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The Effects of Increased Intra-Abdominal Pressure on Bacterial Translocation

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In this study, we investigated the effect of different values of intra-abdominal pressure on bacterial translocation. Twenty-four Wistar-Albino rats were divided into four groups. The animals belonging to the Control group were not subjected to any increased intra-abdominal pressure. In groups I, II and III, an intra-abdominal pressure of 14, 20, and 25 mmHg, respectively, was established by carbon dioxide pneumoperitoneum for a period of 60 minutes. Four hours after the pneumoperitoneum, all animals were sacrificed to evaluate the degree of bacterial translocation at this time. Liver, spleen and mesenteric lymph nodes were excised under sterile conditions. Bacterial growth was assessed using standard bacteriological techniques and compared statistically. The Kruskal-Wallis and Mann-Whitney U tests were used for the statistical analysis. Different amounts of bacterial growth were found in all of the animals subjected to increased intra-abdominal pressure, except for the controls. Bacterial translocation was detected at an intra-abdominal pressure of 14 mmHg but this finding was not statistically significant ($p>0.05$). There was a significant increase in bacterial growth in animals subjected to an intra- abdominal pressure of 20 mmHg or above ($p<0.001$). As a result, we found that bacterial translocation started when the intra-abdominal pressure reached a level of 14 mmHg. Patients should be closely monitored for septic complication risks following laparoscopic procedures in which the intra-abdominal pressure exceeds 20 mmHg.

Key Words: Intra-abdominal pressure, pneumoperitoneum, laparoscopy, bacterial translocation

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INTRODUCTION

Bacterial translocation (BT), has been defined as the movement of viable enteric bacteria to the mesenteric lymph nodes (MLN) and distant organ sites such as the liver and spleen. This definition was initially described by Berg, et al. and Deitch, et al.[1,2] It is well known that BT has been observed after various types of stress including total parenteral nutrition, shock, sepsis, thermal injury, severe trauma, obstruction of the intestinal or bile tract, malignant disease, immunosupression and inflammatory bowel disease.[3-11] Likewise, several studies[12-14] reported that the existence of a relationship between BT and intra-abdominal pressure (IAP).

Increased intra-abdominal pressure (IAP) is defined as a transiently or persistently elevated IAP value. This condition was firstly described as Abdominal Compartment Syndrome more than 125 years ago by Marey and Burt.[14] Significantly elevated IAP values are reportedly associated with various medical and surgical problems, including blunt and penetrating abdominal trauma, surgery for ruptured abdominal aortic aneurysms, peritoneal sepsis, intraperitoneal or retroperitoneal hematomas, neoplastic diseases, pancreatitis, ascites, obesity, liver transplantation and small bowel obstruction.[15] Increased IAP is also observed as a result of intraperitoneal gas insufflation during laparoscopic procedures. The advantages afforded by laparoscopic surgery have led to the current trend towards more extensive and time-consuming intra-abdominal procedures.

In light of this information concerning new approaches, such as laparoscopy, in our study, we aimed to investigate the effect that varying the IAP values would have on BT. Despite the increasing use of laparoscopic methods, in the carbon dioxide (CO_2) pneumoperitoneum (P) model, the effect of varying IAP values on BT has not yet been investigated. Increased IAP has important deleterious effects on many organs and tissues. Among the adverse effects of increased IAP, decreased splanchnic blood flow, as reflected by the reduction of gut intramucosal pH following increased IAP, is particularly worrisome.[16]

Therefore, in this randomized controlled experimental study, the effect of varying the IAP value on BT in rats was evaluated, in order to provide answers to this clinically relevant question.

MATERIALS AND METHODS

Animals

In this experimental study, 24 Wistar-Albino rats with a weight of 200 to 250g were used. All animals were cared for in accordance with the "Guide for the Care and Use of Laboratory Animals", published by the National Institute of Health, as well as following institutional guidelines. All effort was made to avoid unnecessary suffering and stress throughout the study. All animals were fed a standard chow diet and allowed access to tap water ad libitum. The animals were randomized into four groups with 6 animals in each group. All animals were housed under standard laboratory conditions (temperature 21 ± 2℃; relative humidity 55 ± 10%; light and dark cycles of 12 hours duration). None of the rats were allowed feeding for 12 hours before the operation; but they were allowed water. They were also subjected to fasting after the pneumoperitoneum.

The model for studying the effects of pneumoperitoneum (P)

All animals were anaesthetized with intramuscular 100 mg/kg ketamine HCl (Ketalar®) EIP, Istanbul, Turkey) following induction with ether inhalation. The operating field on the abdomen was shaved just before the operation, cleaned with 10% povidone-iodine, and covered by a sterile drape. Using sterile instruments, a mini laparotomy was performed to insert a sterile catheter (Mediflon Catheter, 20 × 1.1 × 33 mm, Eastern Medikit Ltd, Udyog Vihar, Gurgaon Haryana, India) into the abdominal cavity. Purse string sutures (4/0 monofilament polypropilene; Serapen, Bayern, Germany) were applied around the catheter to prevent gas leakage.

The rats in the Control Group (Group C; n=6) were not subjected to increased IAP; they were only exposed to insertion of a catheter. CO_2 was insufflated into the abdominal cavity until the IAP reached a level of 14 mmHg (Group 1; n=6), 20 mmHg (Group 2; n=6) and 25 mmHg (Group 3; n=6) respectively. IAP was recorded continuously using a monitor system (Surgiflator 9100; NISCO, Tokyo, Japan). CO_2 insufflation was terminated after 60 minutes of increased IAP. In all groups, the catheter site was closed with running sutures (4/0 silk, Dogsan, Trabzon, Turkey) with 4-0 silk.

Microbiologic assessment of bacterial translocation (BT)

All animals were sacrificed by an overdose of ether anesthesia 4 hours after the P. Afterwards, tissue samples were taken from the liver, spleen and MLN and these samples were weighed under sterile conditions. Then, the collected samples were carried to the microbiology laboratory in a Carry-Blair transport medium. After homogenization, all tissue specimens were cultured in brain-heart infusion broth (Oxoid, UK) in a quantitative manner with 1 : 10 fold serial dilutions. Broth cultures of homogenates which showed turbidity were subcultured onto 5% blood agar and Eosin Metilen Blue agar (Oxoid, UK). They were then evaluated following incubation under aerobic conditions at 37℃ for 24 - 72 hours. The growth of bacteria was recorded as colony forming units (CFU) per gram tissue. For bacterial identification, conventional microbiological methods were used and, in case of necessity, confirmation was obtained by means of a Crystal ID system (BBL, MD, USA) and grouping latex agglutination (Oxoid, UK).[17]

Statistical Analyses

Results were evaluated by investigators blinded to the groups of the animals, who reported their results using the code number of each animal. The results were decoded by the principal investigator and analyzed statistically at the completion of the study. Values of growth (CFU) are presented in the form of mean(standard error of mean (SEM). The mean CFU and the average number of bacterial growth for each group were compared using the Kruskal-Wallis and Mann-Whitney U test. P values of less than 0.05 were considered to be statistically significant.

RESULTS

All animals survived for the duration of the experiment. For the animals in Control Group, no BT was detected. The incidence of BT in all of the groups increased with rising IAP. The total amounts of BT in the various groups are presented in Fig. 1.

The numbers of translocated bacteria, as expressed in colony forming units per gram (CFU/g), are given in Fig. 2.

Fig. 3 represents the organ involvement of BT. The BT value showed a linear correlation with the IAP level. It was found that BT started in rats with Group 1 which were subjected to 14 mmHg of IAP, but that this difference was not statistically significant ($p > 0.05$). In rats subjected to 20 and 25 mmHg of IAP', a statistically significant difference in BT value was observed compared to the control group. This difference became more prominent when the IAP was 20 mmHg or above ($p < 0.001$) (Fig 1).

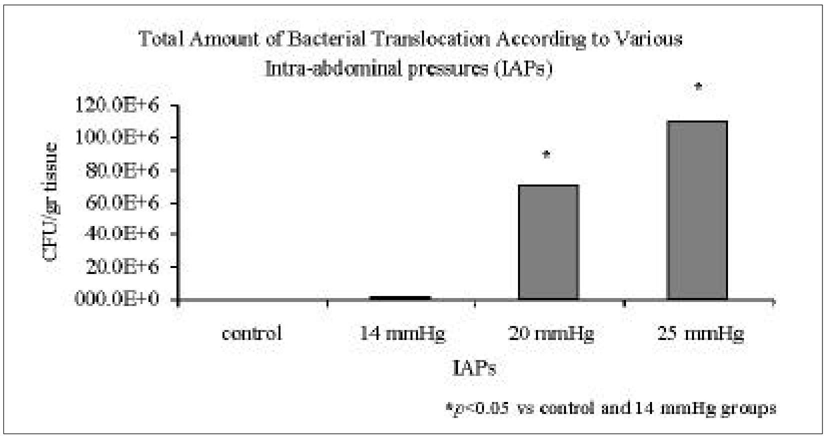

Fig. 1. Total bacterial translocations for each group. BT started when the IAP attained 14 mmHg. BT was more prominent at the 20 and 25 mmHg IAP levels (BT: Bacterial Translocation, IAP: Intra- abdominal pressure, CFU: Colony Forming Unit).

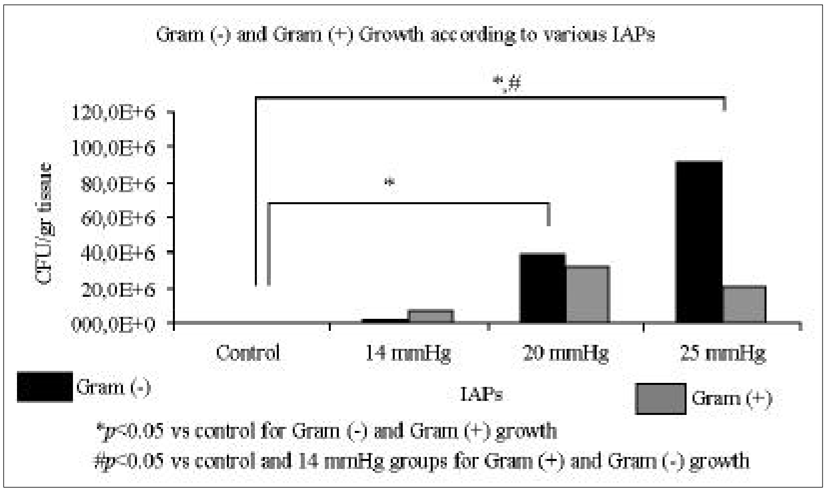

Fig. 2. BT according to gram species growth. There were a statistically significant difference between the Gram (-), Gram (+) and total number of bacteria in the 20 mmHg and 25 mmHg groups vs the control group. The values were also higher in the 25 mmHg group than in the 14 mmHg group (CFU: Colony Forming Unit).

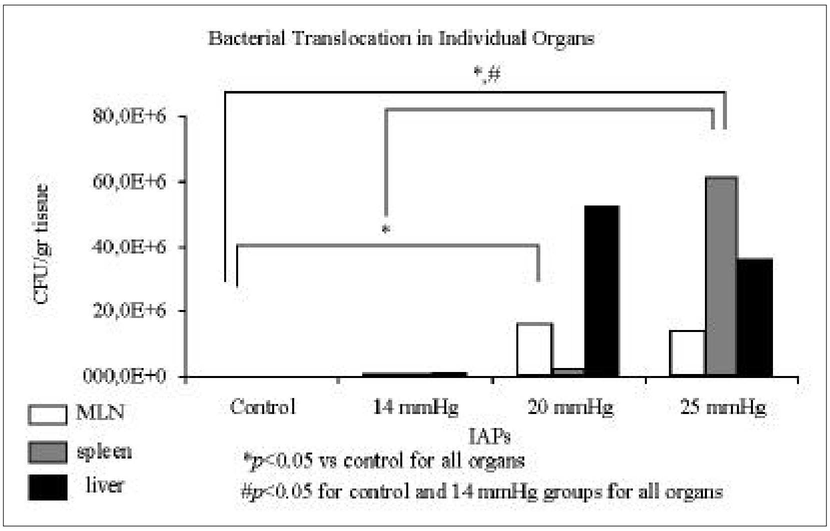

Fig. 3. BT according to individual organs. There was a statistically significant difference in the involvement of all organs in the 20 mmHg and 25 mmHg groups vs the control group. The values were also higher in the 25 mmHg group than in the 14 mmHg group (MLN: Mesenteric lymph node, CFU: Colony Forming Unit).

The growth of Gram (-) bacteria was more frequently observed than that of Gram (+) bacteria, especially when the IAP was increased to a level of 25 mmHg (Fig. 2). However, these differences were not statistically significant. Escherichia coli was the most frequently isolated microorganism from all tissues.

DISCUSSION

It has been well documented that laparoscopic surgery, which is a method that can be used for the treatment of almost all benign or malignant abdominal surgical disorders, is superior to its open counterpart in terms of there being less pain, a shorter hospital stay, a shorter convalescence period, and lower morbidity. Laparoscopy necessitates the creation of a P and the maintenance of a constant IAP of between 10 and 12 mmHg in order to be able to perform the operative procedure. CO_2 insufflation is the most widely used method to create P in laparoscopic surgery, however this technique may lead to the development of operative complications resulting from needle or trocar insertion, hypercapnia and increased IAP.[18,19] The detrimental effects of high IAP on cardiac, respiratory, intestinal and renal functions have been described in many clinical and experimental studies.[20-23] In our previous study, we also showed that P performed during laparoscopy decreased the bursting pressure of intestinal anastomosis and delayed the process of healing.[23]

During laparoscopic surgery, there is always a possibility that the IAP could increase accidentally, transiently or permanently. This increased IAP can cause severe splanchnic ischemia,[20,22,24] because an IAP of 10 - 15 mmHg is even higher than the normal pressure in the portal system, which is 7 - 10 mmHg. Diebel, et al. reported that portal venous blood flow fell by 27% at an IAP of 10 mmHg and by 45% at an IAP of 30 mmHg.[25] Likewise, Rasmussen et al. also found that PVBF decreased significantly when the IAP was 15 mmHg or above.[22]

The insufflation and desufflation of the abdominal cavity with CO_2 represents a typical ischemia-reperfusion model, because of the direct mechanical compression of the abdominal vasculature, the release of vasoactive hormones and the effects of hypercapnia.[26,27] Splanchnic ischemia may cause the conversion of oxygen into free radicals in tissue undergoing reperfusion.[28,29] The amount of oxygen free radicals generated during the process of ischemia-reperfusion depends on the degree and duration of ischemia. Ischemia and reperfusion which result from increased IAP can cause severe BT and septic complications.

The failure of intestinal mucosa to act as a barrier against BT has been accepted as a potential cause of sepsis and subsequent organ failure.[12,13,30,31] BT may occur due to various pathophysiological conditions. The alteration of the host defense, the loss of the intestinal mucosal barrier function and the overgrowth of intestinal flora are the most common causes of BT.[32-34]

Splanchnic hypoperfusion is one of the major causes of BT.[35] Although Eleftheriadis, et al. demonstrated that 15 mmHg of IAP resulted in the production of free oxygen radicals which disrupt the mucosal integrity and BT Tuğ, et al. reported that an IAP of 15 mmHg caused only intraluminal bacterial colonization and not BT.[20,36] The previous studies performed on this subject usually dealt with the peritonitis model. Evasovich et al. investigated the effects of CO_2 insufflation with peritonitis at 15 mm Hg of IAP and reported an increase in bacteremia with CO_2 insufflation.[37] In contrast to these findings, Jacobi and his colleagues found no difference in bacteremia or intraperitoneal abscess formation in rats receiving a fecal inoculum by means of CO_2 P as compared with laparotomy.[38] Likewise, Ozmen and associates reported no difference in bacteremia in the CO_2 and laparotomy groups, but they also observed a significant increase in BT to the lung and spleen in the CO_2 group.[39] The effects of different gases on BT have also been investigated. It has been reported that helium significantly decreased both bacteremia and abscess formation in rats with peritonitis, and constituted a safe alternative to CO_2 insufflation.[40] Likewise Matsumoto, et al. also demonstrated that the presence of gas in the intraperitoneal space modified both the host cytokine response and the BT, but that changes in the IAP had no effect.[41]

Although extensive research has been carried out on the effects of varying the IAP', surprisingly the effect on BT caused by varying the level of CO_2 P during laparoscopy has not yet been studied. Therefore, we designed the present study to determine the effect of varying the level of P, on BT to the MLN, liver and spleen; which to the best of our knowledge has not been previously described.

In the present study, the degree of BT was positively correlated with the IAP. The bacterial counts per gram tissue of Group 1, which was exposed to an IAP of 14 mmHg, did not display a statistically significant difference from the Control Group ($p > 0.05$). In Groups 2 and 3, however, which were exposed to an IAP of 20 and 25 mmHg, respectively, severe BT was observed ($p < 0.001$) (Fig. 1). This effect may be explained by submucosal macrophages phagocytose enteric bacteria adhering to the mucus layer or invading the impaired intestinal barrier and then being carried through the intestinal wall, before finally being liberated from the phagosome.[42] Another interesting result of this study is that a rising correlation between the gram(-) BT and IAP levels of 20 mmHg and above was observed, which may reflect the degree of damage caused to the intestinal mucosa.

In conclusion, we found that BT started when the IAP reached 14 mmHg. More prominent BT was observed when the IAP attained the 20 or 25 mmHg levels. Close monitoring of patients should be performed with respect to the associated potential septic complication risks, especially in the case of laparoscopic surgical procedures involving an IAP of 20 mmHg or above.

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