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# Efficacy of Hyaluronic Acid for Reduction Post-surgical Adhesions Following Experimental Ventral Hernial Repair in Dogs

Wissam Abdullah Alhayani, Ahmed Sami Jarad, Majid A. Alkhilani,
Waleed Hamid Farhan and Khalid Hatem Aljumaily

***Abstract---*** *The point of this research was to assess productivity of hyaluronic acid (HA) for reducing post-surgical adhesions following Observational hernial ventral recovery in dogs. Twelve stable adult dogs were split at random through two equal groups (n=6). In group A(Control), a 3x3 cm of abdominal defect was made In dog's midline abdominal layer and polypropylene mesh reconstruc2on (PP) only, while in group B, , which a 3x3 cm of abdominal defect was made in the midline abdominal wall of dogs and reconstruc2on with PP mesh coated with HA. Clinical outcomes on the basis of post-surgical complica2ons including adhesion forma2on, pain evalua2on and mesh shrinkage after 8 weeks of mesh hernioplasty. The result showed the efficiency of HA for reducing adhesion forma2on with less pain and mesh shrinkage. In conclusions: The PP mesh coated with HA is acceptable and reliable for ventral repair in dogs with less post-surgical adhesion.*

***Keywords---*** *Hernia, Hyaluronic Acid, Polypropylene Mesh, Adhesions, Dogs.*

## I. INTRODUCTION

Hernia is a bulge of an organ or tissue from its usual space via an opening (Tiwari *et al*.,2004). The breach may be caused by a split in the abdomen, or a normal opening(JeSennavar *et al*.,2010).The hernia comprises of three sections, such as the ring, the sac and the contents (Read and Bellenger, 2003).ventral hernia is an acquired hernia that occurs due to blunt trauma, surgical trauma or overpressure at abdominal wall opera2on site (Anjum *et al*.,2016). Hernia can be diagnosed by observation, palpation, plain or contrast radiography and ultrasonography (Abdin-Bey and Ramadan, 2001). Hernia could be handled with a non-operative and surgical reduction; the non-surgical hernial reduction can be Bandage or irritant solutions applied around the hernial ring after physical hernia elimination. Herniorrhaphy is the surgical repair of a hernia by a primary closure of defects or by using permanent synthetic mesh material (Iqbal *et al*., 1994). The mesh is used for large hernial repairs and may reduce the risk of hernia come back and also provide tension free hernioplasty (Amed and Khan,1995) Polypropylene (PP) meshes are made of non-absorbable, braided monofilaments has been extensively used for hernia repair, it is associated with greater post-operative complication when placed directly over the intra-abdominal organs, and may lead to severe complications, Including an immune system response that leads in adhesion, leading to fibromyalgia (Baptista *et al*.,2000; Schumpelick and Klinge, 2003 and Lee *et a*l.,2005). However, many techniques were used to overcome intraabdominal adhesion forma2on such as topical application of honey (Jalali *et al*., 2006). Hyaluronic acid (HA)

*Wissam Abdullah Alhayani, Department of Veterinary Surgery and Obstetrics, College of Veterinary Medicine, University of Fallujah.*
*Ahmed Sami Jarad, Department of Pathology and Poultry Disease, College of Veterinary Medicine, University of Fallujah, Iraq.*
*E-mail: dr.ahmed.s.jarad@uofallujah.edu.iq*
*Majid A. Alkhilani, Department of Veterinary Surgery and Obstetrics, College of Veterinary Medicine, University of Fallujah.*
*Waleed Hamid Farhan, Department of Pathology and Poultry Disease, College of Veterinary Medicine, University of Fallujah, Iraq.*
*Khalid hatem ALjumaily, Student at College of Veterinary Medicine, University of Fallujah, Iraq.*

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Derivatives have proven effective in preventing post-operative adhesions in laboratory studies (Becker *et al*., 1996). Therefore, our research attempted to determine the utility of HA with polypropylene mesh for reducing abdominal adhesion of subsequent hernial recovery.

## II. Materials and Methods

### *1. Experimental Animal*

This work was carried out on 12 stable mature mixed breed dogs (8 ± 2.8) months old, weighing (20± 4.7) kg from both sexes. These dogs were split into two teams (n=6): group A, 3x3 cm defect produced in the abdominal wall close the umbilicus and rectified with HA-coated polypropylene (experimental group). Group B (control group) a 3x3 cm defect was made defect created in the site of abdominal wall close to the umbilical region and the flaw corrected by polypropylene received normal saline only.

### *2. Anesthesia*

Until anesthesia the dogs were fasted for 12 hours. Anesthetization of the animals by intramuscular injection of a xylazine mixture (1mg/ kg) (Adwia Company, Egypt) and ketamine (10 mg/kg) (Alfasan International Company, Holland) according to (Haskins et al., 1986).

### *3. Surgical Technique*

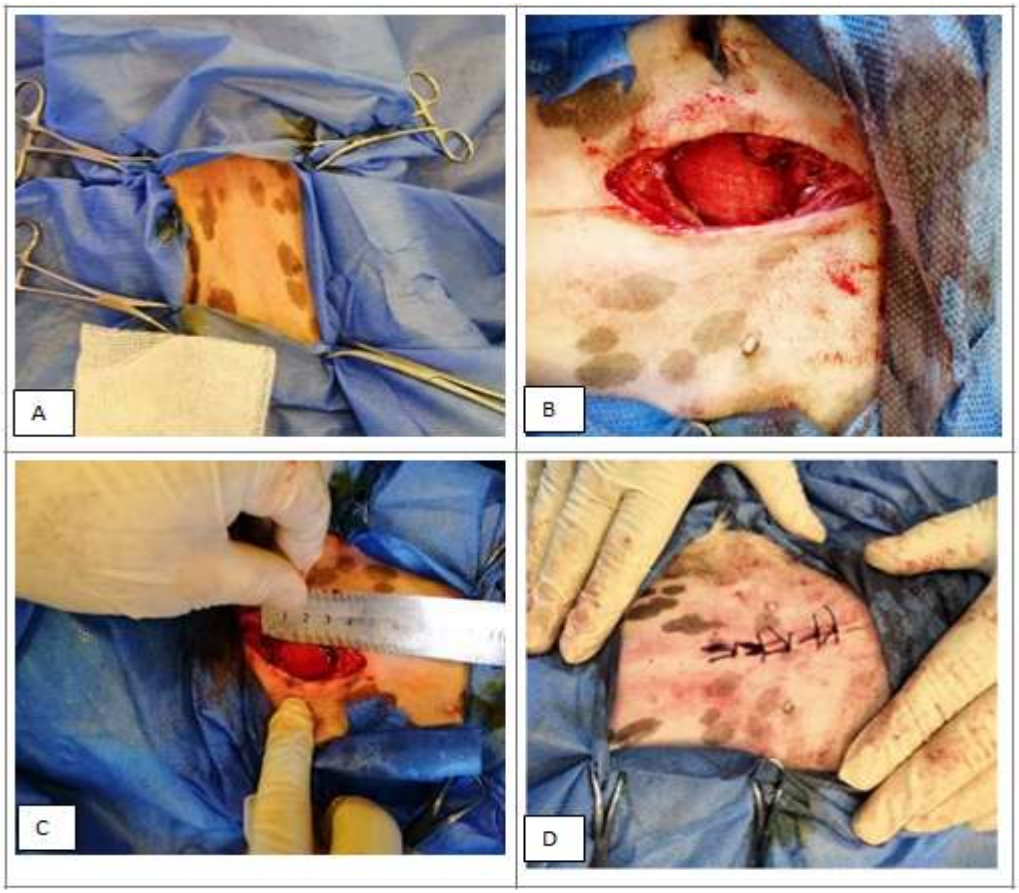


Fig. 1: Opera:on surgery in all Experimental Dogs

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The animals were prepared for aseptic surgery and submitted to surgical procedure to create a defect in the abdominal wall. A 6 cm midline incision was made over the umbilicus scar. The skin and subcutaneous tissue was dissected and reflected, then a 3x3 cm excision of rectus abdominis muscle and peritoneum was removed **(Fig. 1)**. In the group A, the abdominal defect was closed by fixing polypropylene (PP) mesh (Propy-Mesh® Atramat, Mexico) on muscle defect edge using no. 2 silk suture. While in the group B the abdominal defect was closed by PP mesh coated with sodium hyaluronic acid (HA) (Op2flex®, Moss Vision In., UK).

***4. Closure of Laparotomy Incision***

After successful mesh placement, length and width of the mesh were measured using a linear scale for calcula2on of mesh area at the 2me of mesh implanta2on. After this, Subcutaneous 2ssues were applied using polyglycolic suture (PGA) suture 3/0 (DemeTech Company, USA) in a con2nuous suture method. Eventually, the skin was sealed with a clear interrupted suture pattern u2lizing silk no.2 (Ethicon, USA; size 2).

***5. Postopera1ve Care***

The experimental dogs received five days of I.M path injec2on with an2bio2cs such as (penicillin-streptomycin 10,000 I.U./Kg BW and 15 mg / kg BW respec2vely) (Norbrook Company, UK). Dogs were kept in individual wire cages for two months under con2nuous clinical evalua2on.Mesh was removed from groups A and B, respec2vely, after the $8^{th}$ weeks, postsurgically. For mesh explanta2on, a laparotomy was performed under general anaesthesia. The defect in rectus muscle belly was re-opened and mesh removed, then rectus muscle belly, anterior rectus sheath, subcutaneous 2ssue and skin were closed as before.

***6. Parameters of Evalua1on***

***6.1. Adhesion Scoring***

Adhesions at the surgical site were assessed by two methods:

A. Adhesions were evaluated according to (Greca *et al*., 2001) Measuring the amount of mesh coated with adhesions (Table 1).

B. Adhesions were evaluated according to (Evans *et al*., 1993) to measure the strength of adhesion(Table 2).

C. Histology evaluation, six sample collected after 8 weeks from each groups including meshes with connected abdominal wall tissue immediately after wash with normal saline fixed in 10% NBF for 3 days to complete fixation and After routine tissue preparation to sections the sample and cut them at 4 to 6 micrometer and stained by hematoxylin and eosin to evaluated by a pathologist (Jarad *et al*., 2018).

***6.2. Pain Scoring***

Pain at the site of surgery was assessed post-operatively during regular examination and palpation in experimental groups one every two weeks all the end of experiment using a pain grading scale (Table 3). The pain grades were assigned according to (Anjum *et al*., 2016) depending on the severity of pain during examination.

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Table 1: Greca's Scoring System

| Scores | Percent adhesions |
|---|---|
| 0 | No adhesion |
| 1 | Less than 25% |
| 2 | 25%-50% |
| 3 | More than 50% |

Table 2: Evans's Scoring System

| Scores | Percent adhesions |
|---|---|
| 0 | No adhesion |
| 1 | Spontaneously separa:ng adhesions |
| 2 | adhesions separa:ng by trac:on |
| 3 | adhesions separa:ng by dissec:on |

Table 3: Pain Grading Scale for Assessment of Pain at Surgical Site

| Scores | Grades of pain |
|---|---|
| 1 | None |
| 2 | Mild |
| 3 | Moderate |
| 4 | Severe |
| 5 | Unbearable |

***6.3 Mesh Shrinkage***

The percentage mesh contraction was assessed according to (Byrd *et al*., 2011) by area measurements of the mesh, both at the time of surgery (implantation measurement) and at the end of experiment (explants measurement).

Percentage mesh contraction = (*Implantation Immepalasunrtaetmioenntm –eaesxuprleamnetsnt measurement*) x100

***7. Sta1s1cal Analysis***

The data gathered were analyzed using the Chi-square adhesion and pain scoring test and the Student's t quan2ta2ve data test (Mesh shrinkage) using SPSS statistical software (Version 25).Sta2s2cally important values of P= 0.05 were found.

## III. RESULTS

***1. Assessment of Adhesions***

Mesh repair sites in both the groups were intact but adhesions were found in all animals. Adhesions involving the omentum with different degree **(Fig. 2,3).** The results of the macroscopic assessment of adhesions are summed up in **(Fig. 5,6).**

The Histopathology result showed in **(Fig. 4. A,B, and C).** Group A histological analysis showed adherence of omentum to abdominal wall and polypropylene mesh meanwhile the group B histology examines showed less or no adherence with omentum and enhanced granula2on tissue formation.

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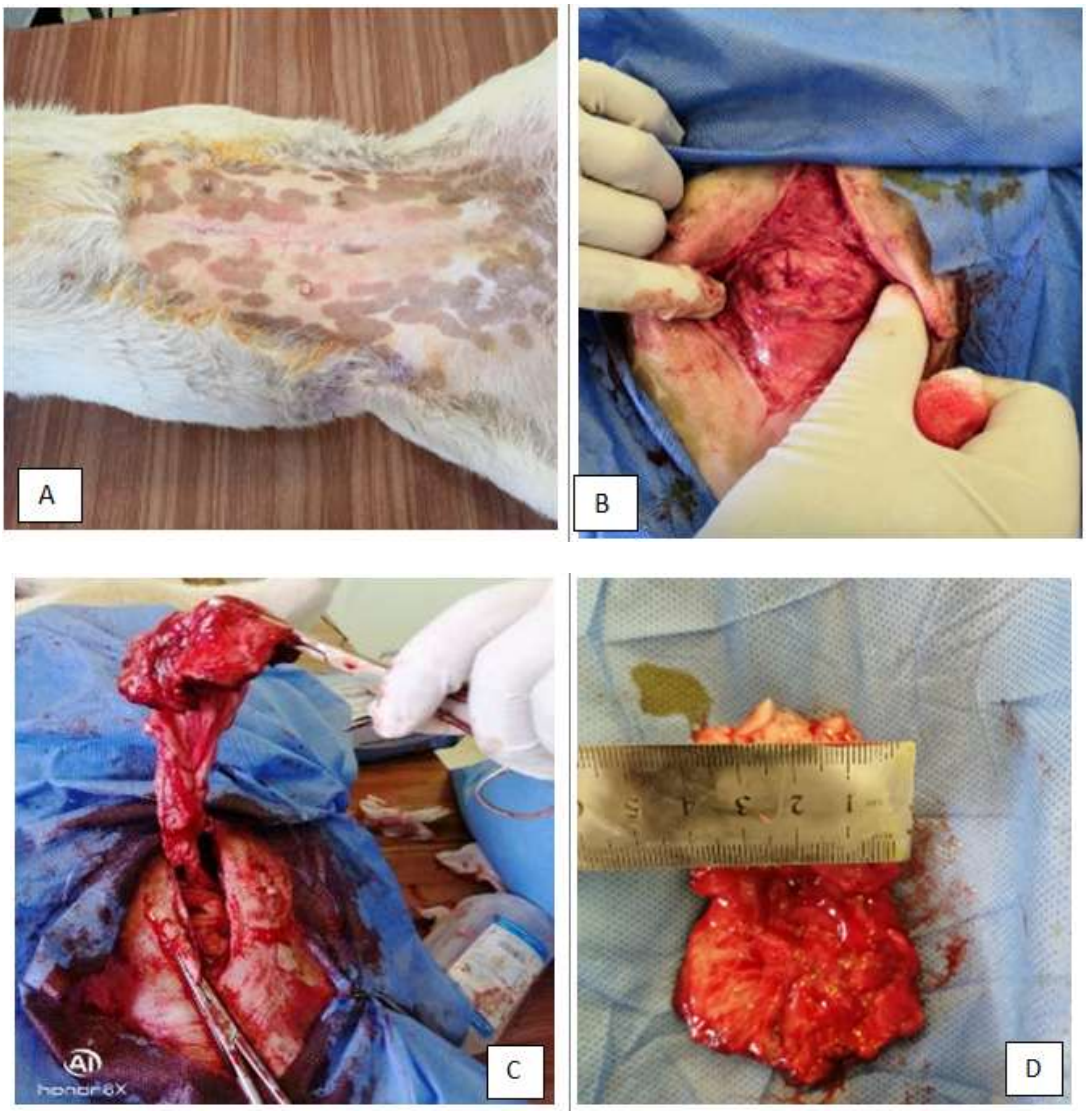
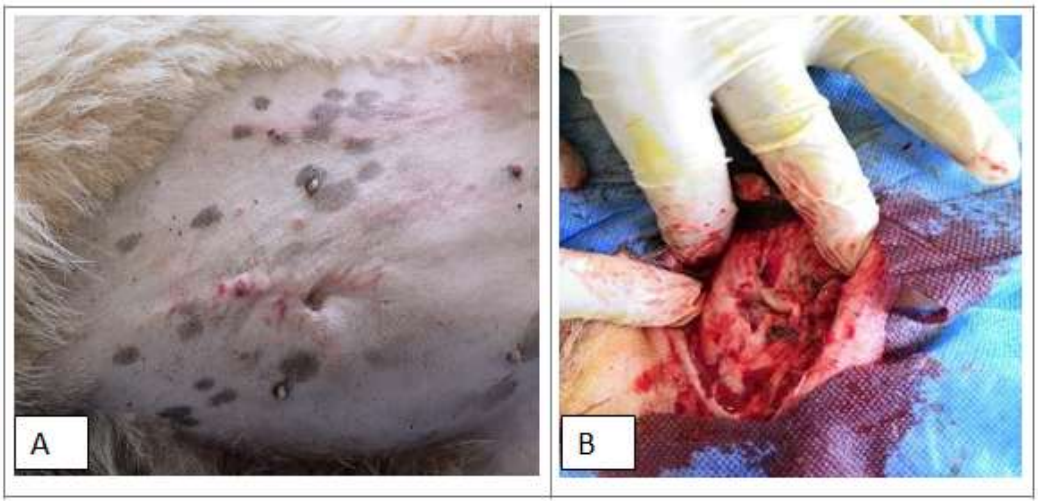



Fig. 2: Macroscopic Analysis and Adhesion Analysis in Group Later 8 Weeks of Surgery

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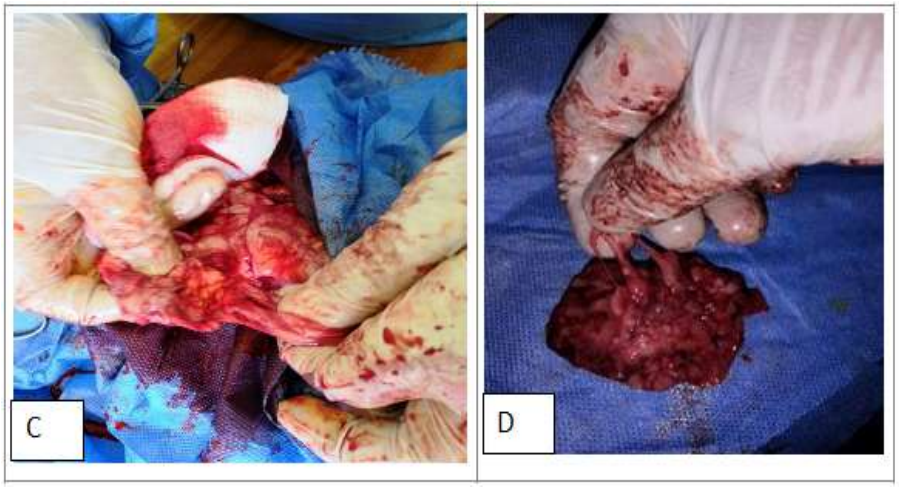


Fig. 3: Macroscopic Analysis and Adhesion Analysis in Group B later 8 Weeks of Surgery

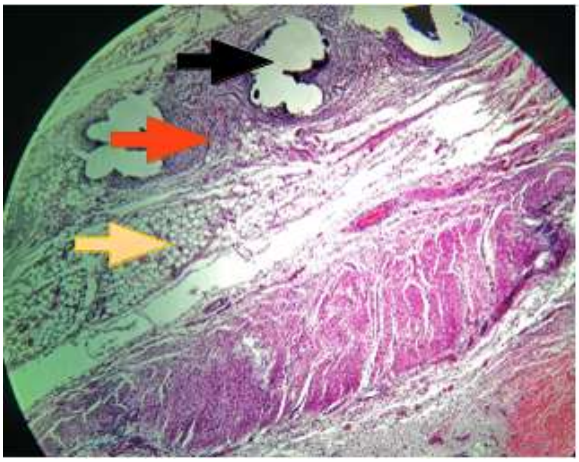

Fig. 4 A: Histophotographic from Group B at Site of Hernia Showed Mesh (Black Arrow) adhesions of omentom (Yellow Arrow) with Fibirosis Formation (Red Arrow) H&E Stain X4

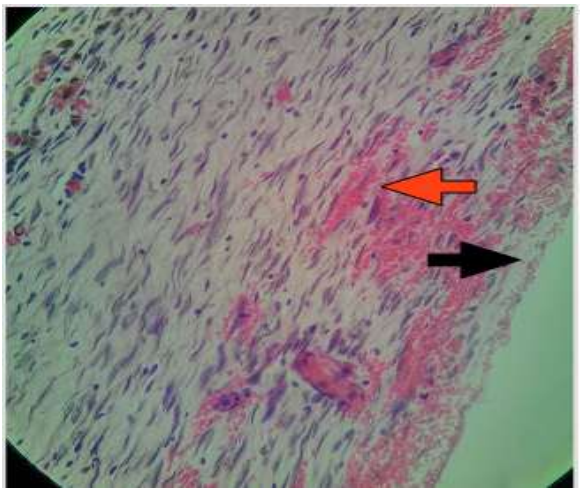

Figure 4: B. Histophotographic from group A at site of hernia showed no adherence at the edge site with (black arrow) with active angiogenesis (red arrow) H&E stain X

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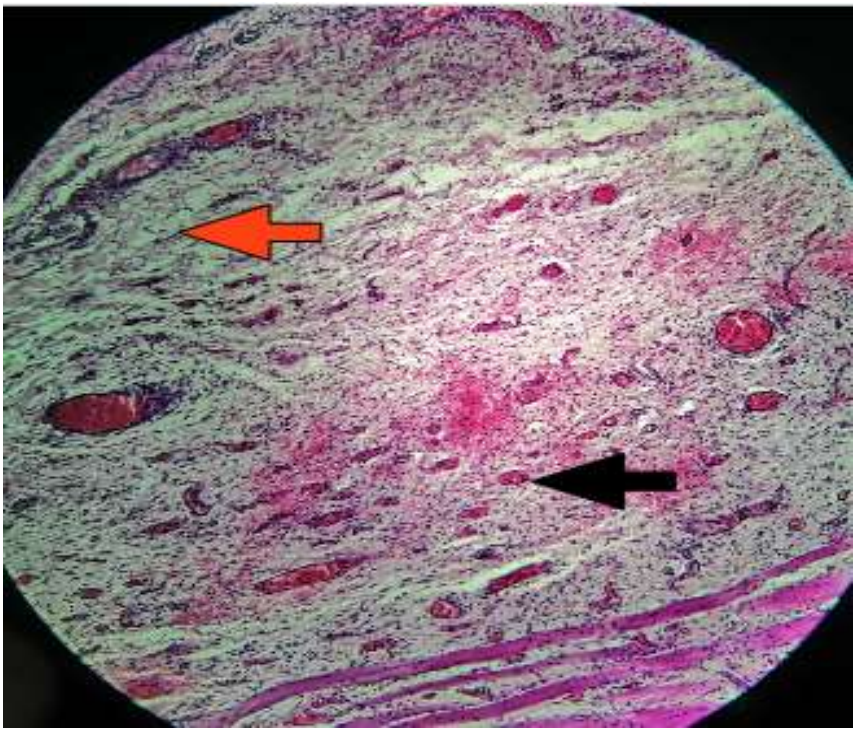

Figure 4: C. Histophotographic from group A at site of hernia showed granulation tissue formation include new blood vessels formation (black arrow) and fibroplasia (red arrow). H&E stain X10.

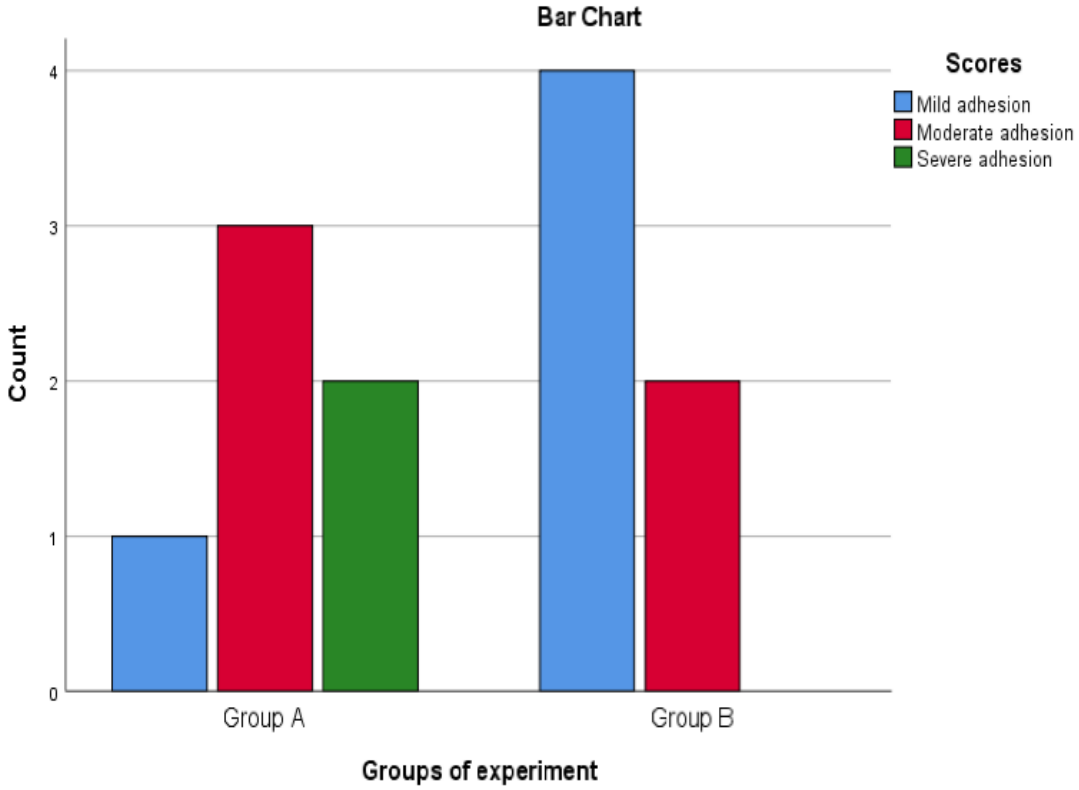


Fig. 5: Grading of intra-abdominal adhesions according on Greca's scoring system in the studied groups (P<0.05)

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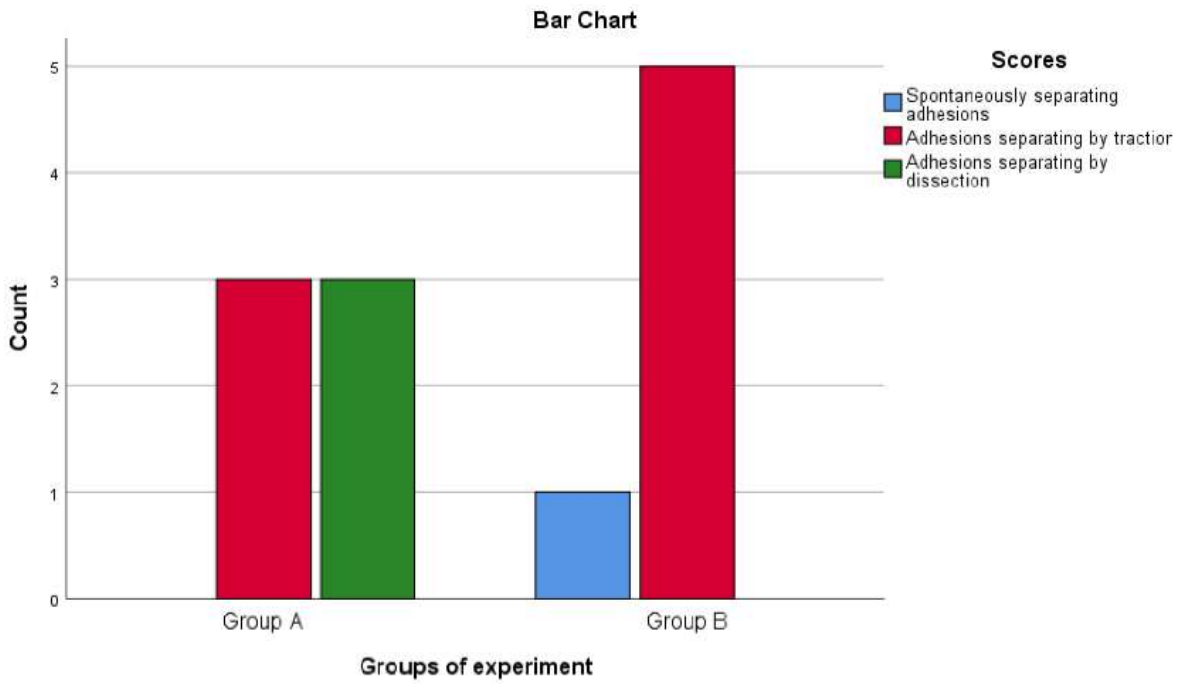


Fig. 6: Grading of intra-abdominal adhesions according on Evans's scoring system in the studied groups (P<0.05).

***2. Pain Scoring***

Pain in group B (P<0.05) was substan2ally weak, scoringin control manifested moderate pain, while in experimental group was mild pain.

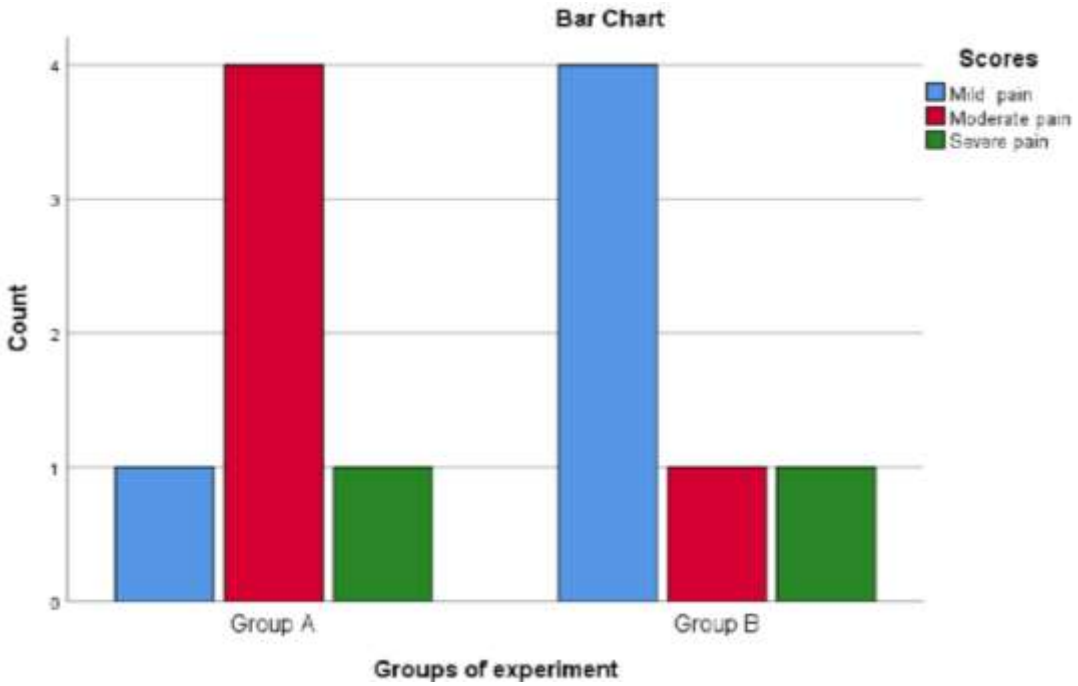


Fig. 7: Pain Scoring in Experimental Dogs (P<0.05)

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### *3. Mesh Shrinkage*

The area of each mesh at the time of insertion was (16±0.3) $cm^2$ in group A and (16±0.3) $cm^2$ in the group B. Calculation of the remaining mesh area at the time of biopsy showed more shrinkage in group A (13.5± 1.7) $cm^2$ than in the group B (14.6± 0.7) $cm^2$ (P<0.05) **(Table 4)**.

Table 4: Mesh Shrinkage in Experimental Groups (P<0.05)

| Groups | Area ($cm^2$) a: me of surgery | Area ($cm^2$) later 8 weeks | % Mesh Contra:on |
|---|---|---|---|
| Group A (control) | (16±0.3) | (13.5±1.7) | 15.62% |
| Group B | (16±0.3) | (13.5±1.7) | 8.75% |

## IV. DISCUSSION

Adhesions occur frequently after abdominal operations lead to bowel obstruction and chronic abdominal pain. Though the pathophysiology of adhesion crea2on is generally understood, there is still no absolute way to solve this issue **(**Vrijland *et a*l., 2002). In the our findings, the adhesion was significantly less in the dogs that received polypropylene (PP) mesh coated with HA compared with the control group that received PP mesh only. This finding is compatible with the findings of Vrijland et al., 2002, which conducted a randomized clinical trial to determine the importance of HA– Carboxymethyl cellulose membrane in reducing the incidence and severity of adhesions in human patients undergoing major abdominal surgery (Vrijland *et al*., 2002), also the histopathological results showed increase in healing rate (jarad et al., 2020), with decrease in adherence to mesh and this agreement with Burns *et al*.,(1996) and Yuan et al. (2016).

In our experimental study, level of postopera2ve pain was significantly decrease in group B at P<0.05. The results were in agreement with Nohuz *et al*., 2014 who reported adding the HA based compound Preserve surgical repair consistency and longevity, and rising postoperative discomfort in rat ventral hernia.

Mesh shrinkage was one of the most important parameters studied. PP mesh Shrinkage is a severe concern, as a major cause of discomfort and recurrence of pelvic or ventral hernia, mesh shrinkage manifested a statistically significant difference of P<0.05. Consequently, group B lesser mesh shrinkage than group A and due to its associated complications, was considered less advantageous and inferior. These findings also agree favorably with the reports of García-Ureña *et al*., 2007 who reported greater inflammatory reaction and mesh shrinkage in polypropylene mesh treatment. In conclusion that, the ventral hernia reconstruction with polypropylene mesh coated with hyaluronic acid is safer and more effec2ve with fewer post-operative complications and better outcomes as compared to the polypropylene mesh alone in experimental ventral hernia in dogs.

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