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To perform operative procedures in an optimized local atmosphere: Can it reduce post-operative adhesion formation?

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ABSTRACT

Background: Adhesion formation is a major problem following abdominal surgery as it creates a considerable economic burden in addition to an increased risk for complications. In the present study, an effort was made to reduce post-operative adhesion formation by creating an artificial atmosphere within and around the abdominal cavity during an open surgical procedure.
Methods: 82 Wistar male rats (Clr:WI) (200 gr, 7 weeks) were randomized into two groups. The abdominal cavity of the control group was exposed to the normal atmosphere of the operating-theatre during surgery (21% O_2, 21 °C, 40–47% relative humidity (RH)), while the abdominal cavity of the study group was exposed to an artificial atmosphere during surgery (3–6% O_2, >75% CO_2, 95–100% RH, 37 °C). Adhesion induction consisted of a laparotomy along linea-alba, four lesions in the anterior abdominal-wall, blood from the tail vein dripped inside the abdominal cavity and exposure to the atmosphere around the wound by use of self-retaining retractors. In addition, a liquid-sample for quantitative bacteriologic cultivation and bacterial load (CFU/ml) calculation was taken just before closure. After 3 weeks the abdominal cavity was scored for the extent, tenacity and severity of adhesions before the rats were euthanized. The two-sample-Wilcoxon-rank-sum test was used in the analysis.
Results: Highly significant differences in postoperative total adhesion score, extent-, severity- and tenacity-score were found ($P < 0.01$). No differences were found between the two groups regarding mean bacterial load ($P > 0.05$).
Conclusions: The rats exposed to the warmed and humidified artificial atmosphere consisting of more than 75% carbon dioxide and 3–4% oxygen during surgery had more severe and more post-operative adhesions compared to the rats that were exposed to the ambient air during surgery.

1. Introduction

Adhesion formation is a major problem following abdominal surgery. After abdominal procedures, 70–90% of the patients develop adhesions.[1] Adhesions can cause complications, such as intestinal obstruction,[1] female infertility,[2] and increase the risk for bowel perforation during reoperation.[3] Depending on the underlying disease, the incidence of bowel perforation during open surgery in patients who previously have had intraabdominal surgery can be as high as 20%.[3] The delayed detection of bowel perforation is associated with a high mortality and morbidity and adhesiolysis before being able to continue the planned procedure is often time consuming.[3]

In a retrospective analysis performed in Sweden, the annual cost of readmissions due to intestinal obstruction caused by adhesions was estimated to 39.9–59.5 million euro's.[4] A cost-of-illness study performed in the United States of America found the annual adhesion-related expenditures to be 1,3 billion dollars.[5] In addition, a ten year follow-up of 12584 patients who underwent lower abdominal surgery showed that approximately a third of the patients were readmitted for possible adhesion related problems during the subsequent 10 years.[6] These observations show that adhesion formation creates a considerable economical burden in addition to an increased risk for complications.

Extensive research on the possible causes of adhesions has been performed throughout the years and although the exact pathogenesis

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of adhesion formation is complex and incompletely understood, damage to the mesothelial monolayer seems to be the trigger.[7] Potential causes of damage are for example ischemia from sutures, abrasion from gauze swabs, irrigation fluid, foreign materials, overheating, desiccation, infection and mechanical forces. Also, during open surgery the mesothelium is exposed to ambient air which contains airborne bacteria that can cause infection[8] and the fact that it is dry and cold could lead to the desiccation of tissues.[9] In addition, ambient air has an oxygen saturation of approximately 21%, which causes hyperoxia and the development of Reactive Oxygen Species (ROS). These factors all increase adhesion formation trough different mechanisms.[10,11]

Several previous studies have focussed on possible ways to reduce adhesion formation. Changing the properties of the insufflation gas used in laparoscopic surgery has shown promising results. Warming and humidifying the insufflation gas during laparoscopic procedures can reduce desiccation of the mesothelium[12] compared to the use of cold-dry insufflation gas. This reduces adhesion formation, since desiccation has been found to enhance adhesion formation.[12] Studies also suggest that an oxygen saturation of 3–4% of the insufflation gas is associated with less adhesion formation than an insufflation gas with a higher or lower oxygen saturation.[13] In addition, hypothermia during the laparoscopic procedure has also shown to reduce adhesion formation.[14] However, cooling down the patient might not be feasible from a clinical perspective.[15,16] The idea of manipulating the environment the mesothelium is exposed to might also be applicable to open surgery.

Most of the previous studies on prevention of adhesion formation have focussed on laparoscopic surgery. However, adhesion formation is probably a bigger problem after open surgery.[17] It has recently been suggested that to establish a local atmosphere in and around the wound cavity during open surgical procedures by using intraoperative field flooding with warm, humidified CO_2 might reduce the risk for infection and post-operative adhesion formation.[18–20]

The aim of this study was to create an artificial atmosphere within and around the abdominal cavity during an open surgical procedure that would reduce post-operative adhesion formation compared to an atmosphere consisting of ambient air. The artificial atmosphere in this trial was warmed and humidified and consisted of more than 75% carbon dioxide and 3–6% oxygen.

2. Materials and methods

This study is a randomized experimental study comparing postoperative adhesion formation and bacterial load in rats where the abdominal cavity was exposed to ambient air during surgery (group I) or to an artificial atmosphere during surgery (group II). For this study 82 Wistar male rats (Clr:WI) from 'Charles river laboratories' were used, weighing about 280 g each. The rats were fed standard rat food with tap water ad libitum, kept at standard laboratory conditions, and were humanely cared for. Each animal received a chip under the skin from which a number could be read with a scanner.

The animals were block randomized into two groups of 41 rats each, a control group (ambient air, group I) and a study group (artificial atmosphere, group II). The randomization generator from the following internet site was used: www.randomization.com.

For the purpose of creating an artificial atmosphere, a box as illustrated in Fig. 1 was designed. The box was made of Perspex with several access points. There were special openings for the intubation equipment and two openings for the surgeons arms, to enable surgery in the box without exposing the surgeon to the environment within.

Carbon dioxide gas and oxygen gas from wall outtakes in the operation chamber were mixed, so that the resulting gas consisted of 3%–6% oxygen and >75% Carbon dioxide. The mixed gas was then warmed and humidified by several heaters and humidifiers to 37° Celsius and a relative humidity level of 95–100% before it entered the box. The PDG3-IR CO2 and O2 gas analyser (Status scientific controls LTD., Mansfield, UK) and the humidity and temperature sensor 'Testo 625' (Testo LTD., alton, UK) were placed inside the box at intervals for registration of the gas concentration, temperature and relative humidity levels. Based on these measurements, adjustments were made to keep the environment inside as stable as possible.

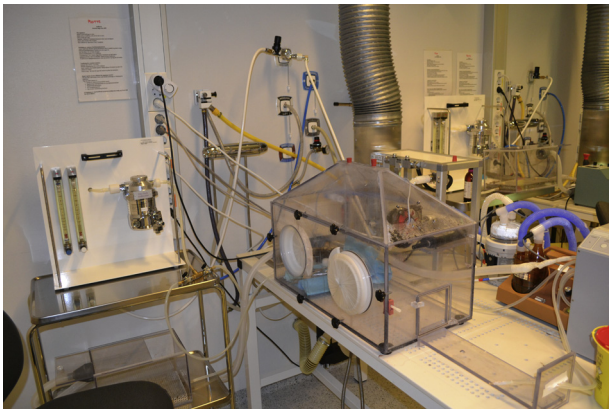

Fig. 1. Perspex box for creation of an 'optimal atmosphere'.

The rats received atropine 20 min before being put under anaesthesia. They were initially anaesthetized with 5% isoflurane, which was inhaled in a closed chamber. They were then intubated and connected to a rodent ventilator (Harvard Starling 'Ideal' Ventilator, Sydney, Australia) with a stroke volume of 1.5 ml/min, and respiration rate of 80 breaths/min. A plane of anaesthesia for surgery was regulated by delivery of approximately 1.5% isoflurane through a vaporizer with 40% oxygen and 60% nitrous oxide.

After intubation, the abdominal hair of the rat was shaved, the skin was sterilized with chlorhexidine and 12 ml isotonic fluid was administered subcutaneously. A midline laparotomy was then performed inside the box on the rats that were included in the study group, and outside the box on the rats included in the control group. The rats operated in the ambient air outside the box were kept warm during the operation with a warming blanket. In order to induce adhesion formation four standardized lesions were made in the anterior abdominal wall, one in each quadrant and the abdominal cavity was exposed to the atmosphere around it by keeping the laparotomy wound open, using self-retaining retractors.

The abdominal cavity of the rat was exposed to the surrounding atmosphere for approximately 70–75 min before it was filled with 5 ml warm isotonic saline. After 2 min, a fluid sample was taken. The volume of the sample was measured before a quantitative bacteriologic cultivation on chocolate agar and blood agar was performed. The agars were incubated for 3 days and the colony forming units (CFU) were counted, which enabled the calculation of the bacterial load for each sample (CFU/ml).

After sampling the fluid, more intra-abdominal adhesion formation was induced using the method described by Graeme Ryan et al.[21] The tip of the tail was cut and nine drops of blood were dropped inside the peritoneal cavity in a standardized pattern. Afterwards, the abdominal cavity was closed with PDS sutures. After closure, the rats in the study group were taken out of the artificial atmosphere. The total time the abdominal cavity was open and exposed to the surrounding atmosphere, until it was closed again with sutures, was approximately 85–90 min.

Immediately after surgery, Buprenorphine (0.05 mg/kg s.c. Temgesic, Reckitt and Coleman, Hull, UK) was administered subcutaneously to reduce acute postoperative pain. Based on the animals general behaviour, alertness and posture, additional pain medication was administered.

After 3 weeks[22,23] the adhesions were scored and the animals euthanized. In order to score the adhesions, the animals were put in an isoflurane anaesthesia administered by an isoflurane mask, before the anterior abdominal wall was removed and any adhesions were scored.

A total number of six scoring sites were used. The first adhesion scoring site[1] was the area around the scar of the laparotomy. The other four were each a quarter[2–5] of the remaining area. The intestines formed the last scoring site. They were searched for any adhesions along their entire length.

The sites were individually scored macroscopically for extent (0 = no adhesions, 1 = 1–25% covered in adhesions, 2 = 26–50%, 3 = 51–75%, 4 = 76%–100%), type (0 = no adhesions, 1 = filmy, 2 = dense, 3 = capillaries present) and tenacity (0 = no adhesions, 1 = adhesions easily fall apart, 2 = adhesions require traction, 3 = adhesions require sharp dissection).[14] The total score for each site was the sum of the quantity-, severity- and tenacity score. The total adhesion score was the sum of all six sites, with a maximum score of 60.

The study was investigator blinded: those who scored the adhesions or counted the number of CFU/ml did not know whether the abdominal cavity of the rat was exposed to the artificial atmosphere or the ambient air of the operating chamber.

The software SPSS 19 (IBM SPSS Statistics, New York, US) was used for analysis of the data. For both groups it could not be assumed that the data was normally distributed after doing a normality test on the distribution of the data in both groups ($P < 0{,}05$). Neither could it be assumed that the bacterial load data from both groups had a normal distribution ($P < 0.001$). This is why we used the Wilcoxon–Mann–Whitney rank sum tests instead of the two samples *T*-tests.

The study was approved by Norwegian Animal Research Authority (NARA).