Effects of increased intra-abdominal pressure and volume expansion on renal function in the rat

Pernilla Lindström, Jonas Wadström, Anna Ollerstam, Cecilia Johnsson and A. Erik G. Persson

1Division of Integrative Physiology, Department of Medical Cell Biology, Uppsala University and
2Department of Surgery, Uppsala University Hospital, Uppsala, Sweden

Abstract

Background. The effects of increased intra-abdominal pressure (IAP) and volume expansion on renal function in the rat were studied to gain more knowledge of the oliguria seen during laparoscopic procedures and to reduce the detrimental renal effects of IAP.

Methods. IAP was elevated to 5 or 10 mmHg by insufflation of CO2 and maintained for 2 h in anaesthetized and mechanically ventilated rats. Rats with normal IAP served as controls. An angiotensin II receptor I antagonist, candesartan, was given as a bolus injection and a 5% volume expansion was achieved by i.v. saline infusion. An angiotensin-converting enzyme (ACE) inhibitor was also given. Renal parameters were the glomerular filtration rate (GFR), urine production, the urinary concentrations of sodium and potassium and the osmolality in the urine. The arterial acid–base balance and blood pressure were also monitored.

Results. The GFR deteriorated by 70% during pneumoperitoneum (PP) of 10 mmHg. There was a dramatic drop in sodium excretion (88–97%). With candesartan and elevated IAP, there was a drop in mean arterial pressure (from 90 to 55 mmHg) and the negative renal effects were very pronounced. Renal function was better preserved during elevated IAP in combination with volume expansion.

Conclusions. Pneumoperitoneum suppresses renal function, especially in combination with angiotensin II receptor 1 blockade and ACE inhibition. Volume expansion reduces the deleterious effects of PP on renal function during elevated IAP. The results suggest that patients should not be given pharmaceuticals blocking the renin–angiotensin–aldosterone system prior to procedures that may increase IAP. It may be beneficial, however, to reduce angiotensin II tension by volume expansion.

Keywords: candesartan; glomerular filtration rate; intra-abdominal pressure; oliguria; pneumoperitoneum; volume expansion

Introduction

The first laparoscopic nephrectomy for live donor transplantation was reported in 1995 by Ratner et al. [1]. The technique has now found widespread acceptance in living donor nephrectomies [2–4], though some concerns regarding the renal function of both donor and recipient still remain. One renal graft loss was reported after laparoscopic nephrectomy due to ischaemic injury, prolonged renal hypoperfusion and graft cortical necrosis [5]. The transient elevation of donor creatinine level was also greater than expected [5].

During laparoscopy, pneumoperitoneum (PP) is created by insufflation of CO2 into the abdominal cavity, to achieve working space. This elevates the intraperitoneal pressure. During laparoscopic procedures and PP, oliguria is seen [6–8]. The mechanism by which oliguria occurs during PP is not yet fully understood, though several mechanisms have been put forward for discussion. Compression of the renal vein, the renal parenchyma and/or the ureter, along with a decrease in cardiac output, are possible mechanisms. Increased release of hormones, such as antidiuretic hormone (ADH), endothelin and/or hormones of the renin–angiotensin–aldosterone system (RAAS), has also been proposed. Contradictory results have been reported in studies of cardiac output and release of ADH and endothelin in combination with PP [9–12], whereas compression of the ureter has now been ruled out as a factor contributing to the oliguria [13–15].
CO₂ gas is chosen for insufflation in the clinical situation because it is low in price, easy to handle, does not burn or explode, can be eliminated easily through ventilation and carries a low risk of gas embolism [16]. CO₂ in tissues has a direct vasodilatory effect, and a decrease in systemic vascular resistance would be expected during capnoperitoneum. However, several studies investigating haemodynamic changes report an increase in systemic vascular resistance by some vasoconstrictor after PP [10,17,18]. It is possible that angiotensin II is released at an increase of intra-abdominal pressure (IAP) with CO₂.

The purpose of the present study was to investigate whether changes in renal function occur in connection with increased IAP in a rat model. In particular, we wanted to investigate whether the RAAS is significantly involved. This was done by the administration of candesartan, an angiotensin II receptor I antagonist, and captopril, an angiotensin-converting enzyme (ACE) inhibitor. In addition, rats were subjected to volume expansion and treated or not with candesartan during the elevation of IAP.

Subjects and methods

The study was divided into three series of experiments. Series 1 established the model and changes in renal function due to capnoperitoneum with 5 and 10 mmHg. The influence of acute candesartan treatment on renal function during PP was studied in series 2. In series 3, volume expansion was added to the experimental protocol of PP and acute candesartan treatment. Additional experiments were performed to measure the concentration of aldosterone.

The study was approved by the independent Local Ethics Committee in Uppsala, Sweden. Male inbred Dark Agouti rats [n = 51, body weight (BW) 201–293 g; B&K International, Sollentuna, Sweden] were used. The rats had free access to food and water and were fasted for 10 days prior to operation. Anaesthesia was induced with 3% halothane (Fluothane; AstraZeneca, Macclesfield, Cheshire, UK) and maintained with 1.75% halothane. The trachea was cannulated and the rats were ventilated in a small animal ventilator (Rodent Ventilator Model 683; Harvard Apparatus, Holliston, MA, USA) with 33% oxygen in air. The acid–base balance (AVL Compact 3; AVL LIST, Graz, Austria) was measured and the respiration rate adjusted accordingly, to maintain arterial partial pressure of CO₂ (pCO₂) within normal range. The rats were placed on a servo-regulated heating pad with a rectal probe to maintain their body temperature at 37.5°C. Catheters were placed in the left jugular vein for maintenance infusion and in the left carotid artery for blood sampling and monitoring of mean arterial pressure (MAP). The abdomen was opened by a small midline incision and the urinary bladder was catheterized for urine collection. Two catheters were inserted through the abdominal wall guided by a 20 gauge needle. One of the catheters was connected to the CO₂ gas supply and the other to an overflow valve to maintain IAP at the desired level. The muscle layer and skin layer of the abdominal wall were closed separately by silk sutures in an airtight manner. To measure the glomerular filtration rate (GFR), a 0.5 ml primary bolus injection of 2.5 μCi/ml [³H]methoxy-inulin (NEN, Boston, MA, USA) in saline was given, followed by a continuous saline infusion (0.9% NaCl, 5 ml/kg BW per hour) with inulin (1.25 μCi/ml) intravenously. Urine was collected during two 60 min periods and blood samples were drawn at the midpoint of each period for haematocrit and acid–base status measurements and to determine plasma concentrations of inulin.

Series 1

This series consisted of three groups. After an equilibration period of 60 min following the preparatory surgery, IAP was elevated to 5 (CIAP 5 group, n = 6) or 10 mmHg (CIAP 10 group, n = 6) by insufflation of CO₂ and maintained for 2 h. Rats treated in the same manner but without insufflation of CO₂ served as controls (C group, n = 8). The intraperitoneal pressures were chosen to mimic the clinical situation, where a capnoperitoneum of <15 mmHg is used. Due to the smaller size of the rat, we chose the levels of 5 and 10 mmHg.

Series 2

Pilot series were performed to decide drug and dose to administer in this series. The purpose was to choose a drug blocking the RAAS. This was done by the administration of captopril and candesartan. Captopril inhibits the ACE. Rats were treated with a bolus dose of 3 mg/kg of captopril followed by a continuous infusion of 3 mg/kg/h. Three rats were treated with captopril and otherwise treated according to the protocol described below for the Cand group. Four rats were treated with captopril and had IAP elevated to 10 mmHg.

Candesartan cilexetil CV 11974 (AstraZeneca) is an angiotensin II receptor I antagonist in an administration form for experimental i.v. use. Candesartan was dissolved in saline and NaHCO₃, with a candesartan concentration of 1 mg/ml, and pH was corrected to 7.4. To establish the dose of candesartan for this series, rats were treated as described below with a low dose (n = 5, 0.1 mg/kg BW) or a high dose (n = 5, 1.0 mg/kg BW) of candesartan according to the instruction manual. There was no difference in the GFR between the groups treated with candesartan or compared with the group not treated with candesartan (C group); consequently, the lower dose was chosen for our series protocol. An additional five rats were treated with candesartan (low dose) and had IAP elevated to 10 mmHg for 2 h.

It was found that the GFR did not differ between the rats with normal IAP (candesartan 0.6 ± 0.06 and 0.8 ± 0.08 and captopril 0.81 ± 0.08 and 1.06 ± 0.3 vs series 1 control 0.9 ± 0.1 and 1.2 ± 0.25 ml/min/100 g BW). Nor was there a difference in urine production (candesartan 4.3 ± 1.6 and 3.1 ± 0.7 and captopril 3.9 ± 0.34 and 4.0 ± 0.05 vs series 1 control 4.1 ± 0.42 and 3.2 ± 0.04 ml/min/100 g BW). Blood pressures were equal as well. Furthermore, there was no difference between groups treated with candesartan and captopril in their response to the elevation of IAP. Both treatments showed MAP of ~50 mmHg during PP (see Figure 3). There was no urine production in either group.

Due to the simpler administration of candesartan, this drug was chosen in our protocol of series 2 and 3. Series 2 consisted of three groups. After 30 min stabilization, the rats were treated with candesartan as a slow bolus i.v. injection of 0.1 mg/kg BW in 250 μl of saline. The experiment started 30 min later. IAP was either not manipulated (Cand group,
or it was elevated to 5 (CandIAP 5 group, \( n = 5 \)) or 10 mmHg (CandIAP 10 group, \( n = 5 \)) by insufflation of CO\(_2\).

**Series 3**

As in the previous two series, this series also consisted of three groups. Immediately after the surgical preparation, a 5% saline volume expansion was commenced (5% of BW/h) for all groups. Candesartan was administered in the same manner as described for series 2. The VEcandN group (\( n = 6 \)) was subjected to volume expansion and treated with candesartan; the VEcandIAP 5 group (\( n = 5 \)) was subjected to volume expansion, treated with candesartan and had IAP elevated to 5 mmHg; and the VEIAP 5 group (\( n = 5 \)) was subjected to volume expansion and had IAP elevated to 5 mmHg.

**Aldosterone measurements**

Additional experiments were performed to measure the concentration of serum aldosterone. Rats had normal IAP (\( n = 3 \)), IAP elevated to 5 (\( n = 3 \)) or 10 mmHg (\( n = 3 \)) or were subjected to volume expansion and had IAP elevated to 5 mmHg (\( n = 3 \)). The elevation of IAP by CO\(_2\) was maintained for 90 min before withdrawal of blood for aldosterone measurement. Analyses of aldosterone were performed at the Clinical Chemistry routine laboratory, Uppsala University Hospital, using standard clinical chemistry methods. Aldosterone concentration was measured with a commercial radioimmunoassay (DPC, Los Angeles, CA, USA).

**Urinalysis**

The urine volumes were determined gravimetrically. The urinary concentrations of sodium and potassium were measured by flame photometry (FLM3; Radiometer Analytical, Copenhagen, Denmark). Osmolality in the urine was determined by depression of the freezing point (Model 3MO; Advanced Instruments, Needham Heights, MA, USA). Osmolar clearance was calculated with the assumption of a serum osmolality of 290 mOsm/l. The amounts of inulin in samples of urine and plasma were determined in a scintillation counter (PW4700; Phillips, Eindhoven, The Netherlands). The GFR was estimated according to clearance of inulin.

**Statistics**

All data are given as means ± SEM. Two-way analysis of variance (Statview; SAS Institute, Cary, NC, USA) was performed for comparison between groups. Scheffe's multiple comparison test was applied. A \( P \)-value of <0.05 was considered to be statistically significant.

**Results**

**Series 1**

MAP was recorded throughout the experiment and is shown in Figure 1. Throughout the experiment, the C\(_N\) group had a MAP of 92–97 mmHg. The rats that had elevated IAP showed a transient reduction in MAP at the induction of PP. This decrease was significant after 5 and 15 min of PP in the CIAP 5 group and after 5, 15 and 30 min in the CIAP 10 group compared with the C\(_N\) group. Thereafter, the former MAP was restored.

Blood gas analyses were performed during the stabilization period and at the midpoint of both periods. The mean arterial pH, pCO\(_2\) and base excess (BE) for series 1 are listed in Table 1. There was no change over time during both periods in each group (data not shown), so the mean values for the entire experimental period are presented in Table 1. The pCO\(_2\) was not affected by insufflation of CO\(_2\); however, pH was reduced and BE was significantly changed, with
a negative BE at all time points and in both groups with PP.

The GFR and urine production are shown in Figure 2. In the CN group, the GFR was 0.91 ± 0.11 ml/min/100 g BW in the first period and 1.18 ± 0.25 ml/min/100 g BW in the second. The GFR in the C1AP5 group was not significantly changed from that in the CN group. During the first period, when MAP was reduced, the GFR was significantly decreased in the C1AP10 group, and the lower GFR in the C1AP10 group was not significant during the second period. The GFR in the C1AP10 group was slightly increased in the second period compared with that in the first, which could be explained by the restoration of MAP. The CN group had a urine flow of ~3–4 μl/min/100 g BW (Figure 2). Urine production was diminished during PP and the C1AP5 group had a significantly reduced urine flow during the first period compared with the CN group, but the urine production was largely recovered during the second period. The C1AP10 group had diminished urine production at all time points. A striking reduction in mean sodium excretion (88–97%) was seen in the C1AP5 and C1AP10 groups compared with the CN group (Figure 2). During the first period, the C1AP5 group showed a significant decrease in potassium excretion (Figure 2). In the C1AP10 group, the potassium excretion...

Fig. 2. GFR, urine flow, excretion of osmotically active substances and sodium and potassium excretion per 100 g BW in series 1. CN is the control group and the C1AP5 and C1AP10 groups had IAP elevated to 5 and 10 mmHg, respectively. Each period lasted for 60 min. Values are given as means ± SEM. *P < 0.05 vs CN.

Values are presented as means ± SEM.
*The experimental period consisted of the measurements in both periods.
*P < 0.05 vs CN in series 1, CandN in series 2 and VEcandN in series 3.
rate was further diminished and the reduction was statistically significant at all time points. The CIAP5 and CIAP10 groups had a significantly decreased osmolar excretion during both periods compared with the CN group (Figure 2). The osmolar clearance was significantly decreased in both periods when IAP was elevated (CN 42.5 ± 3 and 37.9 ± 3, CIAP5 9.6 ± 2* and 19 ± 5* and CIAP10 5.3 ± 2* and 13 ± 4* ml/min). Also, the free water clearance was significantly increased during intra-abdominal hypertension in both periods compared to the CN group (CN –33 ± 2 and –31 ± 3, CIAP5 –7.1 ± 1* and –14 ± 5* and CIAP10 –4 ± 1* and –10 ± 3* ml/min).

Series 2

MAP is shown in Figure 3. Injection of candesartan at –30 min gave an initial drop in MAP of ~10 mmHg, and this reduction in blood pressure was maintained throughout the recording periods. When IAP was elevated to 5 mmHg (CandIAP5 group), MAP dropped to 60 mmHg and did not recover. In the CandIAP10 group, the effect was even more pronounced.

Blood gas analyses were performed during the stabilization period and at the midpoint of the two experimental periods. The mean arterial pH, pCO2 and BE for series 2 are listed in Table 1. There was no change over time during both periods in each group (data not shown); consequently, the mean values for the entire experimental period are presented in Table 1. There was no significant difference in arterial pH, pCO2 or BE between the CN and CandN groups. The CandIAP5 group did not differ significantly from the CandN group in this regard. Arterial pH of the CandIAP10 group did not differ from that of the CandN group, although the CandIAP10 group had a significantly lower pCO2. A metabolic acidosis was seen as negative BE during the experimental period for the CandIAP10 group.

There was no difference in GFR or urinary output in the CandN group (Figure 4) and the CN group. The CandIAP5 group had a strongly suppressed GFR and urine production, whereas the group with the highest intra-peritoneal pressure (CandIAP10) had no urine production at all and is not presented in Figure 4. In the CandIAP5 group, the excretions of sodium and potassium were significantly reduced (or absent), as was osmolar excretion (Figure 4). Both osmolar and free water clearances were changed in the CandIAP5 group compared to the CandN group; osmolar clearance was decreased (CandN 35 ± 12 and 29 ± 8 and CandIAP5 1.4 ± 1* and 0.3 ± 0.3* ml/min) and free water clearance increased (CandN –25 ± 8 and –22 ± 6 and CandIAP5 –1 ± 0.8* and 0 ± 0.1* ml/min). The CandIAP10 group had no urine production; hence, no excretion calculations could be made.

Series 3

Once again, a decrease in MAP of ~10 mmHg was seen immediately after injection of candesartan (VECandIAP5 and VECandN groups, Figure 5). Thereafter, MAP of all groups subjected to volume expansion was quite stable, although a small drop was seen, from 90 to 70 mmHg. The VECandIAP5 group was affected by the insufflation of CO2, and MAP in this

![Fig. 3. MAP in series 2. The CandN group was treated with candesartan and had normal IAP and the CandIAP5 and CandIAP10 groups were treated with candesartan and had IAP elevated to 5 and 10 mmHg, respectively, during both periods. Arrows indicate the time of blood sampling. Values are given as means ± SEM. *P < 0.05 vs CandN. Dashed and dotted lines indicate MAP in rats treated with captopril: the CaptoprilN group was treated with captopril and had normal IAP and the CaptoprilIAP10 group was treated with captopril and had IAP elevated to 10 mmHg during both periods.](https://academic.oup.com/ndt/article-abstract/18/11/2269/1845670)
group was significantly lower at 15 and 30 min after the induction of PP compared with that in the VEIAP 5 group. The drop in MAP after the induction of PP, as seen in series 1 and 2, is not present in the VEcandIAP 5 group, whose MAP only dropped by ~7 mmHg (not significant) at the induction of PP and was stable throughout the experiment.

The mean arterial pH, pCO2 and BE for series 3 are listed in Table 1. There was no change over time in both period in any of the groups (data not shown); conse-
sequently, the mean values are presented together under ‘Experimental period’ in Table 1. During the experimental period, mean pH was significantly lower in groups VE\textsubscript{IAP5} and VEc\textsubscript{IAP5} than in the VEc\textsubscript{N} group. Mean pCO\textsubscript{2} was lower in the VEc\textsubscript{IAP5} group than in the other two groups. BE was significantly reduced compared with that of the VEc\textsubscript{N} group, with a negative value in both groups with PP.

The GFR is presented in Figure 6, as is urine production. The GFR did not differ between the groups. Urinary output was significantly higher in the VEc\textsubscript{N} and VE\textsubscript{IAP5} groups than in the VEc\textsubscript{IAP5} group or in the CN group in series 1. The VEc\textsubscript{IAP5} group had a lower urine production compared with the VEc\textsubscript{N} group in both periods. There was no significant difference between the VEc\textsubscript{N} and VE\textsubscript{IAP5} groups regarding the urinary excretions of sodium, potassium and osmotic substances (Figure 6). The sodium and potassium excretion in the VEc\textsubscript{IAP5} group was significantly depressed during both periods. Osmolar excretion was significantly decreased in the VEc\textsubscript{IAP5} group during the first period, but not the second, compared with the VEc\textsubscript{N} group. The osmolar clearance decreased in the VEc\textsubscript{IAP5} group compared with the VEc\textsubscript{N} group in both periods (VEc\textsubscript{N} \textsuperscript{1} 1 0\pm 7a \textsuperscript{ and } 97\pm 1 2, \textsuperscript{VEIAP5} 88 \pm 1 5 \textsuperscript{ and } 72 \pm 1 5 \textsuperscript{ and } \textsuperscript{VEc andIAP5} 31 \pm 1 1\textsuperscript{*} \textsuperscript{ and } 46 \pm 1 3\textsuperscript{*} \textsuperscript{ml/min}). The free water clearance was increased in the VEc\textsubscript{IAP5} group, but not in the VEc\textsubscript{N} group, compared with the VEc\textsubscript{N} group (VEc\textsubscript{N} \textsuperscript{5} –50 \pm 2 \textsuperscript{ and } –45 \pm 5, \textsuperscript{VEIAP5} \textsuperscript{5} –46 \pm 5 \textsuperscript{ and } –37 \pm 6 \textsuperscript{ and } \textsuperscript{VEc andIAP5} –17 \pm 5\textsuperscript{*} \textsuperscript{ and } –26 \pm 5\textsuperscript{*} \textsuperscript{ml/min}).

**Aldosterone measurements**

Mean aldosterone concentration for the rats with normal IAP was 3.44 \pm 0.4 nmol/l. For the rats that had IAP elevated to 5 mmHg, it was equal (3.45 \pm 0.6 nmol/l). For the rats with a capnoperitoneum of 10 mmHg, it increased significantly to 6.60 \pm 1.1 nmol/l. When the rats were subjected to volume expansion prior to and during PP, it decreased significantly to 0.77 \pm 0.1 nmol/l.

**Discussion**

In this study, we examined the effects of increased intraperitoneal pressure with CO\textsubscript{2} on renal function in a rat model. Kidney function, seen as the GFR, deteriorates during elevated IAP. The GFR was reduced by \textsuperscript{70\%} at an IAP of 10 mmHg. This reduction is much larger than can be explained by the initial drop in MAP and suggests an effect of local factors within the kidney. This is in line with findings by Harman et al. [15], who subjected dogs to high IAP and found that the GFR diminished. After 40 min, the dogs were subjected to volume expansion until cardiac output was back to baseline; however, the GFR was still reduced. London et al. [19] showed that large amounts of

![Fig. 6. GFR, urine flow, excretion of osmotically active substances and sodium and potassium excretion per 100 g BW in series 3. The VEc\textsubscript{N} group was subjected to volume expansion, treated with candesartan and had normal IAP; the VEc\textsubscript{IAP5} group was subjected to volume expansion, treated with candesartan and had IAP elevated to 5 mmHg; and the VE\textsubscript{IAP5} group was subjected to volume expansion and had IAP elevated to 5 mmHg. Each period lasted for 60 min. Values are given as means \pm SEM. *P < 0.05 vs VEc\textsubscript{N}.](https://academic.oup.com/ndt/article-abstract/18/11/2269/1845670/1845670)
i.v. fluids during PP restored urinary and cardiac outputs but that the GFR did not recover.

In the present study, oliguria was seen during increased peritoneal pressure. Oliguria during elevated IAP is well documented [6,8,14,15], but the aetiology has still not been elucidated. The low urine production during the first period in series 1 can be explained partly by the drop in MAP; however, during the remainder of the experiment, MAP was restored and does not justify the prolonged renal effects.

Laparoscopic living donor nephrectomies are performed with an insufflation pressure of 12 mmHg and take 110–350 min [20,21]. Others who have studied elevated intraperitoneal pressures in rats have used pressures in the same ranges as used in the present study [22,23]. In contrast to our findings, Kirsch et al. [23] found oliguria only at an IAP of 10 mmHg, but not at a lower IAP, and suggest that the decrease in urine production is a result of renal vascular insufficiency from central venous compression. In a study on pigs, McDougall et al. [13] found oliguria and a decreased GFR during elevated IAP, with no changes in blood pressure, though cardiac output was slightly decreased. They reported a decreased renal vein flow as the primary renal event during laparoscopy. In contrast, in a study by Boberg et al. [24] in our laboratory, the renal venous pressure was elevated to 20 mmHg, but even at this high renal venous pressure an elevated urine flow was seen, though the GFR was reduced by ~20%.

The most striking finding in series 1 is the decrease in sodium excretion after the elevation of IAP. Almost no sodium was excreted during PP and the excretion of osmotic active substances was likewise depressed, resulting in diluted urine. One possible explanation for this pronounced effect might be that, when the blood pressure is reduced by the administration of CO₂ intra-abdominally, renin is released and angiotensin II is formed. Angiotensin II is known to increase the sensitivity of the tubuloglomerular feedback mechanism that would act to reduce the GFR more than would be expected to occur by the initial blood pressure drop alone. In addition, it is likely that the increased angiotensin II would stimulate the formation of aldosterone, which could increase sodium reabsorption in the distal tubule. Aldosterone was elevated 2-fold in our setting. The aldosterone effect is unclear though, because the short time period of the experiment and if the time is enough to affect the excretion rate of sodium. The upregulation of hormonal output of the RAAS has also been studied during elevated IAP created by fluid instillation [25].

Many of the effects of angiotensin II can be prevented by ACE inhibition. The blockade of the angiotensin II receptor 1 also blocks the effects of angiotensin II. Renal function in rats after candesartan or captopril treatment without PP was not altered compared with the controls. Blood pressure decreased slightly during the course of the experiment in the groups treated with candesartan and captopril but not in the controls. The difference is therefore likely to be due to the continued influence of angiotensin II in the controls in this setting. In the groups treated with candesartan or captopril and with PP, MAP was decreased during PP so that the renal autoregulation diminished or disappeared. The GFR was decreased and small amounts of urine (or no urine at all) were produced. Candesartan or captopril treatment before the induction of PP prevented the vasoconstriction from restoring blood pressure back to normal, as was seen in series 1. This resulted in a metabolic acidosis (negative BE) due to the perfusion pressure being too low to maintain aerobic metabolism.

Volume expansion is known to reduce the production of renin and the generation of angiotensin II. In series 3, a normal GFR was seen during elevated IAP, though MAP was somewhat lower than in the controls. The high venous infusion rate resulted in a high diuresis along with natriuresis. The elevation of IAP did not significantly affect MAP or renal excretion products. The group subjected to both angiotensin II receptor 1 blockade and PP along with volume expansion (VEcandIAP=) had lower urinary excretion rates than the other groups subjected to volume expansion, but compared with the controls the urine production and sodium excretion in this group was within the normal range. We therefore suppose that volume expansion precludes the release of renin and results in a lower amount of angiotensin II and thus diminishes the effect of candesartan.

The mechanism behind the release of renin deserves comment. At the induction of capnoperitoneum, the insufflated gas compresses the large veins. This results in a reduction of cardiac preload and subsequently a forward failure, seen in these experiments as a decrease in MAP in the rats with relative hydropenia. There is a reduction in renal blood flow that induces renin release [26]. Formation of the potent vasoconstrictor (angiotensin II) results in an increase in systemic vascular resistance [15,17,19].

The present experiments indicate that, during relative hydropenia and intra-abdominal hypertension, there was a production of renin, followed by angiotensin II, which elevates blood pressure and sensitizes the tubuloglomerular feedback mechanism to reduce the GFR. Furthermore, this high angiotensin II production initiates the formation of aldosterone shown in the present study and by Bloomfield et al. [25]. In the present study, the blockade, through candesartan, of the angiotensin II receptor 1 also prevented a normalization of the blood pressure; consequently, the renal excretory function was greatly impaired. These results indicate the important role of angiotensin II in the process. With a saline volume expansion, we could reduce the production of renin and angiotensin II and also reduce the sympathetic tone. In the rats subjected to volume expansion, no effect on MAP was seen, and therefore only small effects on excretory functions were seen during elevated IAP, even after blockade with candesartan of the angiotensin II receptor 1. Blood pressure was kept high by the volume expansion and there was no need for angiotensin II production.
Intra-abdominal pressure and volume expansion in a rat model

From the above findings, it seems reasonable to state with regard to humans that treatment inhibiting the RAAS should be avoided in patients in whom IAP is increased during surgery. In patients with surgery involving increased IAP, it may be beneficial to induce mild volume expansion to prevent blood pressure drop, angiotensin II release and loss of renal function. In cases where patients are already on such medication, volume expansion is an advantageous tool to prevent oliguria and reduction of the GFR.

Conclusions

In this study, the renal effects of PP were investigated in a rat model. Results indicate that capnoperitoneum suppresses renal function, especially in combination with angiotensin II receptor 1 blockade and ACE inhibition. Volume expansion prior to and during PP reduces the deleterious effects of PP on renal function during elevated IAP. The results suggest that the RAAS is important during PP and that patients should not receive pharmaceuticals that block the RAAS prior to operation. It may be beneficial also to reduce angiotensin II formation by volume expansion.

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