Effects of Dexamethasone, Piroxicam and Sterile Aloe Vera Extract on the Prevention of Postoperative Peritoneal Adhesion Formation in Rat

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ABSTRACT

Adhesions are a common and unfortunate consequence of most abdominal surgical operations. Some patients form extensive permanent adhesions that can cause abdominal or pelvic pain, infertility and bowel obstruction. Epidemiological studies have highlighted the extent of this problem and the cost to the Health Service, and although there are numerous approaches to prevent adhesion formation by careful laparoscopic, microsurgical techniques, the use of various adhesion barriers and topical pharmacological agents, no method so far has proved completely efficacious in randomized controlled trials. The most effective product for prevention of postoperative adhesion is yet to be discovered. In this study, we decided to evaluate the effects of peritoneal exposure to dexamethasone, piroxicam and sterile aloe vera extract in post-surgical adhesions in rats. Forty adult male wistar rats were divided randomly into four experimental groups; Group 1: Induction of adhesions (IA) + intraperitoneal administration of normal saline, Group 2: IA + intraperitoneal administration of dexamethasone, Group 3: IA + intraperitoneal administration of piroxicam, Group 4: IA + intraperitoneal administration of sterile aloe vera extract. Under general anesthesia the abdominal midline prepared for surgery. A 4cm midline incision was made and the abdomen was opened. Adhesions were induced by removed a 1.5cm × 1.5cm area of transverses abdominus muscle on the right lateral abdominal wall. All rats were euthanized on the 14th day. Adhesions between omentum and abdominal wall were scored in a blinded manner by 2 surgeons according to the method of Evans model. The frequency and intensity of adhesions were recorded, and the mean of the two observers' scores was used for statistical analysis. Results were expressed as mean ± standard deviation. Differences between groups were evaluated by Kruskal–Wallis variance analysis followed by a post hoc Mann–Whitney U-test. P-values <0.05 were considered statistically significant. Most animals developed adhesions between the omentum and abdominal wall and adhesion grades were no statistical significant difference between the treatment groups. However, adhesion grades were significantly different between the treatment groups with control group. In conclusion, the data presented here show that intraperitoneal dexamethasone, piroxicam and sterile aloe vera extract treatment were effective in the prevention of peritoneal adhesions.

Key words: Dexamethasone, Piroxicam, Aloe Vera Extract, Postoperative Peritoneal Adhesion.

Introduction

Postoperative adhesions are a common complication following a variety of surgical procedures. The word “adhere” means stick or hold together [1]. It is a sort of disruption in the normal physiological process of peritoneal healing. It may appear as thin sheets of tissue similar to plastic wraps or as thick sheets similar to rubber bands. Peritoneal adhesions are a worldwide problem. In most cases they are clinically asymptomatic. Adhesions may involve female reproductive organs, leading to infertility, deep dyspareunia and chronic pelvic pains. Adhesions involving the bowels can cause bowel obstruction [2]. Several methods, materials, and agents have been assessed for their ability to prevent postoperative adhesion, including various surgical procedures, minimally invasive and laparoscopic techniques, topical pharmacological agents that target fibrin formation; and liquids, gels, and solids that can form a mechanical barrier between mesothelial surfaces. Although some of these methods or agents have been found beneficial, complete success was not achieved [3]. Anti-
inflammatory agents are used to decrease the initial inflammatory response to tissue injury. Anti-histamminics with corticosteroids inhibit fibroblast proliferation [4]. Aloe vera gel, administered intraperitoneally, has also been shown to be an effective adhesion inhibitor, without promoting adverse effects [5]. We therefore aimed to compare the use of intraperitoneal dexamethasone, piroxicam and sterile aloe vera extract in the prevention of postoperative adhesion formation.

Materials and Methods

All rats of the present research were cared according to the norms of the Islamic Azad University Faculty of Specialized Veterinary Science Tehran Iran laboratory of animal experimentations; this investigation was approved by the Committee of Ethics in Research with animals in Islamic Azad University.

Forty adult male wistar rats were used in the study from around 10 weeks of age with a typical weight between 300 and 400g. Animals were housed at a constant room temperature with a 12h light and dark cycle. Standard rodent chow and water were provided ad libitum. The animals were divided into 4 groups of 10 according to the treatment:

**Group 1:** Induction of adhesions (IA) + intraperitoneal administration of 5 ml normal saline.

**Group 2:** IA + intraperitoneal administration of 5 ml (1mg/ml) dexamethasone.

**Group 3:** IA + intraperitoneal administration of 5 ml (1 mg/ml) piroxicam solution.

**Group 4:** IA + intraperitoneal administration of 5 ml sterile aloe vera extract

All surgical procedures were performed under aseptic conditions by a single surgeon. Rats were anesthetized with an intramuscular injection ketamine (50 mg/kg) and xylazine (10 mg/kg). All animals received a prophylactic dose of ampicillin (50 mg/kg) subcutaneously immediately prior to the procedure. Each rat was placed on its back on an operating table, and its extremities were fixed to the table using sticking plaster. The abdominal hair was shaved off and the surgical field prepared with 5% antiseptic providone-iodine solution. A 4cm midline incision was made and the abdomen was opened. Adhesions were induced by removed a 1.5cm × 1.5cm area of transverses abdominus muscle on the right lateral abdominal wall. The incision was closed with 3/0 polypropylene sutures (Prolene) using a continuous suture technique. We did not use foreign bodies such as prolene or mesh to purposefully produce a low scoring adhesion model. Postoperative analgesia was obtained with the use of subcutaneous nalbuphine hydrochloride (2 mg/kg). All animals were given water from the first postoperative day; standard rat chow and water were provided on the second postoperative day. The animals’ welfare was monitored with the use of a standard observation chart by experienced animal technicians.

All rats were euthanized on the 14th day after being anaesthetized with overdose intraperitoneal pentobarbital injection (300 mg/kg) before re-celiotomy. Adhesions between omentum and abdominal wall were scored in a blinded manner by 2 surgeons according to the method of Evans model (Table 1). The frequency and intensity of adhesions were recorded, and the mean of the two observers' scores was used for statistical analysis. Adhesions were graded as 0 to 3 based on their severity.

All variables were expressed as mean ± standard deviation. Differences between groups were evaluated by Kruskal–Wallis variance analysis followed by a post hoc Mann–Whitney U-test. P-values <0.05 were considered statistically significant. All data were entered into and processed by SPSS for Windows statistical package.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Grading of adhesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No adhesions</td>
</tr>
<tr>
<td>1</td>
<td>Spontaneously separating adhesions</td>
</tr>
<tr>
<td>2</td>
<td>Adhesions separating by traction</td>
</tr>
<tr>
<td>3</td>
<td>Adhesions separating by dissection</td>
</tr>
</tbody>
</table>

**Results:**

A total of 40 rats were operated. During the study, two animals died; one rat from group 1 during anesthesia, and one rat from group 4 in the following first day after surgery (all were immediately replaced but not included in the study). There were no symptoms before death; dead rats underwent necropsy without significant findings. Deaths were not related to surgery. The remaining 38 animals recovered without incident and resumed preoperative physical activity and feeding patterns by postoperative day 2. There was no wound dehiscence; and incision hernia. The grading of adhesions in each group is summarized in Table 2. Most animals developed adhesions between the omentum and abdominal wall and adhesion grades were no statistical significant difference between the treatment groups. However, adhesion grades were significantly different between the treatment groups with control group.
**Table 2:** Adhesion grading of the groups according to the number of cases.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>N</td>
<td>9</td>
<td>10</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.33±0.70**</td>
<td>1.1±0.99*</td>
<td>1.3±0.94*</td>
<td>1.55±1.13*</td>
</tr>
</tbody>
</table>

*Adhesion grades were no statistical significant difference (P>0.05) between the treatment groups (groups 2, 3 and 4). **Adhesion grades were significantly different (P<0.05) between the treatment groups with control group (group 1).

**Fig. 1:** Necropsy photographs showing intraperitoneal adhesions formation between the omentum and abdominal wall in wistar rats, **a)** shows a degree 0 adhesion or the complete absence of lesions, **b)** shows a degree 2 adhesion between omentum and the abdominal wall (adhesions separating by traction), and **c)** shows a degree 3 adhesion.

**Discussion:**

Postoperative adhesions are a natural effect in the mechanism of wound healing of damaged tissue which may lead to severe postoperative complications and problems [6]. Several attempts have been made to reduce adhesion formation like steroids, nonsteroidal anti inflammatory drugs [7, 8], antibiotics [9] or chlorhexidine [10] with different results. Anti-inflammatory agents are used to decrease the initial inflammatory response to tissue injury. Most animal studies have shown the effectiveness of nonsteroidal anti-inflammatory drugs in the prevention of adhesions [11, 12]. Low-dose aspirin [13] could be effective in reducing adhesion formation by its selective inhibition of thromboxane-A2 over prostacyclin. A study carried out by Rodgers et al. [14] verified the effect of various anti-inflammatory agents as retinoic acid, quinacrine and dipyridamole in reducing adhesions in animals. Despite that, other studies have failed to prove any beneficial effect of intramuscular or intraperitoneal administration of ibuprofen in the reduction of peritoneal adhesions in rat and rabbit models [15, 16]. In an experimental study Maghsodi et al [17] showed that intraperitoneal instillation of piroxicam solution might be useful for preventing peritoneal adhesions. Corticosteroids inhibit fibroblast proliferation. The potential side effects of these agents include immunosuppression with subsequent wound infection, and delayed wound healing with subsequent wound dehiscence or incisional hernia. Non-steroidal anti-inflammatory drugs [18] have an anti-prostaglandin effect, hence blocking the adhesiogenic effect of prostaglandins. In this study, we observed that the intraperitoneal administration of dexamethasone and piroxicam significantly decreases the development of postoperative peritoneal adhesions. In agreement with other studies, we showed that intraperitoneal administration of dexamethasone and piroxicam can inhibit inflammation and alter the intensity and frequency of the formation of adhesions.

Aloe vera is a plant with yellow flowers and triangular leaves [19]. Plant leaves contain abundant amounts of mucilaginous fluid of high viscosity, called aloe vera gel. Peripheral bundle sheath cells of leaves contain a less viscous liquid, called aloe vera juice or aloe vera sap [19]. The aloe vera plant contains 75 potentially active substances, including vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids [20]. Owing to its rich content, it is used in the treatment of many clinical diseases and has been found to be effective in many pathological conditions [21–23]. Aloe vera also accelerates the healing of other types of wounds owing to its anti-inflammatory effects [23–26]. Aysan et al have showed that aloe vera gel can effectively decrease adhesion formation if applied before, but not after, peritoneal trauma. This effect is likely due not to its chemical properties but to its viscosity, providing a covering to prevent peritoneal trauma [25]. We have therefore assessed whether aloe vera can prevent postoperative peritoneal adhesions, by applying aloe vera extract to the peritoneal cavity after the induction of adhesions.
Conclusion:

In conclusion, the data presented here show that intraperitoneal dexamethasone, piroxicam and sterile aloe vera extract treatment were effective in the prevention of peritoneal adhesions. Easy applicability of the intraperitoneal administration of these agents was its major advantage. The combination of these agents should be investigated in future studies for evaluation synergistic effects.

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References


