasing intra-abdominal volume or at improving abdominal wall compliance [8–11]. In patients with IAH, abdominal wall compliance can be decreased as a result of capillary leak and edema of the abdominal wall, leading to a shift of the abdominal pressure–volume curve upwards and to the left. The administration of NMB is thought to improve abdominal wall compliance, reverse this shift of the abdominal pressure–volume curve and thus decrease pressure for any given intra-abdominal volume. Two case reports describing a beneficial effect of cisatracurium on IAP and on urine output were published in 2002 [5] and 2003 [4].

Table 1 Effect of bolus administration of cisatracurium on IAP, MAP, APP, CVP and heart rate

Parameter	Time T0	T15	T30	T60	T120	p
IAP	18 (16–20)	14 (12–16)*	14 (13–17)**	15 (14–17)	17 (14–19)	0.002
MAP	71 (64–76)	72 (62–77)	69 (64–77)	70 (63–77)	70 (62–88)	0.969
APP	53 (48–63)	58 (48–66)	59 (45–69)	56 (48–69)	54 (44–65)	0.674
CVP	18 (13–19)	16 (13–17)	15 (13–17)	15 (14–18)	18 (15–20)	0.146
HR	109 (93–113)	109 (94–115)	109 (96–116)	105 (94–111)	104 (99–110)	0.280

Values are reported as median (interquartile range)
IAP, intraabdominal pressure; *MAP*, mean arterial pressure; *APP*, abdominal perfusion pressure; *CVP*, central venous pressure; *HR*, heart rate
* Significantly lower than IAP at T0 ($p = 0.01$)
** significantly lower than IAP at T0 ($p = 0.02$)

In a series of four patients with non-traumatic brain injury, Deeren et al. found a decrease in IAP from 17.4 to 9.2 mmHg after a single dose of 10 mg cisatracurium [12].

Apart from the decrease in IAP in our study, there was also a trend towards decrease in CVP, although this was not statistically significant. Several authors have described transmission of intra-abdominal pressure to the thoracic compartment in patients or animal models with IAH. The proportion of IAP transmitted to the thorax is estimated at between 20% and 80% [13, 14]. Therefore, the high CVP values at the start of the study are probably falsely elevated due to increased IAP and do not reflect the true preload of the patient. Consequently, the trend towards decrease of CVP after administration of NMB, and the return of the CVP to the baseline value after 2 h, suggest an effect of NMB on the measurement of CVP and not a true hemodynamic effect.

We could not find any effect of NMB on MAP, HR or peak airway pressure. This could be due to the observational design of the study, in which patient treatment was left to the discretion of the attending physician, and to the small sample size, which was not powered to detect differences in these parameters. We did not record any data on the administration of vasopressors or fluids, which could have an effect on MAP and HR. Also, we did not specify a ventilation protocol for the study. Patients were sedated and mechanically ventilated using different ventilation modes including pressure-controlled modes, in which no changes in positive end-expiratory pressure or peak airway pressures were made during the short course of the study. Also, in this small series of patients we did not observe a beneficial effect of NMB on urine output. This could be due to a number of reasons. Diuresis may not have been significantly impaired by the presence of IAH at the start of the study (although IAP values were sufficiently high to produce acute kidney injury), fluid loading may have had an effect on urine output, the decrease in IAP may not have been substantial enough, or the transient decrease in IAP may not have lasted long enough to restore urine output after a single bolus administration of NMB.

Timing of an intervention that targets IAP is believed to be an important issue in the treatment of IAH and ACS [3]. In patients with established ACS, immediate DL is often recommended in order to avoid progression of organ dysfunction and mortality. One could argue that the administration of NMB in a single dose may lead to a delay in definitive treatment for those patients who progress to ACS. However, IAP did not increase after administration of NMB in any of our patients, IAP failed to respond at all to NMB in only one patient, and no adverse effect on organ function was observed in this study. We feel that since the effect of NMB on IAP can be observed at 15–60 min after administration, this small delay can be allowed in order to avoid the possible complications of unnecessary DL.

The use of NMB in the ICU has decreased significantly over the past few years, due to concerns about the possible complications of prolonged use of NMB. Known complications include tachyphylaxis, ventilator-associated pneumonia, peripheral nerve injury, skin breakdown, thromboembolic complications, atelectasis formation, and prolonged muscular weakness [15]. It is clear, however, that the use of NMB can only be recommended after careful consideration of possible risks and benefits.

In conclusion, a single-dose administration of cisatracurium (0.15 mg/kg body weight) can significantly decrease IAP in patients with IAH. Based on the results of the present study, NMB may be used in critically ill patients to reduce IAP in patients with moderately elevated IAP, while other interventions are performed to reduce IAP [16, 17]. Single-dose NMB may also be used as a bridge to DL in patients with ACS when immediate surgery is not available, but further clinical research is necessary to define the role for NMB in the treatment for IAH and ACS.

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