Effect of transgastric natural orifice transluminal endoscopic surgery peritoneoscopy on abdominal organ microcirculation: an experimental controlled study

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Background and Aims: On-demand insufflation during endoscopic peritoneoscopy causes wide variations in intra-abdominal pressure. Its effects on splanchnic microcirculation may differ from those of steady intra-abdominal pressure, because pressure characteristics affect crucial intravascular hemodynamic forces—pressure and shear—adapting flow to local metabolic needs. Our aim was to assess the effect of natural orifice transluminal endoscopic surgery (NOTES) peritoneoscopy on splanchnic microcirculatory blood flow.

Methods: Twenty-one swine were randomized to the following: cholecystectomy by transgastric NOTES (n = 8), cholecystectomy by standard laparoscopy (Lap) (n = 8), and a sham group (n = 5). During NOTES, CO_2 was manually insufflated with a maximum allowed pressure of 30 mm Hg. In the Lap group, intra-abdominal pressure was maintained at 14 mm Hg. Systemic hemodynamics were measured, and microcirculatory blood flow was quantified by using colored microspheres.

Results: Mean intra-abdominal pressure was lower in NOTES than in the Lap group ($P = .038$). In both groups, cardiac index and preload remained unchanged, whereas systemic vascular resistances increased over time, with a lesser increase in the Lap group (2-way analysis of variance; $P = .041$). In pneumoperitoneum groups, microcirculatory blood flow decreased similarly in the renal medulla, stomach, small bowel, colon, and mesocolon by 30%, 45%, 34%, 32%, and 37%, respectively. In NOTES, there was a greater microcirculatory blood flow decrease in the renal cortex (NOTES 41% vs Lap 35%; $P = .044$) and mesentery (NOTES 44% vs Lap 38%; $P = .041$).

Conclusions: These findings suggest that both types of pneumoperitoneum have similar physiologic effects on microcirculatory blood flow. However, on-demand pneumoperitoneum (NOTES group) caused a greater microcirculatory blood flow decrease in areas with low metabolic needs, redistributing blood flow toward metabolically active areas. (Gastrointest Endosc 2016;83:427-33.)

Since Kalloo et al[1] announced a successful liver biopsy through a peroral transgastric approach, natural orifice transluminal endoscopic surgery (NOTES) has become the next step in the evolution of minimally invasive surgery.[1-3] NOTES eliminates the need for abdominal incisions, resulting in less pain, faster convalescence, and diminished risk of wound-related adverse events. However, this relatively sterile procedure involves problems, such as the risk of portal contamination and the difficulty of successful viscerotomy closure, which have been the subject of arduous laboratory research.[4,5] Furthermore, insufflation through a flexible endoscope is not controlled by a constant insufflator device but performed on-demand by operators and is subject to visibility difficulties that may arise at any time. Studies with animal models have reported large fluctuations in intra-abdominal pressure but

Abbreviations: Lap, laparoscopy; NOTES, natural orifice transluminal endoscopic surgery.

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with no great impact on systemic hemodynamics and airway pressure from that of pneumoperitoneum performed by standard laparoscopy.[6-8]

However, there is compelling experimental evidence that intra-abdominal pressure increase causes pressure-related adverse effects on splanchnic blood flow and microcirculation,[9-11] although clinical studies have reported contradictory results.[12-15] The factors involved in these conflicting results include cardiac reserve, body position, sympathetic activity, and—to a lesser extent—the absorbed CO_2 effect. What is certain is that distended pneumoperitoneum increases intra-abdominal pressure and thus alters the intravascular hemodynamic forces, pressure and shear, which are crucial in adapting microcirculatory blood flow to local metabolic needs through upregulation or downregulation of vasoactive mediators.[16-19] However, it is not known whether hand-activated insufflation through flexible endoscopes, which generates large variations in intra-abdominal pressure, with high and low episodes, will affect splanchnic microcirculation in the same way as during the steady level of intra-abdominal pressure generated by insufflator devices.

The objective of this randomized, controlled, experimental study was to evaluate the effect of on-demand CO_2 insufflation during NOTES peritoneoscopy on abdominal organ microcirculation and to compare this effect with that of standard laparoscopic pneumoperitoneum.

MATERIAL AND METHODS

Animal model

This study was approved by the Institutional Review Board of the University of Barcelona's Animal Ethics Committee and the Spanish National Animal Research Committee. After overnight fasting with free access to water, 21 female Yorkshire pigs, weighing 25 to 30 kg, were sedated with intramuscular injection of azaperone (Stresnil, Laboratorios Esteve, Barcelona, Spain) 10 mg/kg. Anesthesia was induced by sodium thiopental (15 mg/kg), and the animals were then endotracheally intubated and mechanically ventilated (Fabius Tiro, Dräger Medical, Lübeck, Germany). Anesthesia was maintained with desflurane (Dräger Medical) and fentanyl (75 μg/h), and atracurium (1 mg/kg/h) was given for muscle relaxation. Ventilator settings were periodically adjusted to maintain end-tidal CO_2 between 35 and 40 mm Hg and arterial PaO_2 between 200 and 240 mm Hg with a positive end-expiratory pressure of 5 cm H_2O. Fluid was repositioned with Ringer's solution (Ringer Lactate, Fresenius-Kabi, Barcelona, Spain) (8 mL/kg/h) and 6% hydroxyethyl starch solution in order to maintain preload stability. Core temperature was monitored and maintained between 36.5°C and 38°C by using heating lamps and warm intravenous fluids. After completion of the study, the animals were euthanized with a deep overdose of thiopental and intravenous potassium chloride.

ANIMAL INSTRUMENTATION AND MEASUREMENTS

Systemic hemodynamic study

Anesthetized animals were placed in a supine position. Under aseptic conditions, surgical dissection of the neck was performed. Cardiac output was measured by a thermodilution technique and monitored continuously by pulse contour analysis. For such purposes, a thermodilution catheter (PiCCO, Pulsion Medical Systems AG, Munich, Germany) was introduced into the right common carotid artery, and a single-lumen catheter (Arrow International, Teleflex, Morrisville, NC) was inserted into the right jugular vein.

Hemodynamic parameters measured were as follows: cardiac index (L/minute/m^2); global end-diastolic volume index (mL/m^2) to evaluate preload; systemic vascular resistance index (dyn.s.cn^5.m^2) to evaluate afterload; heart rate (beats per minute or bpm); and mean arterial pressure (mm Hg).

Intra-abdominal microcirculation blood flow study

Intra-abdominal organ blood flow microcirculation was determined by using colored microspheres (Dye Trak; Triton Technology, San Diego, Calif) with a diameter of 15 μm. These microspheres lodge in capillary beds throughout the body and do not pass into the venous system. The delivery of microspheres to different tissues depends on the tissue perfusion at the time of microsphere injection, and tissue concentration is therefore proportional to blood flow at that time. For the colored microspheres technique, two Arrow catheters were introduced. One of them, via the left carotid artery, was advanced until the morphology and the ventricular pressure curve indicated that it was positioned just above the aortic valves. The second one, placed into the left femoral artery, was used to obtain the arterial reference blood sampling of microspheres. The colored microspheres were administered at 3 time points: (1) baseline, before pneumoperitoneum, (2) 60 minutes after starting the surgical procedure (before deflation); and (3) 30 minutes after pneumoperitoneum release. A detailed description of the colored microspheres technique can be found elsewhere.[20] Briefly, at each study time, microspheres were injected into the left ventricle for 20 seconds. Starting 15 seconds before microsphere injection and continuing for 75 seconds, a femoral artery reference blood sample was drawn at a fixed rate of 5 mL/minute, from the reference sample perfusion (mL/minute), by a constant rate extraction pump (Harvard Infusion Pump; Harvard Bioscience, Holliston, Massachusetts, USA). Thirty minutes after pneumoperitoneum release, the animals were euthanized, and tissue samples were harvested carefully from abdominal organs: renal cortex and medulla, stomach, small bowel and mesentery, and ascending colon and colonic mesentery. In each