Evaluation of topical application of honey in prevention of post-operative peritoneal adhesion formation in dogs

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Summary

The objective of this study was to determine the effectiveness of topical administration of honey in prevention of or reduction in post-surgical peritoneal adhesions in dog. The study was conducted on 18 adult female mixed-breed dogs with a mean ± SD weight of 20 ± 4.25 kg. A standardized surgical trauma (serosal trauma model) was made in the dogs' descending colon to induce adhesion formation. The control group (n = 9) received saline treatment. In the experiment group (n = 9), the lesions were covered with honey. Three weeks after laparotomy, the dogs were sacrificed and the adhesions were graded according to the Evans's scoring system. Overall, 67% (n = 6) of the control and 22% (n = 2) of the experiment animals presented with moderate (grade-2) and severe (grade-3) adhesions. In the control group, there were 3 (33%) dogs with grade-0 or grade-1 adhesions, while in the experiment group there were 7 (78%) dogs with the same grades of adhesions. The difference between the two groups was significant ($P<0.05$). It was concluded that honey is a useful covering for damaged peritoneal surfaces and has high effectiveness in reducing post-operative adhesions.

Key words: Honey, Intra-abdominal adhesion, Topical, Dog

Introduction

Adhesion formation is considered to be an inevitable consequence of surgical trauma to the peritoneal surface of the abdominal cavity (Menzies and Ellis, 1989; Burns *et al*., 1996; Rogers *et al*., 1997). For the development of adhesions between two surfaces inside the peritoneum, there must be peritoneal mesothelial damage on at least one surface (Hellebrekers *et al*., 2000). Major complications that arise from post-operative peritoneal adhesions include intestinal obstruction, intra-abdominal abscess formation, ureteral obstruction, infertility and chronic pain (Montz *et al*., 1991). In human, the incidence of adhesion formation after a single abdominal operation is high, with an incidence over a lifetime of 47% after appendectomy and up to 91% after pelvic surgery (Ray *et al*., 1993; Becker *et al*., 1996; Burns *et al*., 1996). With the hope of decreasing the post-surgical adhesion formation, investigators have developed a variety of techniques to minimize the surgical trauma and several agents have been introduced to decrease the inflammatory responses of the peritoneum (Ellis, 1982; Douglas *et al*., 1997; Ustun *et al*., 1998; Treutner and Schumpelick, 2000). A wide variety of barrier substances have been tested by investigators and biomedical companies to prevent adhesions after open abdominal surgery (Sravelos and Le, 1996; Alponat *et al*., 1997; Rogers *et al*., 1997; Treutner and Schumpelick, 2000). Honey has been a valued part of wound treatment for many centuries. It was first documented as a wound treatment by the Egyptians in 2000 BC (Gelbart, 1999; Tovey, 2000). Unlike other antiseptics, honey is said to cause no tissue damage (Molan, 1999). Physical properties of honey (i.e., hygroscopicity, lower pH and hypertonicity) are suggested to be responsible for its wound healing activities (Kaufman *et al*., 1985;

Efem, 1988; Mathews and Binning, 2002). Honey is used in many medical research studies. However, so far, it has never been utilized in preventing post-operative peritoneal adhesion. Since healing of the peritoneal injury is a kind of wound healing process, the objective of this study was to determine whether peritoneal adhesions may be reduced with post-operative topical honey administration.

Materials and Methods

This study was performed on 18 adult female mixed-bred dogs with a mean ± SD weight of 20 ± 4.25 kg. The animals were selected randomly and divided into two equal groups. Following overnight fasting, all animals were tranquillized with acepromazine maleate (Hoogsrraten, Belgium) (0.05 mg/kg, IM). General anaesthesia was induced and maintained by IM injection of ketamine hydrochloride (Alfasan, Woerden, Holland) (20 mg/kg, IM). The dogs were then placed in supine position and the abdomino-pelvic area was prepared for aseptic surgery. Laparotomy was performed as routine on all animals through a caudal midline abdominal incision of 10 cm length. After the peritoneal cavity was entered, the descending colon was isolated with wet sterile gauze. The effects of intra-abdominal administration of honey on post-operative adhesion formation were evaluated using an established model of serosal trauma (Moll *et al*., 1991; Chase *et al*., 1996), to induce intra-abdominal adhesions. The descending colon was exposed and 10 cm of its terminal portion at antimesentric border, just proximal to the pelvic inlet, was isolated. A dry gauze sponge was rubbed 100 times against the colonic serosa at this point, causing an abraded area approximately 3 × 4 cm. A single 3-0 monofilament nylon suture as a marker was then placed through the seromuscular layer of the colon in the center of the abraded area. In the control group, only the serosal trauma model was performed and the abraded areas were washed with 0.9% NaCl solution. The same area in the dogs in the experiment group was covered with honey (10 ml). In this study, a local natural, unpasteurized honey was used. This honey was produced in Targevar region of Urmia. The average composition of the honey is given in Table 1. The abdominal incision was then closed in two layers with continuous 0 polyglactine 910 (Vicryl®) (Sherwood Davis and Geck, U.K.) suture.

Table 1: Average composition of Targevar honey

Component	Average (%)
Reductant sugars	66.38
Sucrose	3.12
Fructose/Glucose	0.93
Diastase	+
Commercial glucose	–
Mineral components	0.05
Moisture	17.08
Concentration	82.92
Total acid	12.5
pH	3.96

Three weeks later, dogs were sacrificed with an IV injection of an overdose of thiopental sodium. The animals were autopsied and the abdominal cavities were entered. The adhesion grades were evaluated according to the Evans's scoring system: 0 = no adhesion; 1 = spontaneously separating adhesions; 2 = adhesions separating by traction; 3 = adhesions separating by dissection (Evans *et al*., 1993). Biopsy of adhesions was performed in some animals in which moderate and severe adhesions were present. Tissue was removed, fixed in 10% formalin, and stained with haematoxylin and eosin.

Statistical analysis

The Mann-Whitney U-test was used to determine differences in adhesion grading between the control and experiment groups. P-values <0.05 were considered statistically significant.

Results

The frequency of dogs with different degrees of adhesion is shown in Table 2. Comparison of the two groups indicated that the severity of adhesions was significantly less in the experiment group ($P<0.05$; Mann-Whitney U-test).

Histologic analysis revealed that honey did not induce any specific inflammatory reactions and caused a lower fibrotic

Table 2: Grading of intra-abdominal adhesions (based on Evans's scoring system) in the studied groups (P<0.05; Mann-Whitney U-test)

Grade	Group	
	Control	Experiment
0	2 (22%)	3 (33%)
1	1 (11%)	4 (44%)
2	3 (33%)	1 (11%)
3	3 (33%)	1 (11%)

response as compared with the untreated control group. The dominant cells in honey-treated group were macrophages and polymorphonuclear neutrophils. In the control group, the inflammation was more severe than treatment group and polymorphonuclear neutrophils were increased in microscopic field.

Discussion

In this experimental study, we attempted to assess the value of honey on prevention of post-operative peritoneal adhesions due to its effects on promotion of wound healing.

Serosal abrasion and intestinal ischemia models have been used to evaluate methods of preventing adhesion formation (Mueller *et al*., 2000). The serosal abrasion technique requires less anaesthesia and surgical time than ischemic models and consistently produces intra-abdominal adhesions (Mueller *et al*., 2000; Boure *et al*., 2002). In the present study, seven (78%) of nine control dogs showed intra-abdominal adhesions. Therefore, similar to previous reports, this model of serosal trauma reliably induced adhesion formation without excessive morbidity and mortality.

Innumerable substances and methods have been used, either locally or systemically, in an effort to reduce or prevent post-operative adhesion formation. Examples are prophylactic administration of antibiotics, intraperitoneal instillation of dextran, corticosteroid (Sravelos and Le, 1996), sodium citrate, heparin, prostigmine, olive oil, and antihistamines (Ellis, 1982). Organic (ox peritoneum) or bioabsorbable inorganic (Seprafilm, Genzyme Co., USA) membranes were used in order to apply mechanical separation of the peritoneal surfaces (Alponat *et al*., 1997). To the best of our knowledge, none of these therapies were found ideal and these materials had only limited success in prevention of intra-abdominal adhesion formation.

The use of honey as a medicine is mentioned in the most ancient written records.

In the modern medicine, many practitioners have noticed the effectiveness of honey in the healing of various types of wounds, burns and ulcers (Subrahmanyam, 1998).

Honey's high osmolarity, acidic pH, inhibin factor, and nutrient content contribute to its bacteriostatic properties and the promotion of wound healing (Subrahmanyam, 1991; Philips, 1993).

In the present study, although the mechanism of action of honey is still obscure, covering the damaged serosal surface of the descending colon with honey significantly decreased the development of post-operative peritoneal adhesion. This effect is thought to be due to two mechanisms: firstly, the increased healing process caused by honey is due to its physical and chemical properties such as high osmolarity, high acidity, high monosaccharides, low active water and nutrient content; secondly, mechanical separation of damaged peritoneal surfaces by honey. The latter property of honey is probably related to its high viscosity and hypertonicity and also delayed absorption of honey.

However, more detailed studies are needed to clarify the precise effects of honey on the tissue healing process.

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