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Effects of CO_2 pneumoperitoneum on the basilar artery

An experimental study in rabbits

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Abstract
Background: Laparoscopic surgery provides many benefits to the patients. The purpose of this study was to evaluate cerebral blood flow changes and the possibility of ischemia–reperfusion injury occurring during carbon dioxide (CO_2) pneumoperitoneum.
Methods: Forty-eight New Zealand white rabbits were divided into four experimental and two control groups. Rabbits were subjected to CO_2 pneumoperitoneum with an intraabdominal pressure of 8 and 15 mmHg for 60 or 180 min as designed for experimental groups. We then assessed the changes in physiological and transcranial Doppler ultrasonographic parameters, as well as brain malondialdehyde levels.
Results: Transcranial Doppler sonography of the basilar artery revealed elevated mean velocity and decreased resistance index and pulsatility index values with the longer-duration and higher-pressure CO_2 pneumoperitoneum. However, there were no statistically significant difference in malondialdehyde values.
Conclusion: Elevated intraabdominal pressure by CO_2-pneumoperitoneum, which does not lead to ischemia–reperfusion injury of the brain tissue, results in increased cerebral blood flow and reduced cerebrovascular resistance as an autoregulatory cerebral answer for CO_2.

Key words: Laparoscopic surgery — Pneumoperitoneum — Cerebral blood flow

The laparoscopic approach has been widely applied to gynecologic and general surgery over the last 2 decades. Laparoscopic surgery (LS) provides many benefits to the patients, including a shorter hospital stay, decreased pain, an earlier return to normal activity, and better cosmesis [18]. Although LS involves minimal tissue damage, it has potentially serious side effects [18]. Significant data have been reported regarding the influences of increased intraabdominal pressure (IAP) due to peritoneal insufflation with carbon dioxide (CO_2) during LS on cardiovascular–pulmonary systems and blood flow [12]. Carbon dioxide is known to be a powerful stimulant that causes relaxation of the smooth muscles of the arterioles and decreased cerebrovascular resistance [9]. However, little is known about the effects of CO_2 pneumoperitoneum (CO_2 PNM) on cerebral blood flow and the hemodynamic side effects related to it [2, 5, 10, 14].

Transcranial Doppler (TCD) ultrasonography has the advantage of allowing repeatable studies of the dynamic changes in cerebral blood supply. It has been shown that there is a strong correlation between TCD ultrasonographic parameters and cerebrovascular hemodynamics [4]. The use of pulsatility (PI) and resistance indexes (RI) and mean velocity of arterial blood flow (Vm) measurements provide an opportunity to assess the changes related with blood flow [4]. With real-time TCD ultrasonographic imaging of the cerebral arteries of rabbits under physiological conditions and during CO_2 PNM, a noninvasive study of the cerebral blood supply can be performed.

The purpose of this experimental study was to evaluate the cerebral blood flow changes occurring during CO_2 PNM at different IAP levels for various duration times and to look for a possible ischemia–reperfusion injury by determining brain malondialdehyde (MDA) levels.

Materials and methods

In this study, 48 New Zealand white rabbits of both sexes (weighing 4.1 ± 0.3 kg) were randomly divided into six groups consisting of four experimental and two control groups. Under general anesthesia, CO_2 PNM was performed in four experimental groups. Two control groups received anesthesia only for the same duration as the study groups.

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The study was approved by the animal care committee of our institution and met standards set by International Research Animal Care Organization.

Anesthesia and monitoring of animals

Before the procedure, the rabbits were fasted overnight but allowed access to water. Anesthesia was induced in a Plexiglass box with 2.1% isoflurane in 100% oxygen. The vein of the right ear was cannulated and an infusion of 0.9% NaCl solution was started at a rate of 4 ml/kg/h. The artery of the left ear was also cannulated for monitoring of the arterial blood pressure and arterial blood gas sampling. The invasive arterial blood pressure was followed throughout the experiments on a monitor (Hellige SMU 612 PBG, Hellige GMBH, Germany; Hellige, USA). When the neck was exposed, a tracheotomy was performed and a cannula (Portex tracheal tube 3 mm ID; Portex SIMS, Portex Limited, UK) was inserted through it. After a bolus administration of 0.15 mg/kg pancuronium bromide, the rabbit was ventilated with 1% isoflurane oxygen-supplemented room air using a volume-cycled ventilator (Evita 2; Dragerwerg AG, Germany), which was adjusted for maintaining normocapnia at a respiration rate of 20/min, tidal volume 12–15 ml/kg, $PaCO_2$; Arterial partial pressure of carbon dioxide 34–40 mmHg. Isoflurane anesthesia was maintained at a dose <1.5 minimal alveolar concentration (MAC). The end-tidal isoflurane concentrations were adjusted according to the depth of anesthesia. The body temperature of the animals was monitored with a rectal temperature probe during the experiments; it was regulated with a servomechanism at 37.0° ± 0.1 C with a heat lamp.

Surgical procedures

The animals were fixed to a surgical table in a supine position. After steady state had been reached, a right parietal burr hole ~5 mm in diameter was created on the bregma, and the surface of the dura mater was covered with gel for TCD ultrasonographic examination. A Veress needle (US Surgical Corporation, Norwalk, CT, USA) was then placed into the peritoneal cavity, which was later insufflated with CO_2 using an Op-Pneu insufflator (Wisap, Sauerlach, Germany) at a rate of 2–3 L/min until the IAP reached 8 or 15 mmHg. At the end of the experiments, all of the animals were killed 30 min after abdominal deflation to measure the MDA level of the brain tissue.

Experimental protocol

The animals were divided into six groups according to level of IAP and duration of procedure. Each group consisted of eight animal. In group K1 (control group I), the animals were only anesthetized for 210 min; in group K2 (control group II), the animals were only anesthetized for 90 min; in group A, CO_2 PNM was maintained at an IAP of 8 mmHg for 180 min, in group B, CO_2 PNM was maintained at an IAP of 15 mmHg for 180 min; in group C, CO_2 PNM was maintained at an IAP of 8 mmHg for 60 min; in group D; CO_2 PNM was maintained at an IAP of 15 mmHg for 60 min. Groups A and B and C and D were compared with the control groups K1 and K2, respectively.

Monitoring of physiological parameters

The cardiac pulse rate, mean arterial pressure (MAP), and rectal temperature were recorded from the monitor. Partial carbon dioxide pressure ($PaCO_2$), partial oxygen pressure (PO_2), pH, and base excess were analyzed in the arterial blood samples. Hematocrit and glucose levels were measured in the venous blood samples. All of these parameters were measured before the onset of CO_2 PNM (t_0) and at the 1st h in all groups (t_1); they were also measured at the 3rd h in groups A and B (t_3). Measurements were repeated 30 min after deflation of the abdominal cavity in all groups (t_d).

TCD ultrasonographic examination

A 6-MHz convex probe, which was covered by a preservative, was positioned over the exposed dura mater to investigate the basilar artery (BA) with B-mode color Doppler ultrasonography (Sonolayer SSH-140A; Toshiba, Tokyo, Japan). When the optimal angular imaging data and color coding were obtained at a certain position, the spectral analysis recording of the duplex Doppler ultrasonographic data was measured. During the duplex Doppler ultrasonographic examinations, the narrowest sampling slices were adjusted to the vessel lumen of BA. Peak systolic (Vs) and diastolic (Vd), and mean flow velocities (Vm) of BA were measured with the spectral analysis mode. The pulsatility index (PI) and resistance index (RI) were also calculated automatically by the device according to the equations Vs–Vd/Vm and Vs–Vd/Vs, respectively. TCD measurements were obtained before the onset of CO_2 PNM (t_0), at the 1st h (t_1) in all groups and at the 3rd h (t_3) in groups A and B. All of the measurements were repeated 30 min after deflation of the abdominal cavity (t_d) in all groups.

Determination of MDA in brain tissue

When the sampling and recording for physiological parameters were completed 30 min after deflation of the abdomen, the animals were killed and a total craniotomy was performed to remove the brain intactly in each. The brains were preserved for the determination of MDA, has been described elsewhere [6].

Statistical analysis

Comparative analysis of the groups was performed via the repeated analysis of variance (ANOVA) and ANOVA (Sigma Stat Statistical Analysis System, Version 1.02, 1992). All data were evaluated as means ± standard error (SE) of the means, and p values < 0.05 were accepted as statistically significant.

Results

There were no statistically significant differences between the study and control groups in pulse rate, SaO_2: Oxygen Saturation, PaO_2: Arterial partial pressure of oxygen, hematocrit, serum glucose, or body temperature values. Mean arterial pressure values were elevated in all study groups, but the changes were not statistically significant except for groups B and D ($p < 0.05$). The elevated MAP values returned to normal limits within 30 min after deflation in all groups (Table 1). $PaCO_2$ values were elevated after creation of the CO_2 PNM and returned to normal levels in groups A, C, and D (Table 2). However, in group B, baseline values of $PaCO_2$ were not achieved even 30 min after deflation of the abdominal cavity (Fig. 1).

Transcranial Doppler sonography findings of BA revealed that longer duration and higher pressure of the CO_2 PNM elevated Vm significantly (Table 3, Fig. 1). Spectral analysis of BA showed that RI and PI values were decreased as a result of prolonged duration and increased intraabdominal pressure during CO_2 PNM (Table 3 and Fig. 2). The MDA measurements, which exhibited no statistically significant differences in any of the groups ranging between 126 and 130 nmol/mg/protein (Table 4).

Discussion

Laparoscopic surgery has become one of the most common routine operative procedures now practiced in general surgery [18]. The effects of CO_2 PNM on the respiratory and cardiovascular systems are well known [18]. The mainte-

Table 1. Changes in vital measurements

Variable	Group K1	Group A	Group B	Group K2	Group C	Group D
MAP (mmHg)						
t_0	84.1 ± 1.8	84.3 ± 1.7	85.1 ± 1.5	84.1 ± 1.2	84.7 ± 1.5	85.6 ± 1.6
t_1	83.6 ± 1.3	84.4 ± 1.5	91.8 ± 2.7[a,b]	83.7 ± 1.4	85.5 ± 1.7	89.5 ± 1.3[a,b]
t_3	83.5 ± 1.4	86.6 ± 1.6	95.5 ± 3.8[a,b]			
t_d	82.5 ± 1.5	85.3 ± 1.2	87.2 ± 2.4	83.1 ± 1.7	85.1 ± 1.2	86.4 ± 1.3
HR (per min)						
t_0	258.26 ± 22.08	260.07 ± 12.03	263.26 ± 17.01	260.32 ± 27.12	262.18 ± 12.06	259.17 ± 11.46
t_1	259.17 ± 11.46	260.32 ± 27.12	261.18 ± 24.08	258.26 ± 22.08	261.18 ± 24.08	264.68 ± 28.01
t_3	258.22 ± 21.09	261.56 ± 31.01	262.18 ± 12.06			
t_d	260.32 ± 27.12	259.17 ± 11.46	261.56 ± 31.01	260.32 ± 27.12	261.56 ± 31.01	263.26 ± 17.01
Temperature (°C)						
t_0	37.4 ± 0.5	37.5 ± 0.6	37.6 ± 0.5	37.3 ± 0.4	37.5 ± 0.3	37.6 ± 0.4
t_1	37.4 ± 0.3	37.3 ± 0.3	37.4 ± 0.4	37.4 ± 0.5	37.5 ± 0.3	37.5 ± 0.5
t_3	37.2 ± 0.6	37.1 ± 0.4	37.1 ± 0.3			
t_d	37.0 ± 0.5	37.3 ± 0.4	37.2 ± 0.4	37.4 ± 0.4	37.4 ± 0.4	37.3 ± 0.4

MAP, mean arterial pressure; Hr, heart rate; t_0, initial; t_1, 1st hr; t_3, 3rd hr; t_d, 30 min after desufflation
Values given as mean ± SE; $n = 8$ in each group
[a] Data that differ in a group or when compared with control group of certain IAP
[b] Data that differ when compared with control and study groups of certain IAP
Among the vital measurements, only MAP exhibited significant changes in the study groups. MAP increased in all study groups, but significant were registered only in group B and D ($p < 0.05$). Elevated MAP returned to baseline values within 30 min after deflation in all groups

Table 2. Results of the analysis of blood samples

Variable	Group K1	Group A	Group B	Group K2	Group C	Group D
pH						
t_0	7.38 ± 0.01	7.39 ± 0.03	7.39 ± 0.01	7.39 ± 0.01	7.38 ± 0.02	7.39 ± 0.01
t_1	7.38 ± 0.02	7.36 ± 0.02	7.33 ± 0.02	7.38 ± 0.01	7.35 ± 0.01	7.34 ± 0.02
t_3	7.39 ± 0.02	7.33 ± 0.02	7.29 ± 0.01			
t_d	7.39 ± 0.01	7.37 ± 0.02	7.34 ± 0.02	7.38 ± 0.02	7.37 ± 0.01	7.37 ± 0.01
PaO_2 (mmHg)						
t_0	390 ± 6	390 ± 9	390 ± 6	390 ± 8	389 ± 7	390 ± 6
t_1	388 ± 6	389 ± 6	392 ± 11	388 ± 7	388 ± 4	388 ± 7
t_3	383 ± 4	388 ± 4	391 ± 7			
t_d	388 ± 8	391 ± 7	396 ± 7	390 ± 6	391 ± 7	389 ± 5
$PaCO_2$ (mmHg)						
t_0	34.90 ± 0.85	34.50 ± 0.60	34.81 ± 0.85	34.8 ± 0.75	34.3 ± 0.70	34.7 ± 0.65
t_1	35.01 ± 0.70	37.70 ± 0.97[a]	42.66 ± 0.70[a,b]	35.0 ± 0.80	37.1 ± 0.81[a]	43.1 ± 0.36[a,b]
t_3	34.30 ± 0.52	40.90 ± 0.65[a]	48.51 ± 0.68[a,b]			
t_d	33.71 ± 0.84	35.28 ± 0.53	38.1 ± 0.51[a,b,c]	35.7 ± 0.60	35.5 ± 0.47	36.3 ± 0.55
Htc (%)						
t_0	38.2 ± 0.86	37.4 ± 0.50	38.21 ± 0.86	38.1 ± 0.6	38.2 ± 0.8	37.7 ± 0.5
t_1	38.0 ± 0.72	37.28 ± 0.48	38.01 ± 0.72	38.2 ± 0.7	37.9 ± 0.7	37.8 ± 0.6
t_3	37.8 ± 0.65	37.1 ± 0.51	37.85 ± 0.65			
t_d	37.4 ± 0.63	36.8 ± 0.45	37.43 ± 0.63	37.9 ± 0.7	37.4 ± 0.6	37.6 ± 0.6
Glucose (mg/dl)						
t_0	88.6 ± 2.4	88.3 ± 2.3	89.6 ± 2.8	89.01 ± 3.0	88.8 ± 3.1	89.8 ± 2.5
t_1	86.6 ± 1.5	88.1 ± 1.5	90.8 ± 1.2	89.3 ± 3.1	89.2 ± 2.0	89.5 ± 2.6
t_3	88.5 ± 1.7	89.3 ± 1.3	90.6 ± 1.8			
t_d	89.2 ± 2.5	87.0 ± 1.6	89.2 ± 2.0	90.1 ± 2.0	89.1 ± 2.3	90.7 ± 2.2

$PaCO_2$, partial carbon dioxide pressure; PaO_2, partial oxygen pressure; Hct, hematocrit; t_0, initial; t_1, 1st hr; t_3, 3rd hr; t_d, 30 mins after desufflation
Values given as mean ± SE; $n = 8$ in each group
[a] Data that differ in a group or when compared with control group of certain IAP
[b] Data that differ when compared with contol and study groups of certain IAP
[c] Data that differ when compared with all groups
The levels of Htc and glucose did not differ between groups after CO_2 pneumoperitoneum. But a significant increase in $PaCO_2$ was observed in all study groups during CO_2 pneumoperitoneum ($p < 0.05$). Thus, elevated $PaCO_2$ did not return to baseline values in group B after deflation

nance of increased IAP for prolonged periods may lead to adverse hemodynamic effects. The negative effects of CO_2 PNM on the cardiovascular system depend on the degree of IAP, the volume of CO_2 that is absorbed, the patient's intravascular volume, the ventilatory technique, the type of anesthesia, the position of the patient, and general surgical conditions [11, 16]. It has been clearly demonstrated in a variety of experimental and clinical studies that CO_2 PNM leads to significant changes in cardiac, pulmonary, splanchnic, and renal circulation [11, 12].

However, there are still no satisfactory data about the effects of the CO_2 PNM on cerebrovascular dynamics. Only a few reports have examined the cerebral complications of the CO_2 PNM [5, 10]. Muller et al. reported one patient who

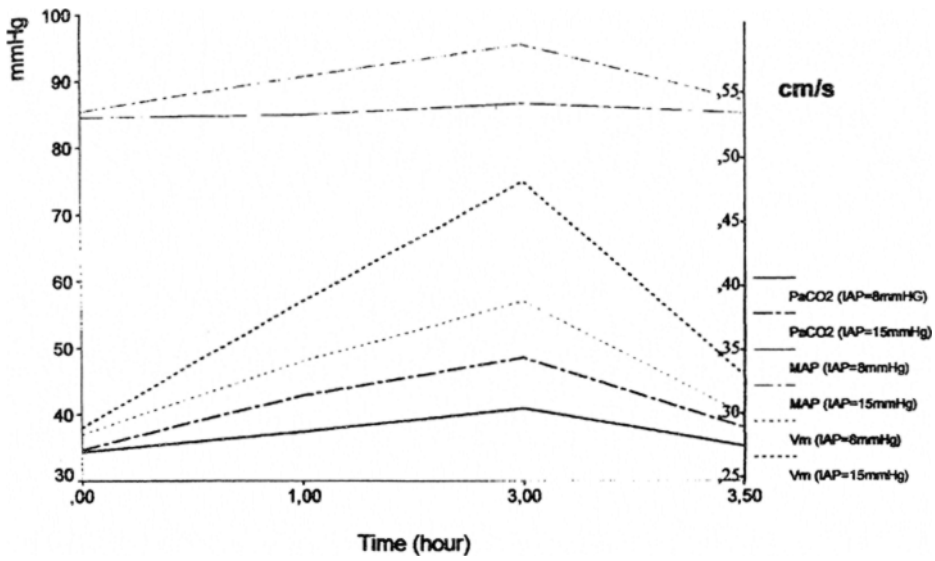

Fig. 1. Time scale of changes in mean flow velocity (Vm), mean arterial pressure (MAP), and partial carbon dioxide pressure ($PaCO_2$) for different intraabdominal pressures (IAP). Elevation of $PaCO_2$ was accompanied by increases in MAP and Vm of basilar artery as long as the CO_2 pneumoperitoneum lasted and as much as IAP increased. Reversal of this situation was observed after deflation of abdomen.

Table 3. Transcranial Doppler (TCD) ultrasonographic evaluation of basilar artery (BA)

Variables	Group K1	Group A	Group B	Group K2	Group C	Group D
Vm (cm/sec)						
t_0	0.28 ± 0.01	0.28 ± 0.01	0.27 ± 0.01	0.29 ± 0.01	0.28 ± 0.02	0.29 ± 0.01
t_1	0.30 ± 0.02	0.33 ± 0.01[a]	0.39 ± 0.01[a,b]	0.30 ± 0.01	0.34 ± 0.02[a]	0.38 ± 0.01[a,b]
t_3	0.30 ± 0.02	0.38 ± 0.01[a]	0.48 ± 0.01[a,b]			
t_d	0.30 ± 0.02	0.30 ± 0.02	0.33 ± 0.01	0.30 ± 0.01	0.30 ± 0.02	0.31 ± 0.01
PI						
t_0	0.95 ± 0.03	0.94 ± 0.03	0.97 ± 0.03	0.95 ± 0.01	0.93 ± 0.02	0.94 ± 0.01
t_1	0.93 ± 0.03	0.79 ± 0.03[a]	0.76 ± 0.01[a,b]	0.92 ± 0.01	0.80 ± 0.02[a]	0.74 ± 0.01[a,b]
t_3	0.94 ± 0.03	0.71 ± 0.04[a]	0.67 ± 0.02[a,b]			
t_d	0.92 ± 0.02	0.87 ± 0.02	0.86 ± 0.01	0.91 ± 0.01	0.91 ± 0.02	0.92 ± 0.01
RI						
t_0	0.53 ± 0.01	0.54 ± 0.01	0.58 ± 0.02	0.54 ± 0.01	0.53 ± 0.01	0.54 ± 0.01
t_1	0.53 ± 0.01	0.50 ± 0.01[a]	0.47 ± 0.01[a,b]	0.53 ± 0.01	0.50 ± 0.02[a]	0.47 ± 0.01[a,b]
t_3	0.52 ± 0.01	0.47 ± 0.02[a]	0.44 ± 0.01[a,b]			
t_d	0.52 ± 0.01	0.53 ± 0.01	0.54 ± 0.01	0.53 ± 0.01	0.53 ± 0.02	0.53 ± 0.01

Vm, mean flow velocity; PI, pulsatility index; RI, resistance index
Values given as mean ± SE; $n = 8$ in each group
[a] Data that differ in a group or when compared with control group of certain IAP
[b] Data that differ when compared with contol and study groups of certain IAP
CO_2 pneumoperitoneum led to a significant increase in Vm and decreases in PI and RI values of the basilar artery (BA) ($p < 0.05$)

developed a cerebral circulatory complication following a laparoscopic procedure [14], and Bonatsos et al. described a case of cerebral bleeding that occurred during one of their 1788 laparoscopic cholecystectomy procedures [2]. To our knowledge, the relationship of cerebrovascular hemodynamic changes with possible cerebral ischemia–reperfusion injury due to CO_2 PNM at different IAP levels for various duration times has not been studied yet.

At present, there are several methods that can provide quantitative values for cerebral flood flow (CBF) or blood flow velocity [1, 15]. The use of TCD allows for the repeated and continuous assessment of blood flow velocity and indirect Doppler parameters such as PI and RI, which permits the evaluation of various physiological and pathophysiological aspects of cerebral hemodynamics. It does not measure flow rate (ml per min) or tissue perfusion, but it evaluates the direction and velocity of blood flow, which has been found to be well correlated with CBF [20].

A rabbit model was chosen because of the anatomic similarity of its cerebral vessels with the human vasculature. Many physiological characteristics of rabbit resemble those of humans, including arterial blood pressure, cerebrovascular responses to changes in $PaCO_2$, and blood pressure [4].

Cerebral blood flow may be affected by changes in systemic blood pressure, serum glucose and hematocrit level, body temperature, $PaCO_2$, PaO_2, blood viscosity, intracranial pressure, and the anesthetic agents used during surgery [3, 19]. All rabbits were anesthetized with isoflurane at a level of 1.2 MAC, which has less impact on cerebral autoregulation than other volatile drugs. As has been shown previously, isoflurane does not alter cerebral autoregulation unless it is sustained under 1.5 MAC [13].

It has been reported that cerebral autoregulation remains intact if MAP and $PaCO_2$ are maintained between 50 and 150 mmHg, and 20 and 60 mmHg, respectively [7, 10]. In the present study, all parameters except for MAP and

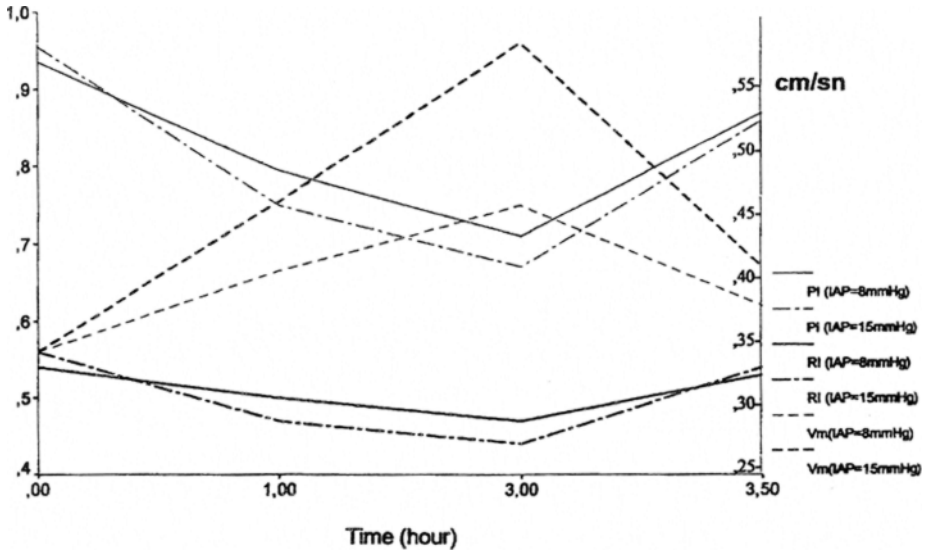

Fig. 2. Time scale of transcranial Doppler (TCD) ultrasonographic changes for different intraabdominal pressures (IAP). Vm = mean flow velocity; PI = pulsatility index; RI = resistance index. Simultaneous TCD ultrasonographic changes were observed while the increase in partial carbon dioxide pressure($PaCO_2$) and mean arterial pressure (MAP) were determined. While PI and RI values were declining, Vm was increasing significantly as long as the CO_2-pneumoperitoneum lasted and as much as IAP increased. The opposite of this correlation was observed as the abdomen was desufflated.

Table 4. MDA levels after CO_2 pneumoperitoneum

Variable	Group K1	Group A	Group B	Group K2	Group C	Group D
MDA (nmol/mg/protein)	126.5 ± 7.7	127.5 ± 5.6	129.1 ± 7.4	129.5 ± 6.7	127.3 ± 7.1	128.1 ± 6.1

MDA, malonyldialdehide
The measurements of brain MDA levels failed to demonstrate an ischemia–reperfusion injury, since no significant increase was determined in study groups ($p > 0.05$)

$PaCO_2$ were stable during the experiments and did not show any statistically significant difference. Thus, both MAP and $PaCO_2$ were maintained within those ranges, indicating the presence of a normal autoregulatory response. In addition, the existence of intact autoregulatory responses throughout the experiments was supported by the brain tissue MDA measurements. The determinations of MDA in the brain tissue revealed no significant difference between the study and control groups, indicating that CO_2 PNM insufflation and deflation at IAP of 8 and 15 mmHg did not lead to ischemia–reperfusion injury.

With a normal cerebrovascular system and a normal blood pressure, even modest alterations in $PaCO_2$ can result in a marked alteration of CBF [8]. Cerebral blood flow shows an alternation of 2.5% for every 1 mmHg change in $PaCO_2$ if it is within the range of 20–60 mmHg [18]. Carbon dioxide causes this response by relaxing the smooth muscles of the arterioles and reducing cerebrovascular resistance, thus greatly increasing CBF [9].

It was previously shown that cerebral blood flow velocity correlates with cerebral blood flow [10]. To evaluate the blood flow characteristics of brain tissue, we used Vm, PI, and RI measurements of TCD. The values of PI and RI are indirect parameters of vascular resistance [4]. Decreases in PI and RI reflect the distal vasodilatation or proximal stenosis or vazospasm of the vascular structures. The decreases in PI and RI values after CO_2 PNM that we observed indicate a possible distal vasodilatation of the arterioles rather than a proximal vasoconstriction, because there was no evidence of the development of a prominent vasoconstriction of the BA. The mechanism that triggered the initiation of this autoregulatory response might have been an accumulation of CO_2 during CO_2 PNM. After the CO_2 PNM was created, $PaCO_2$ increased significantly over baseline values. This hypercarbia should have been due to an increased CO_2 load caused by transperitoneal or subcutaneous absorption of insufflated CO_2. The increase in ventilatory death space, reduction of diaphragmatic movements, and decrease in pulmonary excretion might have contributed to the settling of hypercarbia.

Our results showed that reversal of $PaCO_2$ levels to baseline values could not be achieved at 30 min following deflation in group B, in which CO_2 PNM was maintained at 15 mmHg for 180 min. This result was closely correlated with the finding that longer duration of the procedure and higher intensity of IAP caused an increased deposition of CO_2 in muscle and soft tissue as soon as the limit for the pulmonary CO_2 elimination had been exceeded. Sechzer et al. also reported that there was often an increase in peripheral arterial blood pressure, which can be explained by an outpouring of catecholamines from adrenal glands provoked by CO_2 [17]. Since the autoregulation was kept intact during our study, increased CBF due to reduced cerebrovascular resistance might have induced the sympathetic nervous system to increase peripheral vascular resistance. This would have inevitably resulted in an increase in MAP. The aim of this reflex should have been to maintain normal cerebral perfusion pressure, thus preventing further elevation of intracranial pressure by the increased CBF due to lowered cerebrovascular resistance. High IAP might have contributed not only to the facilitation of CO_2 absorption but also to the direct stimulation of MAP increase. The peripheral

vascular resistance might have also increased as a response to elevated IAP because of the reduced inferior vena cava blood flow and diminished cardiac return. In our study, there was a significant increase in MAP in groups B and D, in which CO_2 PNM was maintained at 15 mmHg for 180 min.

A prolonged CO_2 PNM at high IAP resulted not only in CO_2 accumulation but also an increase in MAP. Doppler sonographic findings of increased Vm and decreased PI and RI values of BA are related to the cerebral autoregulatory response to CO_2. However, we could not demonstrate any finding that would support the occurrence of cerebral ischemia or the production of free radicals due to changes occurring during laparoscopy. We believe that the safety of the laparoscopic procedure should always be questioned in subjects who cannot tolerate minor changes in cardiovascular parameters and those who are susceptible to alterations of intracranial pressure because of the very rare cerebral complications reported in the literature.

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