

# **PERITONEAL FIBRINOLYSIS DURING PNEUMOPERITONEUM AND LAPAROSCOPIC SURGERY**

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av

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leg läkare

Avhandlingen baseras på följande delarbeten:

- I. Peritoneal response to pneumoperitoneum and laparoscopic surgery.  
Bergström M, Ivarsson ML, Holmdahl L,  
*Br J Surg* 2002;89(11):1465-9
- II. CO<sub>2</sub> promotes plasminogen activator inhibitor type 1 expression in human mesothelial cells  
Bergström M, Falk P, Holmdahl L,  
*Surg Endosc* 2003;17(11):1818-22
- III. Effect of acidosis on expression of mesothelial cell plasminogen activator inhibitor type-1  
Bergstrom M, Falk P, Holmdahl L,  
*Surg Endosc* 2006;20(9):1448-52
- IV. Peritoneal and systemic pH during Pneumoperitoneum with CO<sub>2</sub> and helium in a pig model  
Bergstrom M, Falk P, Park PO, Holmdahl L,  
*Surg Endosc* 2007, e-pub ahead of print
- V. Clinical evaluation of peritoneal acidification and fibrinolytic response during laparoscopy, a randomized parallel group study comparing Helium and Carbon dioxide  
Bergstrom M, Falk P, Park PO, Bengtsson JP, Haglind E, Holmdahl L,  
*in manuscript*

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## BACKGROUND

Laparoscopic surgery is believed to induce less postoperative adhesion formation compared with open procedures, but information regarding biological impact of a laparoscopic approach is limited.

## MATERIAL & METHODS

Peritoneal response to laparoscopic surgery was assessed in human peritoneal tissue in two clinical trials (paper I & V). Human mesothelial cell response to CO<sub>2</sub> was assessed in cell culturing media (paper II & III). Measurements of peritoneal pH was evaluated in an animal model (paper IV), and then performed in patients (paper V). Assays of the key fibrinolytic enzymes t-PA and PAI-1 were done at protein (paper I-III & IV) and mRNA levels (paper II & III).

## RESULTS

The initial clinical study showed a similar decrease in peritoneal t-PA activity during both open and laparoscopic cholecystectomy. However, there was a higher initial peritoneal PAI-1 concentration in the laparoscopic group, which might be attributable to prior exposure to CO<sub>2</sub>. The *in vitro* studies showed an up regulation of PAI-1 mRNA production in cells exposed to CO<sub>2</sub> or acidic conditions, and that acidification could be caused by CO<sub>2</sub>. *In vivo* studies of peritoneal pH showed an immediate decrease to 6.5 during insufflation, reproducing the CO<sub>2</sub> effect during surgery. He did not affect peritoneal pH. When initial peritoneal exposure to CO<sub>2</sub> was controlled for, peritoneal levels of t-PA decreased and PAI-1 increased during laparoscopic surgery regardless of gas used. These findings are consistent with observations done in open surgery and indicate that the effect is related to the surgical trauma. However, the t-PA activity was better preserved using CO<sub>2</sub> suggesting that use of CO<sub>2</sub> might have less adverse effect on peritoneal fibrinolysis than He.

## CONCLUSION

Peritoneal fibrinolytic response during laparoscopic surgery is similar to open surgery, but CO<sub>2</sub> elicits specific biological effects. Exposure of peritoneum and mesothelium to CO<sub>2</sub> leads to a local and systemic acidosis and seems to have direct effects on key fibrinolytic enzymes. The systemic acidosis is manageable through controlled ventilation. The clinical implication of the effect on peritoneal fibrinolysis is unclear, but the observations done in humans are consistent with a reduced propensity for adhesion formation.

Key words: Laparoscopy, Peritoneum, Fibrinolysis, Mesothelial cells, Carbon dioxide, Helium

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