The effects of experimentally induced intraabdominal hypertension on adrenal glands

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Aim: To investigate the effects of intraabdominal hypertension (IAH) on adrenal glands.

Materials and methods: Forty male Wistar albino rats were divided into 4 groups: the control group, sham control group, and 2 study groups. In the study groups, the animals were subjected to IAH of up to 20-25 mmHg for 3 h. At the end of the study, blood samples were collected for cortisol analysis and adrenal gland samples were extracted via laparotomy for histopathological examination.

Results: Cortisol levels were decreased compared to the control group (P < 0.05). There were no statistically significant differences demonstrated among the other groups (P > 0.05). Upon examination of the adrenal gland, no pathological alterations were found in the control and sham control groups, while hydropic degeneration and vascular congestion were demonstrated in the study groups.

Conclusion: The effects of experimental IAH on adrenal glands were statistically significant. The alterations of the adrenal glands could be the result of the direct effects of IAH, which is a severe trauma for the organ, or could be the effects of other organ systems that were influenced by the IAH.

Key words: Abdominal compartment syndrome, adrenal gland, intraabdominal hypertension

Deneysel olarak oluşturulan karın içi yüksek basıncın börek üstü bezler üzerine etkisi

Amaç: Artmış karın içi basınçın adrenal bezler üzerinde olan etkilerini araştırmak.

Yöntem ve gereç: Kirk erkek Wistar albino rat kontrol, sham kontrol ve iki çalışma grubuna ayrıldı. Çalışma gruplarında denklerde 3 saat süre ile 20 ve 25 mmHg’lık basınç oluşturdular. Çalışma sonunda kortizol düzeyleri için kan örnekleri, histopatolojik çalışma için laparotomi ile adrenal bezler alındı.

Bulgular: Kontrol grubuna göre diğer gruplarda kortizol düzeyinde azalma saptandı (P < 0.05). Diğer grupların kortizol düzeyleri arasında anlamlı bir fark saptanmadı (P > 0.05). Adrenal bezlerin histopatolojik incelemesinde kontrol ve sham kontrol gruplarında herhangi bir patolojik bulgu saptanmazken çalışma gruplarında hidropik dejenerasyon ve vasküler konjesyon saptandı.

Sonuç: Deneysel olarak oluşturulan intraabdominal basınç artışının adrenal glandlar üzerinde istatistiksel olarak anlamlı değişikliklere neden olduğu kanatının varlığı. Oluşan bu değişiklikler organizmaya büyük bir travma olan intraabdominal basınç artışının direkt bir sonucu olabileceğini gibi abdominal kompartman sendromunda etkilenen diğer organ sistemlerinin etkileri sonucunda da oluşmuş olabilir.

Anahtar sözcükler: Abdominal kompartman sendromu, adrenal bezler, intraabdominal hipertansiyon

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Introduction

Normal intraabdominal pressure (IAP) is equal to or slightly below atmospheric pressure in species with a pulmonary system. Elevation of IAP above the defined level is called intraabdominal hypertension (IAH) (1).

Abdominal compartment syndrome (ACS) can be defined as the physiopathological changes caused by high IAP (2,3). Clinically, it is characterized by a stiff abdominal wall or abdominal distention, respiratory distress, and reduced urine output despite sufficient fluid replacement (2-4). Recovery from ACS can occur quickly with the correct intervention (5,6). If ACS is not treated in time, it can result in fatal organ failure (7).

Measurement of IAP was defined in 1863 and the reflection of IAP on intravesical pressure was emphasized in 1876. Although it is known that high IAP causes cardiovascular, respiratory, and renal changes, and despite many experimental and clinical studies on this syndrome, some issues remain underexamined. Although previous studies (8,9) determined that an increase in IAP caused splanchnic ischemia, they did not examine how organ functions were affected by the ischemia. Therefore, this study aims to examine the effects of IAH on the cortisol secretion function and the structure of the adrenal glands.

Materials and methods

This study was conducted with the approval of the Ethical Committee of the Faculty of Medicine, University of Gaziantep (Ethical Committee Decision No: B.30.2.GZP.01.00.00.211/246).

The study was carried out in the Experimental Animal Research Laboratory of Gaziantep University, Faculty of Medicine, Department of Physiology. The study included 40 male Wistar albino rats weighing 250-300 g, which were fed a standard diet under equal conditions. All of the animals were kept in an environment with a light/dark photoperiod of 12:12. The animals were fasted for 12 h before the experiment. Because of diurnal variation, the experiments were performed between 1000 and 1200 hours.

The animals were divided into 4 groups, each containing 10 rats, and were then anesthetized using 30 mg/kg of intraperitoneal ketamine HCl and 10 mg/kg of intramuscular xylazine HCl.

Group 1 (control group): Under anesthesia, 3-cm³ blood samples were taken from the subjects and then a midline abdominal incision was performed, both adrenal glands were removed and kept in 10% formalin solution for histopathological examination.

Group 2 (sham control group): Under anesthesia, a 20-G needle was inserted intraperitoneally and left in place. After 3 h, blood and tissue samples were taken from the animals.

Group 3 (first experimental group): Under anesthesia, a 20-G needle was inserted intraperitoneally and a standard insufflator (Karl Storz, Germany) was connected. The abdomen was insufflated with CO₂. The insufflator was left at 20 mmHg of pressure for 3 h to create IAH. At the end of this procedure, the abdomen was desufflated and blood and tissue samples were taken.

Group 4 (second experimental group): The abdomen was insufflated as in Group 3. However, IAH was created by keeping the insufflator at 25 mmHg of pressure for 3 h. At the end of this procedure, the abdomen was desufflated and blood and tissue samples were taken.

The blood samples were transferred from the syringes to vacutainer tubes. The tubes were kept at room temperature for 30 min to allow coagulation before being centrifuged at 5000 rpm for 5 min. Blood serum samples were transferred to Eppendorf tubes (Eppendorf, Hamburg, Germany) and were kept at −80 °C until the biochemical analyses to determine serum cortisol levels. Serum cortisol levels were determined using the electrochemiluminescence (ECLIA) method.

The tissues were dehydrated in alcohol, treated with xylol, and stored in paraffin-embedded blocks. Sections measuring 3-5 μm were taken from the tissues and, after the deparaffinization process, stained with hematoxylin and eosin and examined histopathologically by light microscopy. Histopathological surrenal tissue damage was evaluated as absent, mild, and severe in terms of hydropic degeneration and vascular congestion.
For statistical analysis of serum cortisol levels, mean and standard deviation values were calculated initially and the values were assessed as means ± standard deviations. One-way analysis of variance (ANOVA) was used to determine the differences between the 4 groups. The least significant difference (LSD) method was used to determine the groups from which such differences derived. For all analyses, P < 0.05 was considered statistically significant.

Results
The cortisol levels were 2.79 ± 0.74 ng/mL, 2.12 ± 0.75 ng/mL, 2.19 ± 0.37 ng/mL, and 2.22 ± 0.41 ng/mL in Groups 1, 2, 3, and 4, respectively. The cortisol levels in Group 1 were significantly higher than in Groups 2, 3, and 4 (P < 0.05); no significant difference was found among the other groups (P > 0.05) (Figure 1).

Discussion
Despite comprehensive studies on the effect of IAH on certain organs and systems, there are still matters that have not been clarified. Although previous studies (8,9) determined that IAH caused splanchnic ischemia, they did not examine how organ functions were affected by the ischemia. Therefore, this study...
aimed to examine the effects of increased IAP on the functions of the adrenal glands.

Despite the many causes of IAH, a prolonged pressure increase above a certain level is necessary to affect the organs and systems. Activities such as coughing and lifting heavy items result in IAH, but they do not affect the organs or systems since the effect is short-lived. However, situations such as intraabdominal hemorrhage, peritonitis, and abdominal packing, which cause permanent IAH, generate the above effects. Pneumoperitoneum during laparoscopic surgery causes a controlled increase in IAP. In the present study, the pressure was monitored during surgery to obtain a high IAP. IAH could be generated by injecting fluid or by placing a balloon into the peritoneum; however, pneumoperitoneum is superior to these methods because it regulates distribution of the pressure and avoids potential damage to the organs, which can be caused by contact with these materials. Another advantage of this method is that IAP could be directly measured while simultaneously ensuring the IAH.

The point at which IAH begins is a matter of debate. Although normal IAP was reported as approximately 6.5 mmHg, it could be as low as 0.2 mmHg and as high as 16.2 mmHg. This value depends on the body mass index or previous surgical history of the patients (10). It is standard that the increase and duration of the pressure affect the changes on the organs and systems. In this study, we created 2 study groups with IAH of up to 20 and 25 mmHg for 3 h.

Reduction in the splanchnic blood flow and damage formation on the related organs is possible (8,9,11,12). It is possible to measure the hormone levels produced by the adrenal glands or to conduct a histopathological examination to determine how this gland is affected by prolonged high pressure. To consider the measurements of hormone levels as significant, the duration of IAH must be longer than the half-life of the hormones in the serum. The half-life of the cortisol produced by the adrenal gland is 80-100 min; it is cleared from the blood in 200 min (13). The 3-h increase in IAP in this study was sufficient to observe the effects on the hormone production of the adrenal gland. We could not examine the effects of IAH on the hormonal changes by means of extending the period, since the animals could not tolerate 25 mmHg IAP.

Many studies have examined the effect of IAH on the organ systems, including the endocrine glands. A study by Ortega et al. (14), examining the hormonal changes in laparoscopic cholecystectomy, reported that no significant change occurred in the adrenocorticotropic hormone, cortisol, epinephrine, thyroid-stimulating hormone, thyroxin, insulin, or glucagon levels compared to open cholecystectomy during the preoperative period; however, at 12 and 24 h postoperatively, serum glucose and insulin levels were high in the patients who underwent open cholecystectomy, while there were no differences in the other hormone levels. However, they did not increase the IAP over 15 mmHg and they determined the insufflation period as 70 min.

Byrne et al. (15) reported that there was no significant difference between the laparoscopic and conventional methods in terms of hemodynamic, hematological, and metabolic changes. Recently, Böyük et al. (16) investigated the effects of IAH on the endocrine functions of the pancreas and reported that glucagon levels were increased and insulin levels were decreased with high IAP.

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Our study showed that cortisol levels decreased significantly in the control and sham control groups after 3 h of IAH (P < 0.05). In cases where the IAH level increased, changes were observed in the hormone levels. No significant difference was found between the pressures of 20 mmHg and 25 mmHg (P > 0.05).

Cortisol release is regulated by the autonomous and central nerve system activity and is affected by other hormones. As the induced IAH was a trauma, not only its local effects such as splanchnic blood flow, caused by the high pressure, but also its systemic neuroendocrine effects were expected to affect the cortisol levels.

Many studies on the effects of IAH have been conducted using histopathological examinations, but they did not examine the adrenal glands. By histopathological examination of the pancreas, inflammatory cell infiltration in the peripancreatic fatty tissue, edema in the parenchyma, vascular congestion and slight ductal dilation, capillary congestion in the islets of Langerhans, and congestion in the vascular structure of the peripheral acinar related to IAP increase were observed (16). The present study did not determine any pathological changes in Group 1 and Group 2. In Group 3, hydropic degeneration was observed in the zona fasciculata and zona glomerulosa cells, and vascular congestion was seen in the parenchyma. In Group 4, more common and severe hydropic degeneration was observed in the zona fasciculata and zona glomerulosa cells. Vascular congestion was also observed in the parenchyma in Group 4. The effect of histopathological changes in the adrenal glands on the hormone release might have caused a significant decrease in the serum cortisol levels of IAH-induced rats. However, the decrease in the serum cortisol levels in the sham control group could not be explained, as there was no hydropic degeneration or vascular congestion observed in the sham group.

In conclusion, similar to other traumas, IAH affects the functions of the adrenal gland. However, greater changes were observed depending on the IAH. These changes could be influenced by the effects of IAH on other organs, but they could also affect the functions of organs and systems, thus creating a complex picture in the physiopathology of ACS. Therefore, further studies are required to clarify this interaction.

References

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