Ulusal Cer Derg 2013; 29: 49-53
DOI: 10.5152/UCD.2013.39

Biochemical and histopathological changes of intra-abdominal hypertension on the kidneys: Experimental study in rats

Akın Köşüm[1], Ersin Borazan[2], Göktürk Maralcan[2], Alper Aytekin[2]

ABSTRACT

Objective: This study aimed to evaluate the effects of experimentally induced intra-abdominal hypertension on renal functions, with the combination of biochemical and histopathological properties.

Material and Methods: Thirty male Wistar albino rats were used in this experimental study. Rats were divided into four groups. Group 1 (control group, n=6) only received anesthesia. After the induction of anesthesia, a 20 G catheter was introduced intraperitoneally to Group 2 (sham group, n=8), Group 3 (n=8) and Group 4 (n=8). The intra-abdominal pressure was not increased in Group 2. We applied 20 mmHg intra-peritoneal pressure to Group 3 and 30 mmHg to Group 4 for 3 hours. After withdrawing 3 mL intracardiac blood from all groups, the kidneys were removed for histopathological examination. Serum urea and creatinine levels were measured in all groups.

Results: Biochemical examination showed that blood urea and creatinine levels were statistically different among all groups ($p<0.05$). Serum creatinine levels in Group 3 and serum urea and creatinine levels in Group 4 were significantly increased. In the histopathological examination, the kidneys in Group 1 and Group 2 were classified as normal. In Group 3, areas with congestion were detected in the glomeruli and interstitial regions. In addition to these findings seen in Group 3, dilatation of the pelvi-caliceal structures and proximal ureters were noticed in Group 4.

Conclusion: The levels of serum urea and creatinine are elevated when intra-abdominal pressure is increased due to kidney damage. Foci of hemorrhage in the interstitial area, dilatations in the proximal ureter, renal pelvis, and lymphatics were the pathologic findings seen in the kidneys under such circumstances.

Key Words: Kidney, intra-abdominal hypertension, creatinine, histopathological changes, urea

INTRODUCTION

Normal intra-abdominal (IA) pressure is equal to or lower than the atmospheric pressure in animals making lung respiration (1, 2).

Clinically intra-abdominal hypertension (IAH) manifests with respiratory distress and low urine output despite volume resuscitation, together with abdominal distension. The presence of organ dysfunction in addition to IA pressure elevation is defined as "Abdominal Compartment Syndrome (ACS)".ACS is fatal if not treated (3, 4). Clinical and experimental studies contributed to better understanding of the effects of IAH and physiology of ACS, thus underlining the importance of urgent decompression (5, 6).

The kidneys are susceptible to intra-abdominal hypertension due to their anatomic location and blood supply (7). The first response to IA increase is oliguria. Oliguria develops when IA pressure exceeds 15-mmHg, and pressures over 30-mmHg lead to anuria (8).

Glomerular filtration pressure equals to the difference between mean blood pressure and IA pressure. Filtration gradient is the difference between glomerular filtration pressure and proximal tube pressure. When IA pressure increases, the proximal tube pressure is equal to the IA pressure. With increase in the pressure, the filtration gradient decreases because the mean blood pressure remains constant. The anuria encountered with higher-pressure levels cannot be related to ureteral compression, patients with urethral stents in place also exhibit anuria (9, 10).

An increase in the intra-abdominal pressure causes decrease in the renal blood flow due to decrease in cardiac output, decrease in renal artery and vein flow due to compression, compression to ureters, direct compression to kidney cortex and medulla, increase in the release of renin, aldosterone and ADH.

This study aimed to evaluate the effects of experimentally induced intra-abdominal hypertension on renal functions, with the combination of biochemical and histopathological properties. The purpose is to evaluate the adverse effects of IAH on kidney functions.

[1]Department of General Surgery, Adıyaman Gölbaşı Hospital, Adıyaman, Turkey

[2]Department of General Surgery, Gaziantep University Faculty of Medicine, Gaziantep, Turkey

This study was presented at the 18th National Surgical Congress as a poster (PB-224), 23-27 May 2012, İzmir

Address for Correspondence

Dr. Ersin Borazan

Department of General Surgery, Gaziantep University Faculty of Medicine, Gaziantep, Turkey
Phone.: +90 342 360 60 60
e-mail: ersinborazan@hotmail.com

Received: 02.05.2013
Accepted: 29.05.2013

Available online at www.ulusalcerrahidergisi.org

MATERIAL AND METHODS

The study was initiated after obtaining an ethical board approval from Gaziantep University Medical Faculty Ethics Board (Approval No: 06-2008/124, Date: 30.06.2008).

This study was planned in Gaziantep University Medical Faculty Department of General Surgery. The specimen were evaluated at the pathology laboratory.

The study includes 32 male Wistar albino rats with weights between 250-300 grams and fed with a standard diet under similar conditions.

The subjects were randomized into four groups. Two rats from the control group that died during experiments were excluded. Group 1 (control) contained 6 rats, ant the other Groups (Group 2, Group 3, Group 4) 8 rats each.

The subjects were not given oral diet 12 hours prior to procedures. Anesthesia induction was done with 85 mg/kg ketamine hydrochloride intraperitoneally (Ketalar®, %5 solution, Parke-Davis licensed Eczacıbaşı Pharmaceuticals, Levent, Istanbul).

Group 1 (Control Group): Following induction of anesthesia 3 mL intracardiac blood was withdrawn. Both kidneys were removed and preserved in 10% formaline solution.

Group 2 (Sham Group): Following induction of anesthesia a 20 G catheter was replaced and fixed intraperitoneally. Three hours later 3mL intracardiac blood was withdrawn. Both kidneys were removed and preserved in 10% formaline solution.

Group 3 (First Study Group): Following induction of anesthesia a 20 G catheter was replaced, creating a 20 mmHg intraperitoneal pressure with an insufflator (Figure 1). At the third hour of experimentally induced IAH, 3 mL intracardiac blood was withdrawn. Both kidneys were removed and preserved in 10% formaline solution.

Group 4 (First Study Group): Following induction of anesthesia a 20 G catheter was placed, creating a 30 mmHg intra-peritoneal pressure with an insufflator. At the third hour of experimentally induced IAH, 3 mL intracardiac blood was withdrawn. Both kidneys were removed and preserved in 10% formaline solution (Figure 2).

In this experimental study, the IA pressure in rats was created by insufflation of CO2 into the abdomen. In this manner, the pressure was diffusely distributed throughout the abdominal cavity and target pressure levels were precisely reached.

The blood samples that were withdrawn for biochemical analysis were kept in room temperature for half an hour for clotting and centrifuged for 5 minutes in 5000 rpm. Serum urea and creatinine levels were measured for all the subjects.

The kidney tissues were cleared with xylol after dehydration with alcohol and embedded in paraffin blocks. Sections of 5-µmthickness were cut from tissues and deparaffinized. They were stained with Hematoxylin eosin and evaluated under light microscopy for histopathology.

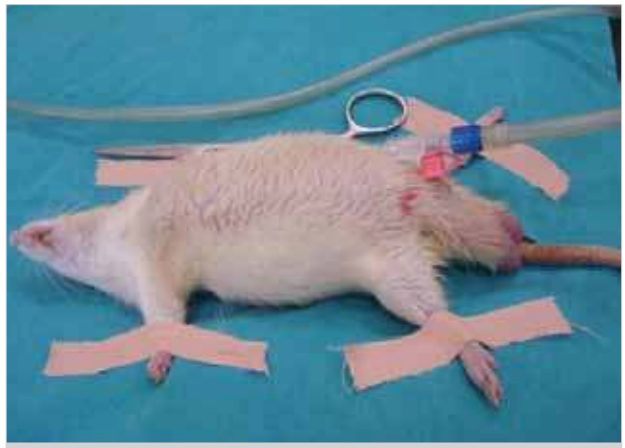

Figure 1. A rat with intraabdominal hypertension

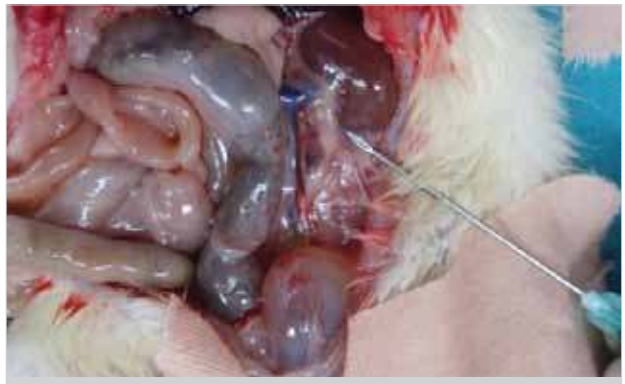

Figure 2. Macroscopic appearance of kidneys from a rat in Group 4

Statistical analysis

Serum urea and creatinine levels were stated as descriptive statistics, median (minimum-maximum) values. The groups were compared by the Kruskal Wallis test, if this test failed to show any difference between the groups, then they were compared in pairs by Mann-Whitney U test. Statistical analysis were done by SPSS 15,0 for Windows, a value of $p<0,05$ was accepted as significant.

RESULTS

Serum urea and creatinine levels of all groups are shown in Table 1 as median (minimum-maximum) values.

The groups showed significant difference in their urea ($p=0.004$) and creatinine ($p<0.001$) levels. The serum urea and creatinine levels were elevated as the IA pressure increased.

The comparisons in pairs are shown in Table 2. The difference in urea levels between Group 1 and Group 4 ($p=0.005$), was more prominent than the difference between Group 1 and Group 3 ($p=0.051$). This might be accepted to arise from the difference in pressure.

With regards to creatinine levels, Group 1 and Group 2 were similar (p=0.296). The creatinine levels were significantly higher in groups that IA was increased. As compared to Group 1 (Control group), creatinine levels in Group 3 (p=0.004) and Group 4 (p=0.002) were statistically significant.

Although a higher IA pressure was applied in Group 4, there was no significant difference between Group 3.

Table 3 summarizes histopathologic findings. Groups 1 and 2 did not show any abnormal findings in their kidneys (Figure 3). Group 3 revealed glomerular congestion (Figure 4) and interstitial hemorrhage foci (Figure 5). Group 4 exhibited dilatation in renal pelvis, lymphatics and proximal ureter (Figure 6) in addition to glomerular congestion and interstitial hemorrhage foci (Figure 7).

Table 1. Urea and creatinine levels in Groups

Intergroup Comparison (Krusker Wallis Test)	Urea (mg/dL) Median values (Min-Max) p=0.004	Creatinine (mg/dL) Median values (Min-Max) p<0.001
Group 1	51.50 mg/dL (47-59)	0.465 mg/dL (0.43-0.50)
Group 2	51.00 mg/dL (47-61)	0.475 mg/dL (0.44-0.51)
Group 3	58.50 mg/dL (51-64)	0.545 mg/dL (0.48-0.60)
Group 4	61.50 mg/dL (55-69)	0.580 mg/dL (0.53-0.62)

Table 2. Intergroup comparison in pairs (Mann-Whitney U test, p values)

Groups	1&2	1&3	1&4	2&3	2&4	3&4
Urea	1.000	0.051	0.005	0.039	0.005	0.102
Creatinine	0.296	0.004	0.002	0.007	0.001	0.139

Table 3. Histopathologic findings of the Groups

Pathology	Group 1	Group 2	Group 3	Group 4
Glomerular congestion	-	-	+	+
Interstitial hemorrhage	-	-	+	+
Pelvicaliceal dilation	-	-	-	+
Ureteral dilation	-	-	-	+

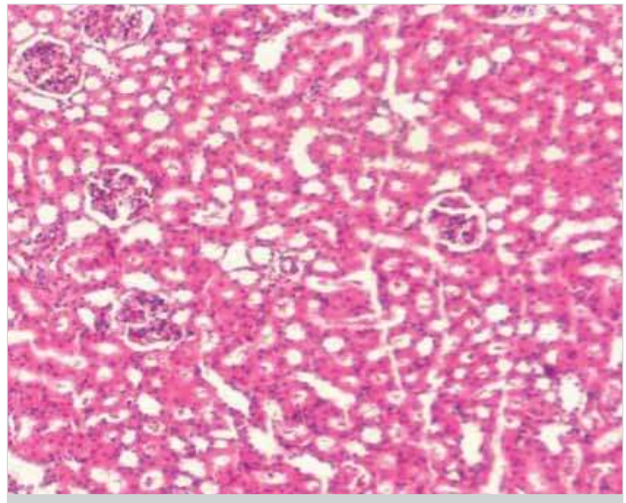

Figure 3. Normal kidney tissue in histopathologic examination of a rat kidney from Group 1 (HE x100)

DISCUSSION

The intra-abdominal pressure can be monitored via a Foley catheter. It is emphasized that the IA pressure increase may lead to organ dysfunctions and it can be fatal if not treated (11). Various studies have shown that IAH is a common problem amongst critically ill patients (6, 12). IAH emerged as a current investigation area, based on the facts that it is now accepted as a main factor to contribute to morbidity and mortality in intensive care patients and that laparoscopic procedures are evolving (2, 13).

In studies where the effects of normal intra-abdominal pressure on kidneys are evaluated, biochemical parameters are well reported whereas not many studies focus on the histopathologic changes in kidneys. This study, evaluated the effects of IAH on kidneys both with serum urea and creatinine levels and with histopathologic changes.

Oliguria and anuria refractory to fluid replacement, diuretics and dopaminergicsupport are renal signs of ACS (2, 3, 8, 14). When IA pressure exceeds over 15 mmHg oliguria develops, and over 30-mmHg anuria is expected (8). In experimental studies, in normovolemia, if the intra-abdominal pressure exceeds 20 mmHg the GFR decreases 75%, and over 40 mmHg it decreases by 100%. The decrease in glomerular filtration rate is refractory to volume load. The renal changes seen in IA pressure increase are due to the compression on the renal vessels and kidney parenchyma rather than decrease in cardiac output. We believe the congestion areas seen in glomeruli and interstitium are the result of compression due to IA pressure increase. The dilatation in renal pelvis and proximal ureter is thought to result from compression on the ureters.

Ma et al. (15) reported that when IA pressure increases, the urinary output is significantly impaired and serum creatinine levels increase. Küçük et al. (16) stratified their 25 patients with increased IA pressure into four groups according to their pressure levels, finding out that the group with IAP of 31-40 cm H_2O had a significant increase in urea and creatinine levels they concluded that the critical threshold for decompression is 30 cm H2O (1 cm-H_2O=0.735 mmHg). In our study, serum urea and creatinine levels were significantly higher in the second study group as compared to controls. Although the increase was significant the levels were within the normal range, we believe the reason to be the experiment period was limited because the subjects could not resist longer durations of high pressures.

In conclusion, it was found that experimentally induced IAH in rats has significant biochemical and histopathologic effects on kidneys. Patients with increase in IA pressures should be carefully monitored in order to prevent formation of these adverse effects on kidneys. We think early surgical intervention should always be kept in mind for ACS.

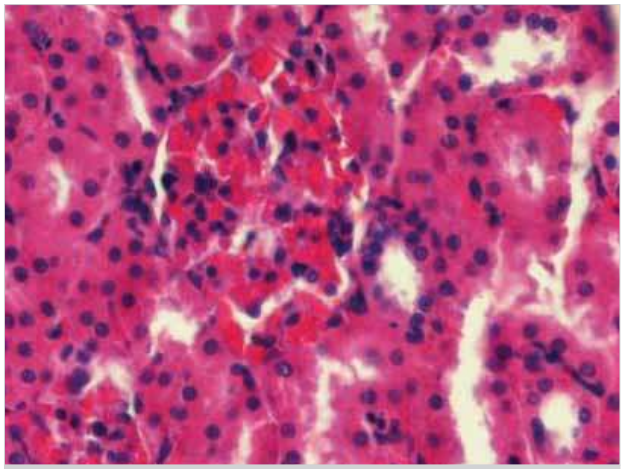

Figure 4. Glomerular congestion in histopathologic examination of a rat kidney from Group 3 (HEx400)

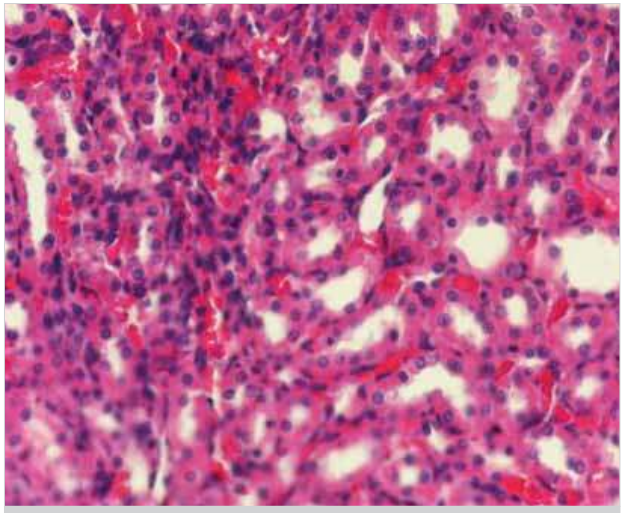

Figure 5. Interstitial hemorrhage in histopathologic examination of a rat kidney from Group 3 (HE x400)

CONCLUSION

The study results show that as normal intra-abdominal pressure increases, serum urea and creatinine levels significantly increase. Histopathologic glomerular congestion was observed together with IAH. IAH resulted in interstitial hemorrhage foci in kidneys. It was seen that it resulted in dilation of the proximal ureter with compression to the ureters. Additionally, dilation was seen in the renal pelvis and lymphatics.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Gaziantep University School of Medicine (30.06.2008, 06-2008/124).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - G.M., A.K.; Design - G.M., E.B., A.K.,; Supervision - G.M., E.B.; Funding - A.K., A.A.; Materials - A.K., A.A.; Data Collection and/or Processing - A.K., A.A.; Analysis and/or Interpretation - G.M., E.B., A.K.; Literature Review - A.K., A.A.; Writer - A.K., E.B., G.M.; Critical Review - G.M., E.B.

Conflict of Interest: No conflict of interest was declared by the authors.

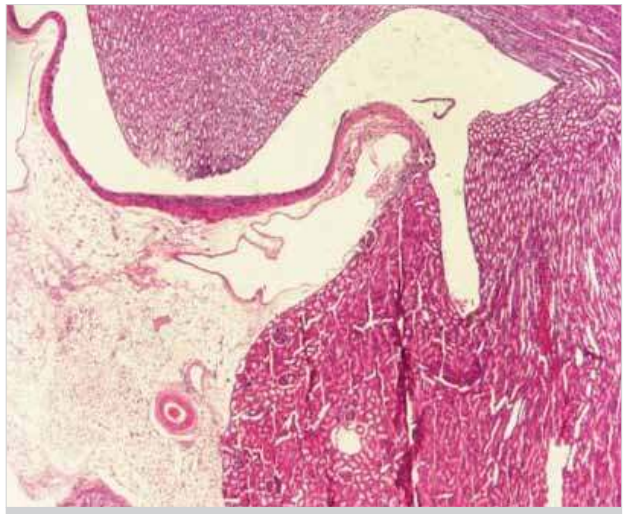

Figure 6. Dilation of renal pelvis and lymphatics in histopathologic examination of a rat kidney from Group 4 (HE x40)

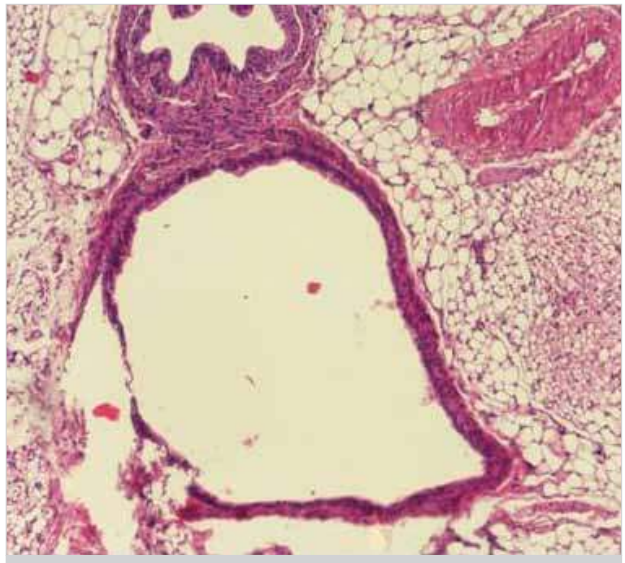

Figure 7. Ureteral dilation in histopathologic examination of a rat kidney from Group 4 (HE x100)

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Hunter JD, Damani Z. Intra-abdominal hypertension and the abdominal compartment syndrome. Anaesthesia 2004; 59: 899-907. [CrossRef]
2. Saggi BH, Sugerman HJ, Ivatury RR, Bloomfield GL. Abdominal compartment syndrome. J Trauma 1998; 45: 597-609. [CrossRef]
3. Cullen DJ, Coyle JP, Teplick R, Long MC. Cardiovascular, pulmonary, and renal effects of massively increased intra-abdominal pressure in critically ill patients. Crit Care Med 1989; 17: 118-121. [CrossRef]
4. Akbilen A, Çarkman S, Salihoğlu Z, Köksal S, Şirin F. Prosthetic greft application in preventing ıntraabdominal hypertension. Bakırköy Tıp Dergisi 2007; 3: 130-133.
5. Richards WO, Scovill W, Shin B, Reed W. Acut renal failure associated with increased intra-abdominal pressure. Ann Surg 1983; 197: 183-187. [CrossRef]
6. Schein M, Wittman DH, Aprahamian CC, Condon RE. The abdominal compartment syndrome: the physiological and clinical consequances of elevated intra-abdominal pressure. J Am Coll Surg 1995; 180: 745-753.

7. De Waele JJ, De Laet I. Intraabdominal hypertension and the effect on renal function. Acta Clin Belg Suppl 2007; 2: 371-374.
8. Harman PK, Kron IL, McLachlan HD, Freedlender AE, Nolan SP. Elevated intra-abdominal pressure and renal function. Ann Surg 1982; 196: 594-597. [CrossRef]
9. Katz R, Meretsky S, Gimmon Z. Abdominal compartment syndrome due to delayed identification of a ureteral perforation following abdominoperineal resection for rectal carcinoma. Int J Urology 1997; 4: 615-617. [CrossRef]
10. Chiu AW, Azadzoi KM. Effects of intra-abdominal pressure on renal tissue perfusion during laparoscopy. J Endourol 1994; 8: 99-103. [CrossRef]
11. Kron IL, Harman PK, Nolan SP. The measurement of Intra-abdominal pressure as a criterion for abdominal re-exploration. Ann Surg 1984; 199: 28-30. [CrossRef]
12. Ertel W, Oberholzer A, Platz A, Stocker R, Trentz O. Incidence and clinical pattern of the abdominal compartment syndrome after damage-control laparotomy in 311 patiens with severe abdominal and/or pelvic trauma. Crit Care Med 2000; 28: 1747-1753. [CrossRef]
13. Ivatury RR, Sugerman HJ. Abdominal compartment syndrome: A century later, isn't it time to pay attention? Crit Care Med 2000; 28: 2137-2138. [CrossRef]
14. Jacques T, Lee R. Improvement of renal function after relief of raised intra-abdominal pressure due to traumatic retroperitoneal haematoma. Anaesth Intensive Care 1988; 16: 478-482.
15. Ma YM, Qian C, Xie F, Zhou FH, Pan L, Song Q. Acut renal failure due to abdominal compartment syndrome. Zhonghua Yi Xue Za Zhi 2005; 85: 2218-2220.
16. Küçük HF, Çevik A, Kurt N, Bildik N, Gülmen M. The effect of abdominal compartment syndrome on blood urea and creatinine levels. Ulusal Travma Dergisi 2002; 8: 11-15.