Research Article

Changes in mesenteric blood flow during intracranial hypertension due to acute elevations in intra-abdominal pressure

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Elevated intra-abdominal pressure (IAP) has been associated with increased intracranial pressure (ICP) and diminished splanchnic blood flow. We investigated superior mesenteric artery flow and ICP following an increase in IAP. A flowmeter was placed on the superior mesenteric artery in five pigs and ICP was measured with an intraparenchymal bolt. IAP was elevated to 10 and 20 mmHg with nitrogen pneumoperitoneum. Changes in ICP, central venous pressure, mean arterial blood pressure and superior mesenteric artery blood flow were recorded at each level of IAP. Analysis of variants and paired t-test analyses were performed. ICP was increased and superior mesenteric artery flow decreased following IAP elevation. These changes were statistically significant when IAP was raised to 20 mmHg (ICP: p = 0.02; superior mesenteric artery flow: p = 0.006); central venous pressure was also increased. There was no significant change in mean arterial blood pressure and cerebral perfusion pressure. We have demonstrated a simultaneous effect of IAP on ICP (increase) and superior mesenteric artery blood flow (decrease). Further studies are warranted to evaluate the complete mechanism of these findings. In addition to direct transmission of pressures from the abdominal cavity, indirect effects of intra-abdominal hypertension may play a role in these documented changes.

Earlier in the 20th century, increased intraabdominal pressure (IAP) was recognized as an important clinical entity in association with abdominal compartment syndrome (ACS) in various surgical conditions [1,2]. More recently, the development of laparoscopy has further focused attention on increased IAP and its physiological effects.

An acute elevation of IAP may be observed in trauma patients due to abdominal bleeding and visceral swelling [2,3] or during laparoscopy when the abdominal cavity is insufflated with gas to achieve adequate working space [4]. Elevated abdominal pressure was found to have adverse effects on several physiological systems, depending on pressure levels. Among the most important changes observed are increased mean arterial pressure and systemic vascular resistance, elevated venous pressure, respiratory changes, and decreased renal and visceral perfusion [5–7].

Elevated IAP has also been shown to increase intracranial pressure (ICP). Experimental animal models have demonstrated a significant increase in ICP following elevation of IAP during pneumoperitoneum [8]. The immediate effect of IAP on ICP is attributed mainly to the transmission of pressure from the abdominal cavity to the venous system above the diaphragm leading to a reduction of venous return from the brain [9]. While ICP elevation appears to be directly related to mechanical transmission of pressures, the various hemodynamic effects, including a decrease in visceral perfusion are more difficult to explain.

Changes in the perfusion of abdominal organs during increased IAP are more pronounced than can be accounted for by direct compression of arterial vessels or changes in cardiac output [10].

It has been suggested that increased IAP may lead to an initiation of local [11] or central [12] mechanisms that contribute indirectly to these changes, including the theory that ICP elevation following increased IAP may lead to a neurohormonal response of stress hormones that may influence visceral perfusion [12]

The aim of this study was to investigate changes in ICP and superior mesenteric arterial (SMA) blood flow simultaneously, following the increase of IAP using a large animal model.

Material & methods

This protocol was approved by the University of Miami Animal Care and Usage Committee. Five male Yorkshire farm pigs, weighing 20 to 25 kg, were used in this experiment.

Animal preparation

Anesthesia was induced by ketamine 10 mg/kg, acepromazine 0.05 mg/kg, atropine 0.22 mg/kg and phentobarbital 8 mg/kg. Phentobarbital con-

tinuous infusion at a rate of 8 to 12 mg/kg/h was used for the maintenance of anesthesia. Following endotracheal intubation, the animals were placed in the prone position and a Camino[®] (Integra Neuro-Care) intraparenchymal pressure-monitoring probe was inserted intracranially in the frontoparietal area. The animals were then placed in the supine position. The femoral vein and artery, as well as the internal jugular vein and the carotid artery, were cannulated by a direct cut-down technique. A midline laparotomy was then performed, and the superior mesenteric artery was isolated. A Transonic® (Transonic Systems) ultrasound flowmeter was placed around the artery. A cystostomy catheter was placed for urine collection. A 10 mm laparoscopic trocar was inserted through the abdominal wall for peritoneal insufflation. The laparotomy was closed, and the animals underwent 15 min of stabilization before proceeding with the experiment.

Experimental protocol

Two different IAP levels were used: 10 and 20 mmHg. Abdominal insufflation was achieved using nitrogen to prevent possible effects of absorbed CO_2 on ICP. A total of 15 mins of stabilization was allowed after reaching the desired pressure, and 15 min of rest at baseline 0 mmHg pressure was taken prior to proceeding to the next level of pressure. At baseline and at each subsequent pressure level, the following parameters were recorded:

- IAP (mmHg)
- ICP (mmHg)
- Mean arterial blood pressure (MABP; mmHg) at the femoral and carotid arteries
- Central venous pressure (CVP; mmHg) at the superior vena cava (measured through the jugular vein) and at the inferior vena cava (measured through the femoral vein)
- SMA blood flow (ml/min)
- Blood gas analysis including arterial PCO₂ (mmHg), PO₂ (mmHg) and pH

At the completion of the experiment, the animals were sacrificed by intravenous euthasol solution (0.2 cc/kg).

Statistical analysis

Results were analyzed using repeated measures analysis of variants (ANOVA) for overall effect of pressure on the measured parameters and paired t-test for comparison of the different pressures to the baseline values; p < 0.05 was considered statistically significant.

Results

All animals survived the procedure. Volume status and respiratory stability were maintained throughout the experiment, as evidenced by the insignificant changes in resting at the superior vena cava and blood gas analysis. CVP at the inferior vena cava was significantly affected by the increasing IAP (p < 0.001) which was seen in all five pigs during pneumoperitoneum. The mean increase in CVP was 3.6 mmHg for IAP of 10 mmHg (11.8–15.4) and 12.4 mmHg when IAP was raised to 20 mmHg (11.4–23.8).

Overall, ICP significantly increased (Table 1) and SMA blood flow significantly decreased (Table 2) in response to elevated IAP. Of note, ICP showed immediate response to the raised IAP (p = 0.04), with some adaptation after 15 min of stabilization. Therefore, the changes in ICP values were not significant at that time (p =0.07). The changes in ICP with IAP of 20 mmHg were significant (p = 0.006). SMA blood flow continued to significantly decrease over time (p = 0.039), after IAP was increased to 20 mmHg. MABP and cerebral perfusion pressure (CPP) calculated from the MABP and ICP did not change significantly during pneumoperitoneum (Table 1).

Discussion

Many investigators have studied and described the hemodynamic effects of IAH. The most prominent changes observed are increased systemic vascular resistance, increased CVP, and increased blood pressure [6]. In trauma settings, it has been shown that the abdominal pressure generated in abdominal compartment syndrome might also cause increased ICP [8].

Recently, experimental animal models of pneumoperitoneum established a linear correlation between the IAP created during laparoscopy and ICP elevation [9,13]. The primary suggested mechanism for this phenomenon is a mechanical transmission of pressure. Elevated IAP produces cranial displacement of the diaphragm and increased intrathoracic pressures. This leads to high filling pressures of the right atrium, increased jugular vein pressure and subsequent reduction of the venous return from the brain, increasing the ICP [14,15]. Another pathway for pressure transmission is the obstruction of venous outflow from the spinal cord via the pelvic and lumbar veins due to increased pressure in this region. This results in increased cerebrospinal fluid compartment pressure, transmitted via the subarachnoid space to

Table 1. Intracranial pressure.								
Variable	Condition	Mean	SD	p-value compared with each baseline	p-value compared with first baseline			
ICP	Baseline IAP at 10 mmHg	17.0 19.8	4.6 3.6	0.07				
ICP	Baseline 2 IAP at 20 mmHg	16.4 24.2	3.8 5.2	0.006	0.018			
СРР	Baseline CPP at 10 mmHg	44.4 44.2		NS				
СРР	Baseline 2 CPP at 20 mmHg	44 38.2		NS	NS			

CPP: Cerebral perfusion pressure; IAP: Intra-abdominal pressure; ICP: Intracranial pressure; NS: Nonsignificant; SD: Standard deviation.

the intracranial cavity [14,15]. In our study, the transmission of pressure to the venous system was demonstrated by a significant rise in the measured CVP.

In this study we confirmed these observations and demonstrated the association between ICP and IAP using nitrogen (N_2) instead of CO_2 for pneumoperitoneum creation. Although abdominal insufflation with nitrogen may reduce intestinal blood flow [16] we preferred its use since CO_2 has a substantial effect on ICP [17] and our initial aim was to get a net effect of IAP on ICP.

It is important to note that elevation of ICP is not necessarily associated with reduced CPP, which may be maintained due to elevated MABP [13]. In our study CPP did not significantly change during ICP elevation, although no conclusions can be drawn since MABP was also not significantly changed. In order to get significant results in these parameters, a large number of observations will be required.

Similar to the changes in ICP, we have demonstrated a significant reduction in SMA blood flow by direct measurements. The reduction in flow in our study was significant only in the higher IAP of 20 mmHg. Of note, the new baseline before increasing the IAP to 20 mmHg was somewhat higher than the original baseline at the beginning of the experiment. The return to baseline after the first phase of the experiment (IAP increase to 10 mmHg) was associated with an overshoot phenomenon in SMA flow, thus, creating a new baseline. Ideally, the two phases of the experiment (pressure increase to 10 and 20 mmHg) should have been separated using different animals to achieve a more physiological baseline. However, other studies have documented an absolute reduction in abdominal visceral perfusion following IAP increase [11], including blood flow to the

intestine [18], as well as decreased flow in the portal system [19]. These findings were also demonstrated in patients undergoing routine laparoscopic cholecystectomy [20–22].

The reasons for such a decrease are not completely understood. Hypoperfusion of the splanchnic territory has been attributed to direct effects of IAP with direct pressure on arteries, veins and inferior vena cava and parenchymal compression [6,7]. A secondary effect of reduced cardiac output has also been implicated [6].

However, these mechanical explanations cannot completely explain the magnitude and the different changes observed in abdominal organ blood flow during mild-to-moderate IAP elevation. Even minor elevations of IAP (as in our study) can cause a significant decrease in major abdominal vessel blood flow and the pressures observed in the abdomen are not sufficiently high to cause direct obstruction to arterial flow. Additionally, the effect of elevated IAP is not uniform to all abdominal organs. Caldwell and colleagues [11] demonstrated that increased IAP causes a marked decrease in blood flow to several abdominal organs and also a significant increase in adrenal blood flow. These observations suggest that indirect effects of IAH, local or systemic, may also play a role in these changes.

A possible theoretic mechanism that may be partly responsible for the observed effects of IAH in this study is the release of vasoactive substances in response to elevated IAP. It has been suggested that the increase in ICP itself may further contribute to the diminished blood flow in the splanchic territory [12]. Elevated ICP regardless of its cause leads to vasoconstriction mediated by release of stress hormones [23]. Further studies should be carried out to clarify this relation and characterize the possible hormonal mediators that might play a role in this possible mechanism.

Table 2. Superior mesenteric artery blood flow.							
Variable	Condition	Mean	SD	p-value compared with each baseline			
MBF	Baseline IAP2 at 10 mmHg	249.0 238.8	173.6 143.1	0.61			
MBF	Baseline 2 IAP2 at 20 mmHg	299.8 242.0	185.2 149.9	0.039			

IAP: Intra-abdominal pressure; MBF: Mesenteric blood flow; SD: Standard deviation.

In this study, we focused on the immediate changes of ICP and SMA flow caused by increased IAP. The study was not designed to investigate longer-term effects such as SMA blood flow after longer periods of IAP increase or time recovery of the elevated ICP and reduced SMA blood flow following IAP decrease to baseline. However, these are relevant interesting issues that should be further investigated as well.

Expert commentary & conclusion

We have demonstrated that increased IAP has a simultaneous effect on ICP and SMA blood flow. While ICP elevation is simple to explain by transmission of mechanical pressures the reduction in SMA blood flow might be related, at least partly, to indirect effects of IAP that should be further investigated.

Highlights

- Elevated intra-abdominal pressure causes an increase in intracranial pressure.
- Elevated intra-abdominal pressure causes a decrease in superior mesenteric artery blood flow.
 Intracranial pressure elevation following an increase in intraabdominal pressure can be attributed
- mainly to mechanical transmission of pressures from the abdominal cavity to the venous sytem above the diaphgram leading to a reduction of blood flow from the brain.
- The reduction in superior mesenteric artery blood flow cannot be completely explained by direct transmission of pressures.
- Theoretically, the elevated intracranial pressure may further contribute to the diminshed blood flow of the superior mesenteric artery by leading to a release of stress hormones that cause vasoconstriction. This theory may be further investigated.

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