



Evaluation of the effectiveness of sodium hyaluronate, sesame oil, honey, and silver nanoparticles in preventing postoperative surgical adhesion formation. An experimental study¹

Hamid Reza Khorshidi^I, Amir Kasraianfard^{II}, Amir Derakhshanfar^{III}, Siavash Rahimi^{IV}, Ali Sharifi^V, Hamid Reza Makarchian^{VI}, Manoochehr Ghorbanpoor^{VII}, Seyed Mohammad Reza Javadi^V

^IAssistant Professor, Department of Surgery, Medical Sciences, Hamadan University, Iran. Scientific and intellectual content of the study, Conception and design of the study, critical revision.

^{II}MD, Resident, Department of Surgery, Medical Sciences, Hamadan University, Iran. Technical procedures, manuscript writing.

^{III}Associate Professor, Department of Surgery, Medical Sciences, Hamadan University, Iran. Conception and design of the study, critical revision.

^{IV}MD degree, Faculty of Medicine, Medical Sciences, Mazandaran University, Sari, Iran. Acquisition of data, manuscript preparation.

^VAssistant Professor, Department of Surgery, Medical Sciences, Hamadan University, Iran. Critical revision, final approval.

^{VI}Assistant Professor, Department of Surgery, Medical Sciences, Hamadan University, Iran. Statistics analysis, manuscript preparation.

^{VII}Assistant Professor, Department of Surgery, Medical Sciences, Hamadan University, Iran. Analysis and interpretation of data, technical procedures.

Abstract

Purpose: To evaluate the effectiveness of sodium hyaluronate, sesame oil, honey, and silver nanoparticles in preventing of postoperative surgical adhesion formation.

Methods: Forty male Wistar rats were randomly assigned into five groups with eight rats in each group including control, hyaluronate, sesame, honey and silver groups. After two weeks the animals underwent laparotomy and were evaluated by two different blinded surgeons for severity of adhesions based on the two different classification scoring systems including Nair classification and cumulative adhesion scoring scale.

Results: The scores of severity of adhesions in the hyaluronate and sesame groups were significantly lower than the control group based on the Nair classification (both P-values = 0.02), however based on the cumulative adhesion scoring scale just the score of severity of adhesions in the hyaluronate group was significantly lower than the control group (P-value = 0.02). In the hyaluronate group the severity of adhesions was decreased by 48% based on the cumulative adhesion scoring scale.

Conclusions: Sodium hyaluronate and sesame oil may have a significant effect in preventing postoperative surgical adhesion formation.

Key words: Hyaluronic Acid. Sesame Oil. Tissue Adhesions. Honey. Nanoparticles. Rats.

■ Introduction

Postoperative surgical adhesion is a common consequence of intraperitoneal surgery which may lead to several complications such as adhesive small bowel obstructions, chronic abdominopelvic pain, and female infertility making a significant adverse impact on health care costs¹⁻³.

Many efforts have been made aiming to decrease the rate of postoperative surgical adhesion formation by using anti-inflammatory agents⁴, fibrinolytics⁵, anti-coagulants⁶, mechanical barriers⁷ and anti-biotics⁸. Recently, the anti-inflammatory effect of components of sesame oil has been investigated^{9,10}, although the effect on postoperative surgical adhesion formation has not yet been investigated. Hyaluronic acid which naturally coats serosal surfaces and provides a certain degree of protection from serosal desiccation may work as a mechanical barrier for adhesion formation¹¹. Silver nanoparticles with anti-bacterial properties has also been reported to be effective on postoperative surgical adhesion formation^{12,13}. Recently, honey -with a long history in medicine- has been suggested to have has anti-inflammatory, wound healing and anti-bacterial properties^{14,15}

We conducted the present experimental study aiming to evaluate the effectiveness of sodium hyaluronate, sesame oil, honey, and silver nanoparticles in prevention of postoperative surgical adhesion formation.

■ Methods

We conducted this experimental study after obtaining the approval of the Ethics committee of Medical Sciences, Hamadan University from 2015 to 2016.

Forty male albino Wister rats were studied with weight range of 200 - 220 grams.

They were housed in 21°C temperature and 60% ± 5 humidity and were kept for two weeks under above-mentioned condition for acclimation. Rat pellet and water was accessible *ad libitum*. Animals were randomly assigned into 5 groups with 8 rats in each group including control, hyaluronate, sesame, honey and silver groups.

All were anesthetized with ketamine 80 mg/kg and xylazine 10 mg/kg subcutaneously without use of antibiotic. Anterior abdominal wall was shaved and disinfected. A three cm incision was made and after mobilization of cecum and placing it on a wet gauze the cecum was scraped with a sterilized nylon toothbrush in one cm × one cm dimensions till the petechie was seen. Then, one mL of saline in the control group, one mL of 10% sodium hyaluronate solution in the hyaluronate group, one mL of sesame oil in the sesame group, one mL of undiluted and purely natural honey which was produced in Hamadan province in the honey group, and 100 ppm of silver with size range of 60 - 100 nm in the silver nanoparticles group were instilled on cecum.

After two weeks the animals were euthanized with diethyl ether, underwent laparotomy and were evaluated by two different blinded surgeons for severity of adhesions based on the two different classification scoring systems including Nair classification and cumulative adhesion scoring scale. Nair classification is defined as score zero for complete absence of adhesions, score one for single band of adhesion between viscera, or from viscera to abdominal wall, score two for two bands, either between viscera or from viscera to abdominal wall, score three for more than two bands between viscera or viscera to abdominal wall or whole intestines forming a mass without being adherent to abdominal wall, score four for viscera directly adherent to abdominal wall, irrespective of number and extent of adhesive bands. Cumulative

adhesion scoring scale is defined as point zero for no adhesion and one point for each of the followings: one adhesion band from the omentum to the target organ, one adhesion band from the omentum to the abdominal scar, one adhesion band from the omentum to another place, one adhesion band from the adnexa/epididymal fat bodies to the target organ, one adhesion band from the adnexa/epididymal fat bodies to the abdominal scar, one adhesion band from the adnexa/epididymal fat bodies to another place, any adhesive band other than described above, target organ adherent to the abdominal wall, target organ adherent to the abdominal scar, target organ adherent to the bowel, target organ adherent to the liver or the spleen, any other organ adherent. The final score is the accumulation of the points.

Statistical analyses were performed by using SPSS software (IBM SPSS Statistics for Windows, Version 20.0, IBM Corp., Armonk, NY, USA). Quantitative and qualitative data were analyzed using the Kruskal-Wallis and Mann-Whitney U test, respectively. Statistical significance was defined by $P < 0.05$.

Results

The frequency of scores of severity of adhesions in each group based on the Nair

classification is shown in Figure 1. As shown in Table 1, the scores of severity of adhesions in the hyaluronate and sesame groups were significantly lower than the control group based on the Nair classification, however based on the cumulative adhesion scoring scale just the score of severity of adhesions in the hyaluronate group was significantly lower than the control group. In the hyaluronate group the severity of adhesions was decreased by 48% based on the cumulative adhesion scoring scale. The scores of severity of adhesions in each group based on the cumulative adhesion scoring scale are box-plotted in Figure 2.

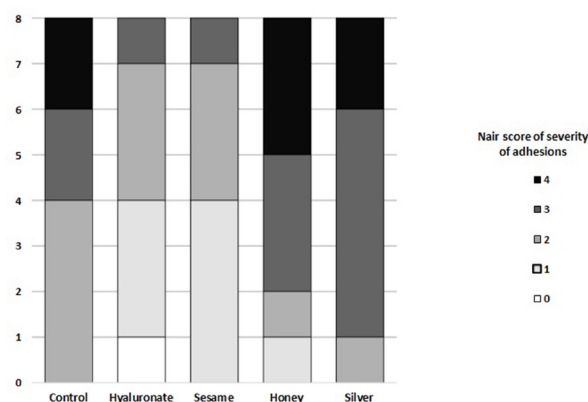


Figure 1 – The frequency of scores of severity of adhesions in each group based on the Nair classification.

Table 1 - The scores of severity of adhesions in each group based on the Nair classification and cumulative adhesion scoring scale.

	Nair classification	P-value*	Cumulative adhesion scoring scale	P-value
Control	2.5 ± 0.886		5.5 ± 2.6	
Hyaluronate	1.5 ± 0.926	0.02	3 ± 1.38	0.02
Sesame	1.5 ± 0.744	0.02	3 ± 1.18	0.07
Honey	3 ± 1.069	0.5	6.5 ± 2.33	0.49
Silver	3 ± 0.641	0.3	6.5 ± 2.56	0.49

*P-values are calculated by comparing each group with the contributed control group

**Data is shown as median ± standard deviation

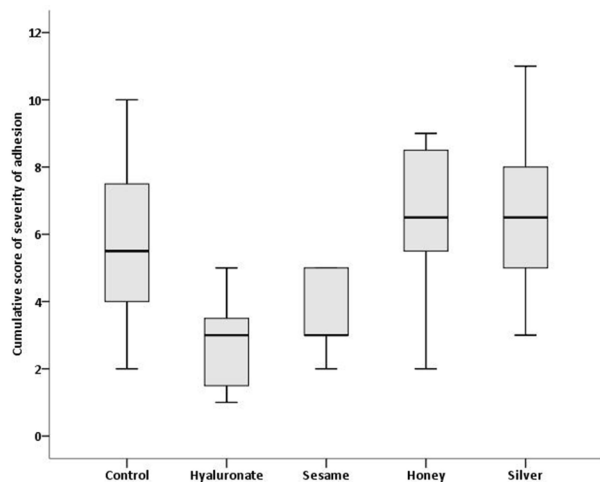


Figure 2 - The scores of severity of adhesions in each group based on the cumulative adhesion scoring scale.

■ Discussion

Adhesion band formation occurs after surgical insult to peritoneum. The damage causes an inflammation with fibrinous exudate that is rich in fibrin which activates the coagulation cascade resulting in thrombin activation and more fibrin deposition. Accumulated fibrocollagenous tissue acts as a matrix for fibroblasts, which produce collagen and further stabilize the adhesion band. Endothelial and mesothelial cells and macrophages produce plasminogen activators, specifically tissue plasminogen activator which converts plasminogen to plasmin that is responsible for fibrin degradation. In the process of adhesion band formation plasminogen activator inhibitor-1 deactivates tissue plasminogen activator¹⁶. Considering this mechanism efforts have been made to break this chain of causality for preventing postoperative surgical adhesion formation.

In our study sodium hyaluronate and sesame oil appeared to be the most effective

in preventing postoperative surgical adhesion. The effect of hyaluronate on postoperative surgical adhesion has been investigated before¹⁷⁻²⁰, all data suggest its role as an anti-adhesive agent but none have used our method of adhesion induction, drug treatment and adhesion band evaluation to show its efficacy. In our study design we investigated the effect of hyaluronic acid as a “free floating” molecule therefore we injected 1 ml of 10% sodium hyaluronate in peritoneal cavity. Thus, beside its direct barrier effect other properties as a signaling molecule is possible to be evaluated. Hyaluronic acid is a natural polysaccharide that can be found in most tissues and fluids of body. Several mechanisms have been suggested for its anti-adhesive properties. It can directly increase proliferation, migration and activation of mesothelial cells to injured area²¹. A possible receptor for hyaluronic acid-mesothelial interaction is cluster of differentiation 44²². Hyaluronic acid also may influence the mesothelial fibrinolytic capacity in response to monocyte-macrophage system and tumor necrosis factor alpha^{23,24}. Our observation indicates that sodium hyaluronate may have a direct biological effect on peritoneum and may suggest that the pathophysiology of postoperative peritoneal repair can be modulated.

Sesame oil obtained from *sesamum indicum* is rich in polyunsaturated and monosaturated fatty acids, which also contains high amount of lignans such as sesamin, sesamol, sesamolin and sesaminol²⁵. These agents have been found to exert anti-inflammatory and anti-oxidative properties²⁶⁻²⁸. Specifically, sesamin has been found to halt proinflammatory cytokine production²⁹. In our study we found that sesame oil may significantly reduce adhesion band formation in comparison to the control group based on Nair classification. Such result was not reproduced in cumulative

adhesion scoring scale, which may be due to methods of evaluation of severity of adhesions band evaluation methods, study design and population. Grading adhesion bands according to Nair is a widely used method of adhesion band evaluation but it is rather weak in distinguishing lesser differences and distinction in high-grade adhesions. Cumulative adhesion scoring scale is quantitative, less reliable on observer and more sensitive, the reason is cumulative adhesion scoring scale avoids the problem of ranking events and; it only counts them to form a sum suitable for statistical analysis. Despite the earlier investigations for adhesion prevention property of honey^{30,31}, we found no statistically significant results. This can be due to composition or physical characteristic of honey used in our study. Similarly, notwithstanding its anti-inflammatory and anti-microbial effect no significant result was seen in group received silver nanoparticles^{12,13}.

■ Conclusion

Sodium hyaluronate and sesame oil may have a significant effect in preventing postoperative surgical adhesion formation. However, the latter showed inconsistent data and needs further research to elucidate its role.

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Correspondence:

Seyed Mohammad Reza Javadi
Shahid Beheshti Boulevard, Besat Hospital
General Surgery Department, Hamadan, Iran
Phone: +988132640020
smrezajavadi@gmail.com

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¹Research performed at General Surgery Department, Besat Hospital, Medical Sciences, Hamadan University, Iran.
