

Use of Colchicine in Reduction or Prevention of Talc-induced Intra-abdominal Adhesion Bands

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Abstract

Background: Postoperative peritoneal adhesion bands are one of the most common complications caused by foreign material.

Objective: To investigate the effect of colchicine on talc-induced peritoneal adhesion bands.

Method: Adhesion bands were induced in 30 short hair England Guinea pigs by introduction of talc-saline solution (10 mL, 10%) into the peritoneal cavity. Afterwards, the pigs were randomly divided into two equal groups and colchicine was orally given to the experimental group. Finally, laparotomy was performed and the adhesion bands in both groups were classified using the Nair classification and compared with each other.

Results: Only four (23%) out of 15 Guinea pigs of the target group developed substantial adhesions, while the other 11 (75%) pigs developed only insubstantial adhesions (grade 0-1). On the other hand, the entire control group developed substantial adhesions.

Conclusion: Colchicine, at a dosage of 0.02 mg/kg, prevented and reduced formation and severity of adhesion bands ($p < 0.05$). Therefore, given the safety, low cost and acceptable side effects, colchicine may be a useful agent for prevention or reduction of adhesion band formation. Human studies on this subject are warranted.

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Keywords • Colchicines • intestinal obstruction • peritoneal adhesion bands • talc-induced

Introduction

Intra-abdominal adhesions are almost inevitable after any major abdominal surgery. Studies on this subject, mostly based on post-mortem laparotomies are surprisingly few. ~~Analysis of large series of cases have demonstrated that approximately one-third of all intestinal obstructions are likely to be due to adhesion.~~¹⁻²

In Weibel and Majno's study, the incidence of adhesion bands in patients with previous history of laparotomy was 67% and after multiple operations the incidence increased to 93%.¹ Previous studies show that anything which damages the endothelium, like rough handling, retraction, surgical denudation, etc, is likely to be followed by

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Grade	Description of adhesive bands	Remarks
0	Complete absence of adhesions	Insubstantial Adhesions
1	Single band of adhesions between viscera, or from one viscus to abdominal wall	
2	Two bands, either between viscera or from viscera to the abdominal wall.	
3	More than two bands, between viscera, or viscera to abdominal adhesions wall, or whole of intestines forming a mass without being adherent to abdominal wall.	Substantial Adhesions
4	Visceral directly adherent to abdominal wall, irrespective of number and extent of adhesive bands.	

adhesion.¹⁻³ Therefore, this became a principle for surgeons that peritoneal injury should be avoided, raw damaged serosal surfaces must be eliminated within the peritoneal cavity and the peritoneal defect must be over-sewn or patched whenever possible.¹⁻³ Injury or inflammation was implicated as the cause. Several efforts, both clinical and experimental, have been made toward solving this problem and prevention of postoperative adhesion bands, such as the enhancement of peristalsis postoperatively or using talc-free gloves. However, the great majority of these efforts were ineffective.

Colchicine is absorbed readily after oral administration and reaches peak plasma levels within 2 hours. It produces its anti-inflammatory effects by binding to the intracellular protein tubulin, thereby preventing its polymerization into microtubules and leading to inhibition of leukocyte migration and phagocytosis. It also inhibits the formation of LTB^{4,5}. In addition to acute gouty attack, colchicine is useful in delaying progression of hepatic cirrhosis, in sarcoid arthritis and also in the treatment of idiopathic pulmonary fibrosis.^{4,5} Because of colchicine's proven anti-inflammatory effects, we attempted to evaluate its efficacy in prevention or reduction of talc induced adhesions.

Material and Method

Our study was performed on 30 short-hair England Guinea pigs, 650-950 g body weight (mean of 730 g), which were randomly divided into two equal groups, the experimental (Group A) and the control (Group B). Only the nurse responsible for gathering the data at the end of the study knew which pig belonged to which group. Therefore, the study was performed blindly and randomized.

At the beginning of the study, all 30 pigs were anesthetized using ketamine 5% (45 mg/kg) and xylazine 2% (5 mg/kg). Afterwards a 2-3 cm midline incision was performed and the skin and fascia were incised. The peritoneum was opened and the talc-saline solution (10 mL-10%, talc 1 g/kg, pre-

pared as 10% solution) was instilled into the peritoneal cavity and the abdominal cavity was closed with nylon 2/0 continuously. No antibiotics were given.

The experimental group (group A) received colchicine (0.02 mg/kg) through a polythens stomach tube. The control group (group B) only received ordinary diet. The animals were housed in a climate-controlled animal care facility (humidity of 45% and temperature of 22-24 °C) with 12 hour light-dark cycles. Standard rodent pellet and water, ad libitum, were provided for both groups. The veterinary personnel responsible for taking care of the pigs didn't know which pig belonged to which group.

All animals were killed after 6 weeks and the peritoneum was investigated for the presence or absence of adhesions and graded for each animal according to the Nair classification (Table 1).

Statistical analysis

For comparisons between groups, Chi square and the t-test were used. The significance level was considered for the values of $p < 0.05$.

Results

Only 4 (23%) out of the 15 guinea pigs of group A developed substantial adhesion (Table 2). The other 11 pigs (75%) developed only insubstantial adhesions (grade 0-1). No adhesion was detected in six (40%) of the 15 guinea pigs of group A. Five

Grade of adhesions	Group A (n=15)	Group B (n=15)
0	6	–
1	5	–
2	2	–
3	-	5
4	2	10

developed grade I adhesions, 2 grade II, and 2 developed grade IV adhesions (Table 2).

In group B, all of the guinea pigs developed grade III-IV adhesions and there were no guinea pigs free of adhesion (Table 2).

The prevalence of adhesion band was significantly higher in the control group, which had not received colchicine, as compared to group A, the experimental group ($p < 0.05$).

Discussion

Postoperative peritoneal adhesions continue to be a serious surgical problem. Indeed, injuries to the serosa of bowel and peritoneal surfaces during the course of surgery, presence of microscopic foreign bodies such as talcum powder, fluff from gauze pads, presence of blood and fibrin exudates and etc. initiate an inflammatory response.⁶⁻⁹ Body tissue response to an inflammatory stimulus is similar, regardless of the nature or the site of stimulus.⁷ Several methods have been tried for prevention of these adhesions and suppression of inflammation. Nair *et al* used proteolytic enzymes¹⁰, Kagoma *et al* experimented on Vitamin E¹¹, Cook performed a study on dogs¹², Kapur *et al* tested anti-inflammatory properties of oxyphenbutazone¹³, Galili *et al* used methylene blue¹⁴ and Davidson administered heparin and dicumarol.¹⁵ However, limited success has been achieved.

Colchicine is an anti-inflammatory drug that is traditionally used for the relief of acute gouty attacks. Recent studies have demonstrated beneficial effect of this drug in prevention of progression of idiopathic pulmonary fibrosis and familial Mediterranean fever.^{4,5} Colchicine is a safe anti-inflammatory drug with acceptable and tolerable side effects. Our results demonstrated that colchicine is effective in preventing and reducing talc-induced adhesion bands. Given the safety, low cost and acceptable side effects colchicine may be a useful agent for prevention or reduction of adhesion band formation. Human studies on this subject are warranted.

Conclusion

The results of our study showed that colchicines administered orally, at a dosage of 0.02mg/kg, prevented and reduced the formation and severity of adhesion bands ($p < 0.05$). Therefore, given the safety, low cost and acceptable side effects, colchicine can be used to prevent or reduce adhesion-band formation.

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