

Comparison of N-Acetyl cysteine and dexamethasone in enterotomy in cats

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ABSTRACT

Background: Peritoneal adhesions develop between organs and tissues. They are an intrinsic component of the recuperative mechanism of the body following surgical intervention or inflammation. N-acetyl cysteine is an affordable drug with a long history of safe usage and is commercially available. Dexamethasone is a long-acting synthetic corticosteroid exhibiting minimal mineralocorticoid action. The presence of a fluorine atom at C9 on the steroid ring is a defining characteristic.

Aim: This study aimed to conduct a comparative analysis of the effects of N-acetyl cysteine against dexamethasone on enterotomy in felines.

Methods: The efficacy of three substances—N-acetylcysteine (NAC), dexamethasone, and normal saline—was assessed for their potential to expedite intestinal healing post-surgery and inhibit adhesion formation. The study included 15 cats, evenly and randomly allocated into three groups. The intestines of cats were incised longitudinally (enterotomy) and subsequently closed with a simple continuous suture in each group. Upon completion of intestinal suturing, the surgical site in each group was irrigated with one of the three agents. The surgical wounds were then closed 3 days after surgery, and the abdomens of a whole cohort of cats were surgically reopened for direct observation. The animal administered the neutral solution displayed considerable intestinal adhesions. The cat administered with dexamethasone exhibited delayed healing along with minor adhesions. NAC-administered cats exhibited fast recovery with negligible edema.

Results: CBC assessment on the third postoperative day indicated an elevation in white blood cells (WBCs) levels in all cats. By the seventh postoperative day, all cats exhibited a significant to moderate reduction in WBC, particularly associated with N-acetyl cysteine. Computed tomography scans revealed adhesions in groups 1 and 2; however, no adhesions were observed in the NAC-administered group.

Conclusion: NAC has a beneficial effect on intestinal healing after surgery and adhesion prevention in this feline model.

Keywords: Dexamethasone, Enterotomy, Hemoglobin, N-acetylcysteine, WBC.

Introduction

Adhesions are fibrous tissue bands that develop between organs and tissues. They are an inherent component of the body's recuperative mechanism following surgical procedures or inflammation. Although generally benign, they might pose complications when they impede organ mobility. The causes include surgery, inflammation, trauma, radiation therapy, and congenital factors. Symptoms include abdominal pain, bloating, nausea, and vomiting; in extreme instances, intestinal obstruction may occur, and in females, adhesions can lead to infertility. Complications include intestinal blockage, prolonged stomach pain, and infertility. N-acetyl cysteine (NAC) is an affordable drug with

a long history of safe usage and is commercially available Aldini *et al.* (2018). N-Acetyl cysteine is not naturally occurring, but cysteine is an amino acid commonly found in foods such as chicken, turkey, eggs, yogurt, and garlic. NAC is a well-tolerated mucolytic agent that reduces the viscosity of mucus and improves the activity of glutathione S-transferase Aslan *et al.* (2017). The oral administration of this drug results in the de acetylation reaction of NAC during its transit through the small intestine and liver, leading to a 4%–10% reduction in bioavailability. NAC stimulates glutathione biosynthesis, acts directly as a free radical scavenger, and promotes detoxification. It functions as a potent antioxidant and a possible

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therapeutic alternative for illnesses (Youssef *et al.*, 2006). Dexamethasone is a prolonged-acting synthetic corticosteroid with minimal mineralocorticoid action. The presence of a fluorine atom at C9 on the steroid ring is a defining characteristic Lee *et al.* (2007). It is 25 times more efficacious than hydrocortisone. The pharmacologic effects may endure due to its intracellular activity, even after plasma concentrations decline. The onset of these effects may need up to 8 hours, and their duration may exceed 36 hours (Lee *et al.*, 2007). Adhesion-prevention strategies can be classified into three categories: minimizing injury through precise surgical techniques and reduced tissue trauma, employing physical barriers between peritoneal surfaces, and utilizing pharmacological agents to influence the cellular response to tissue injury. Aref-Adib *et al.* (2019).

The objective of a computed tomography acquisition is to quantify X-ray transmission through a subject from numerous perspectives.

Materials and Methods

Equipment and instruments

Anesthesia by (Xylazine and Ketamine mixture) intramuscular injection, and the dosage was 2.2 mg Xylazine and 10 mg ketamine, sterile surgical instruments, iodine, gauze, surgical drapes, polyglyactin suture size 20, nylon suture size: 30, antibiotic (penicillin), N-acetylcysteine (NAC), and dexamethasone.

Experimental animals

Fifteen adult (1 years) cats, weighing (1–2 kg) were utilized in this research. The cats were adjusted to their surroundings for 7 days leading up to the beginning of the study. The cats were housed in distinct cages within the animal facility of the University's College of Veterinary Medicine Basra and exposed to the same environment. The dogs were given vaccines and examined clinically to ensure they were healthy.

Experimental design

Animals will be divided into three groups after inducing enterotomy:

Group 1 (5 cats) treated with normal saline (5 cc) and repeated use after 3 days.

Group 2 (5 cats) was treated with dexamethasone and repeated use after 3 days (received 4.5 ml NS + 0.5 ml dexamethasone) (Pejman *et al.*, 2011).

Group 3 (5 cats) was treated with NAC (dose 140 mg/kg) and repeated after 3 days (NAC) was prepared aseptically according to the animal weight at 140 mg/kg per 1 kg body weight, and all animals of group C were weighed before NAC was applied directly to the defect) (Radhi and Abdulrazaq, 2022).

Surgical technique

1-Anesthesia and preparation: The cat is placed under general anesthesia, and the surgical area on the abdomen is shaved and cleaned (Fig. 1).

2-Abdominal Incision: The surgeon makes an incision along the ventral midline of the abdomen to access the small intestine.

3-Bowel isolation: The specific portion of the intestine requiring bowel opening is carefully identified and isolated using wet gauze pads.

4-Preventing leakage: Gentle pressure or painless clamps are applied to the intestine on either side of the intended incision site to reduce intestinal contents leakage using intestinal forceps.

5-Intestinal incision: A small incision is made into the lumen (the inside) of the intestine, usually on the ant mesenteric border (the side opposite the attachment to the mesentery). Incision length (5 cm) in all groups.

6-The bowel was closed using a simple continuous suture, starting with a triple stitch, using polyglactin suture, in a two-layer in-and-out pattern with closely spaced stitches to prevent leakage and bleeding (Fig. 2).

7-A neutral solution was injected near the suture line to check for any possible leakage in the suturing. There was no leakage.

8-The intestines and the wound area were washed with normal saline in the first group, dexamethasone was used in the second group, and an N-acetyl cysteine solution was used in the third group. Then, the intestines returned to their original position.



Fig. 1. Preparing the operating area.

- 9-Muscles were closed with a polyglactin suture in a simple, continuous pattern.
- 10-Then, the skin was closed with simple interrupted nylon sutures, ensuring that no dead space was left to prevent pus formation.

Postoperative care includes the following

Normal saline was given for the first 2 days instead of food by IV. Liquid diet (e.g., chicken soup) to follow. Daily intramuscular injection of 0.5 ml of penicillin for 3 days. The removal of stitches after 10 days.

Statistical analysis

The data were expressed as mean \pm standard deviation ($M \pm SD$), the experiments analyzed by using One-way ANOVA with SPSS (Special Program for Statistical System) version 21.0. The least significant difference test (LSD) was used to determine the differences between groups in the ANOVA test, the level significant set on ($p < 0.05$).



Fig. 2. Intestinal suturing with a simple continuous suture.

Ethical approval

The University of Basra College of Veterinary Medicine—Research Ethics Committee has recently reviewed your responses to comply with the ethical principles of the International Ethical Guidelines for Health-related Research Involving Humans or Animals prepared by the Council for International Organizations of Medical Sciences in collaboration with the World Health Organization, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research entitled "Ethical Principles and Guidelines for the Protection of Human Subjects of Research" (Belmont Report) for the project involving human and human specimens and must follow the framework of the Office International des Epizootics principles on animal ethics guidelines for the project involving animals and animal specimens according to approval number (120/37/2026) 8/1/2025.

Results

Clinical signs observed in different treatment groups

Group 1. Normal saline group

Cats in this group displayed prolonged lethargy, which lasted for more than 3 days. Patients experienced diarrhea for the initial 2 days after surgery. An elevated body temperature of 41°C was recorded. Wound healing was notably delayed. Arched back (kyphosis).

Group 2. Dexamethasone Group

Similar to the normal saline group, these cats exhibited prolonged. Diarrhea was present on the first postoperative day. By the second day, the feces had returned to normal. Wound healing is significantly delayed. Body temperature fluctuated within the range of 39°C–40°C.

Group 3. N-acetyl cysteine group

These cats exhibited lethargy for a shorter duration of 2 days. Normal fecal consistency was observed from the first postoperative day. Their body temperature ranged from 38°C to 39°C. This group exhibited faster wound healing than the other two groups.

Blood tests

White blood cells (WBCs)

The results of WBCs increased significantly ($p < 0.05$) in the NAC group on all days more than in the other groups, and within all groups, the WBCs increased significantly on day 7 more than 0 day (Table 1).

Table 1. Effect on WBC concentration (cell/mm³) in day 0, 3, and 7.

Groups	0 day	3 days	7 days
Group 1	3.34 \pm 1.33 Cb	4.38 \pm 2.14 Bb	13.16 \pm 6.39 Ba
Group 2	6.32 \pm 1.13 Bb	8.36 \pm 1.50 Ab	10.86 \pm 1.92 Ba
Group 3	1.52 \pm 10.24 Ab	9.22 \pm 1.75 Ab	14.00 \pm 5.59 Aa
LSD	3.00	3.98	10.54

Capital letters denote significant differences between groups at level ($p < 0.05$) ($M \pm S D$). Small letters denote significant differences within groups at level ($p < 0.05$) ($M \pm S D$).

Monocytes

The monocyte numbers increased in group n on days zero, three, and seven compared with the other experimental groups. Also, the concentration of Hb increased in groups d and n in day 3, while in day 7 increased in group c more than in the other groups, but there were no significant differences. However, Hb concentration increased significantly within group c on day 7 but significantly ($p < 0.05$) decreased within groups d and n on day 7 of treatment (Table 2).

Hemoglobin

The concentration of (Hb) increased in group d and n on day 3, while on day 7 increased in group c more than in the other groups, but no significant differences. But (Hb) concentration increased significantly within group c on day 7, but significantly ($p < 0.05$) decreased within groups d and n on day 7 of treatment (Table 3).

Red blood cells

showed the results of red blood cells (RBCs) concentration on days 0, 3, and 7 after treatments. RBCs increased significantly in group n more than in other groups on days 0, 3, and 7, but in group d, there were no significant differences with groups n and c, and

there was a less significant number of RBCs in group c. There were also no significant differences within the groups on days 0, 3, and 7 (Table 4).

Computed tomography (CT) scan

All the cats in the study underwent CT scans before surgery (Figs. 3 and 4) and again at 3 days (Figs. 5–7) and 7 days (Figs. 8–11) postoperatively.

From these results, we conclude that the active substance used, NAC, and simple continuous suturing have shown positive results in preventing adhesion formation (Table 5).

Macroscopic examination

On the 3 day of the surgical procedure, a laparotomy was performed on a cat treated with normal saline and compared with a cat treated with NAC (Pejman *et al.*, 2011), and the results of group (1) show sever adhesion (Fig. 12A and B) compared with group (2,3) that absence of adhesion (Fig. 13A and B).

Discussion

The results of our investigation indicated that the NAC group outperformed the other groups in terms of clinical signs, demonstrating lethargy for a shorter

Table 2. Effect on monocyte concentration ($10^9/L$) on days 0, 3, and 7.

Groups	0 day	3 days	7 days
Group 1	0.40 ± 0.33 Bb	0.55 ± 0.32 Cb	1.48 ± 0.68 Ba
Group 2	0.74 ± 0.35 Bc	1.22 ± 1.34 Bb	4.64 ± 1.10 Aa
Group 3	2.14 ± 1.16 Ab	2.10 ± 2.40Ab	3.18 ± 1.42 Aa
LSD	1.40	1.60	1.70

Capital letters denote significant differences between groups at level ($p < 0.05$) ($M \pm S D$). Small letters denote signify differences within groups at level ($p < 0.05$) ($M \pm S D$).

Table 3. Effect on Hb (g/dl) concentration at 0, 3, and 7 days.

Groups	0 day	3 days	7 days
Group 1	8.88 ± 1.55 Bb	8.58 ± 1.26Bb	10.26 ± 1.35Aa
Group 2	10.06 ± 1.37 Aa	10.84 ± 2.05ABa	9.76 ± 1.00Aa
Group 3	11.00 ± 1.24 Aa	11.78 ± 1.73Aa	9.88 ± 1.66Ab
LSD	1.18	3.19	NS

Capital letters denote significant differences between groups at level ($p < 0.05$) ($M \pm S D$). Small-letters denote significant differences within groups at level ($p < 0.05$) ($M \pm S D$).

Table 4. Effect on RBC ($\times 10^9/l$) concentration on days 0, 3, and 7.

Groups	0 day	3 day	7 day
Group 1	7.04 ± 0.29 Ba	7.40 ± 0.97 Ba	7.55 ± 0.52 Ba
Group 2	8.14 ± 1.21 ABa	8.21 ± 0.99 Aba	8.28 ± 1.25 Aba
Group 3	9.16 ± 1.34 Aa	9.01 ± 1.02 Aa	8.34 ± 0.84 Ab
LSD	2.12	1.61	1.14

Capital letters denote significant differences between groups at level ($p < 0.05$) ($M \pm S D$). Small letters denote significant differences within groups at level ($p < 0.05$) ($M \pm S D$).



Fig. 3. During the computed tomography scan, the cat was placed under general anesthesia in a dorsal recumbent position.

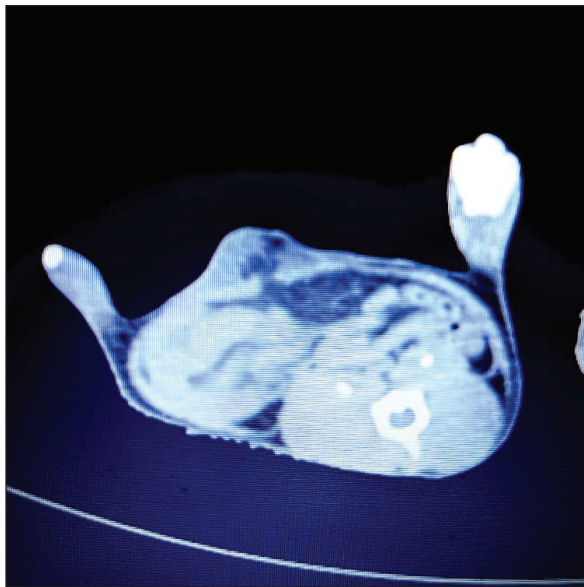


Fig. 4. Normal view pre-surgery (0 time).

duration of 2 days. Normal faecal consistency was noted from the first postoperative day. The present temperature diminished after 2 days in the treatment group, indicating a reduction in inflammation due to the administration of NAC Shahzamani *et al.* (2021), Zomorodi *et al.* (2011). In contrast, the control group exhibited an elevated temperature for 7 days, consistent

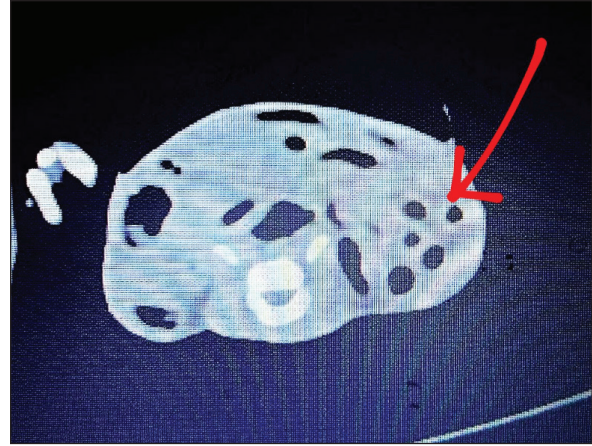


Fig. 5. Cat treated with normal saline after 3 days (severe adhesions).

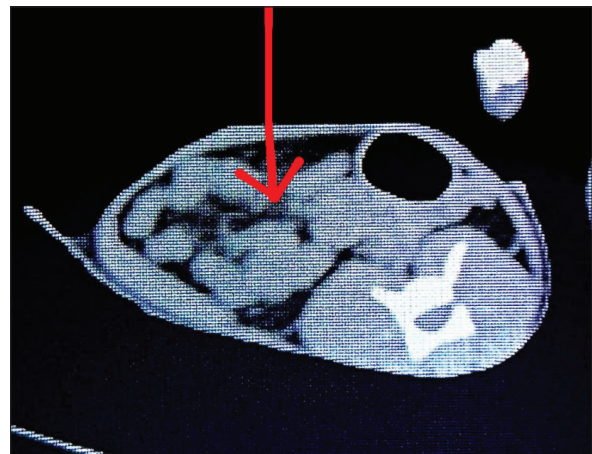


Fig. 6. Cat treated with dexamethasone after 3 days (severe adhesions).



Fig. 7. Cat treated with N-acetyl cysteine after 3 days (mild adhesions).

with the findings of Abdulrazaq *et al.* (2020). This group had accelerated wound healing relative to the other groups. Gross inspection at the surgical site after 3 days revealed that the NAC-treated group had no

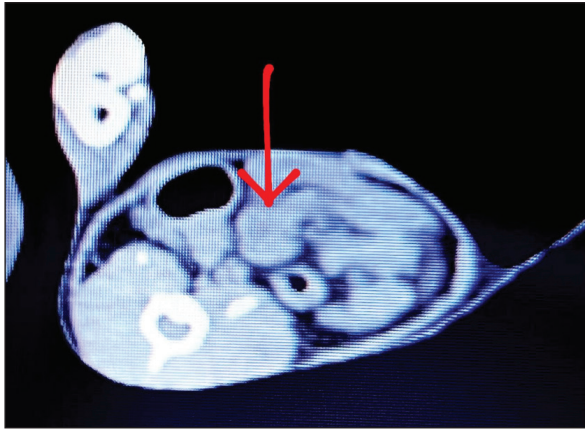


Fig. 8. Cat treated with normal saline after 7 days (severe adhesions).

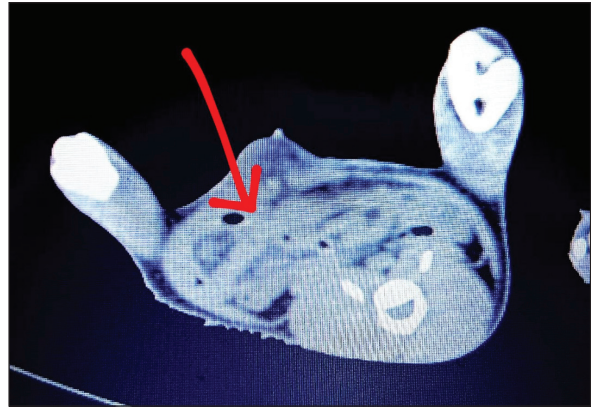


Fig. 10. Cat treated with N-acetylcysteine after 7 days (normal).



Fig. 9. Cat treated with dexamethasone after 7 days (mild adhesions).



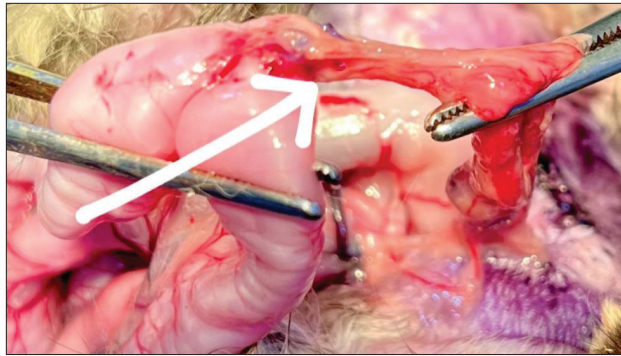
Fig. 11. Cat treated with N-acetylcysteine after 7 days (normal).

Table 5. CT scan analysis.

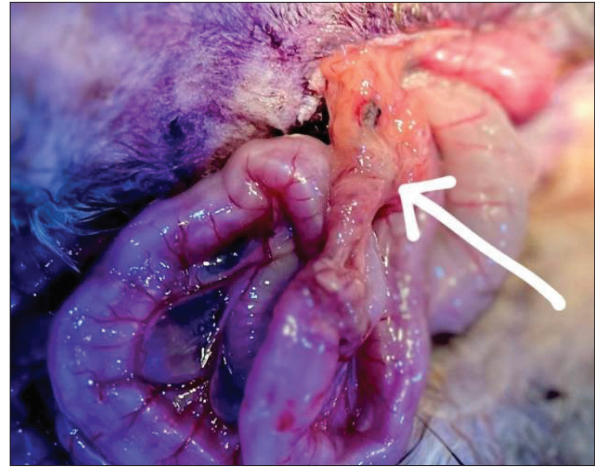
CT scan	0 Day	3 Day	7 Day
Group 1	+	+++	+++
Group 2	+	+++	++
Group 3	+	++	+

adhesions between the intestine and adjacent organs in the abdominal cavity or between the intestine and peritoneum. The intestinal lining in the treated group was healthier than that in the control group, corroborating the findings of Aktunc *et al.* (2010). Postoperative peritoneal adhesions represent a significant complication following intra-abdominal surgery,

resulting in potentially life-threatening conditions and various issues that disrupt normal gastrointestinal function, including severe rigidity and intestinal obstruction, which can lead to chronic abdominal and pelvic pain (AlQadhi and Al-Hasan, 2013; Karimi *et al.*, 2016). Approximately 60%–90% of individuals after abdominal surgery develop intraperitoneal



(A)

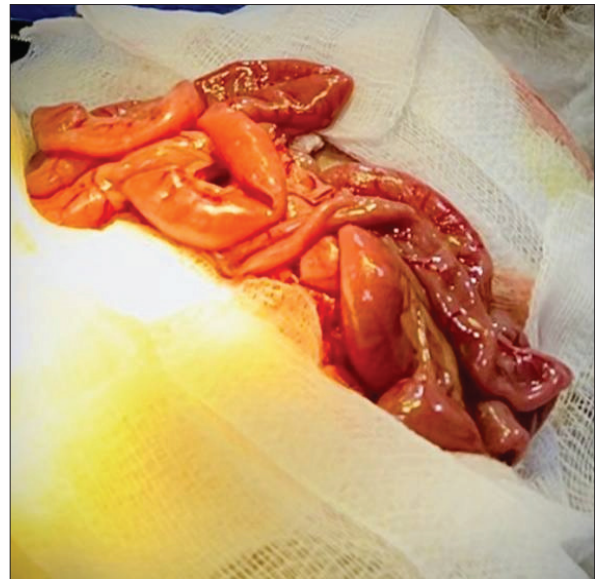


(B)

Fig. 12. A and B: The control group showed severe adhesions.



(A)



(B)

Fig. 13. A and B: the N -acetyl cysteine group showed no adhesions.

adhesions, frequently necessitating a subsequent surgical intervention for their removal (Parsaei *et al.*, 2013). In recent years, numerous initiatives have been undertaken to prevent or address this issue, and various substances have been evaluated for this purpose, including glucocorticoids, heparin, dextran 70, normal saline, antibiotics, promethazine, antihistamines, antioxidants, prostaglandin synthesis inhibitors, lactated Ringer's solution, calcium channel inhibitors, streptokinase as a fibrinolytic agent, rofecoxib as a cyclooxygenase inhibitor, methyl blue, and octreotide. Regrettably, no agent can successfully avert peritoneal adhesions during intra-abdominal surgery (Parsaei *et*

al., 2013; Karimi *et al.*, 2016). Post-surgical adhesions may arise from various sources, including surgical trauma, tissue ischemia, and foreign substances, all of which compromise tissue integrity and subsequently lead to inflammation, cytokine release, and oxidative stress that trigger adhesion development. Adhesion fibroblasts acquire a my fibroblast phenotype, and it has been demonstrated that these mesothelial cells react to cytokines and extracellular matrix signalling, thereby facilitating the my fibroblast phenotype (Parsaei *et al.*, 2013; Karimi *et al.*, 2016). N-acetyl cysteine comprises L-cysteine and glutathione, which diminish reactive oxygen species. N-acetyl cysteine dramatically

reduces peritoneal oxidative stress by directly altering membrane-associated oxidases. Chu *et al.* (2011) demonstrated that NAC intraperitoneal treatment decreased adhesion formation while enhancing peritoneal fibrinolytic activity and antioxidant defences, without affecting normal anastomotic wound healing (Chu *et al.*, 2011). Furthermore, Moon *et al.* (2010) demonstrated that NAC effectively diminished the oxidative burst of neutrophils, RhoA activity, and myeloperoxidase activity, alleviating oxidative stress and inflammation. Ion. Aslan *et al.* (2017) assessed the impact of localized NAC treatment on intra-abdominal adhesion development following laparotomy in rats. The results demonstrated a considerable reduction in tissue fibrosis and inflammatory cells after 10 days, consequently inhibiting adhesion. Our investigation yielded comparable findings, particularly among the NAC group after 3 days. The present study employed nanoscience due to the rising application of modern technology, particularly in the creation of Rascals. NAC particles possess distinct biological and chemical characteristics relative to their bigger equivalents (Hala *et al.*, 2021). The impact of NAC on the blood profile revealed no significant variations in RBC and WBC counts before and after the surgical intervention; however, a substantial rise ($p < 0.05$) in haemoglobin concentration was observed in the NAC-treated groups 7 days postoperatively. Ion. Furthermore, significant increases ($p < 0.05$) in monocyte levels were observed in the control group at 7 days postoperatively; however, no increases were detected in the NAC-treated group (Moon *et al.*, 2010). Radhi and Abdulrazak (2022) demonstrated that NAC significantly influences cell proliferation and repair when lied. It engulfs and eliminates invading pathogens via phagocytosis and intracellular destruction; monocyte elevation during inflammation is a vital component of the immune response. These cells are summoned to the locus of injury or infection, where they facilitate pathogen elimination and tissue restoration via phagocytosis and diverse inflammatory media secretion. Monocytes execute phagocytosis and then mature into macrophages within tissues, which are extremely effective phagocytic cells essential for resolving the inflammatory cess. The antioxidant and anti-inflammatory properties of NAC serve as the molecular basis for addressing numerous conditions linked to oxidative stress and inflammation. The primary antioxidant action of NAC is its ability to augment intracellular glutathione (GSH) levels, the essential bio thiol that regulates cellular redox equilibrium. Rum. As an anti-inflammatory agent, NAC suppresses the activity of nuclear factor kappa B, thereby reducing the concentrations of tumour necrosis factor-alpha and interleukins (IL-6 and IL-1 β). Notwithstanding the considerable therapeutic potential of NAC, its efficacy in clinical trials targeting diverse pathological conditions remains limited, as indicated by extensive experimental studies (2018). NAC is

a pharmaceutical agent that provides bioavailable cysteine for glutathione restoration and mitigating oxidative damage and inflammation. It also results in the synthesis of GSH in the body (Abd Alrahma *et al.*, 2020 Hiba M. Abd Alrahma *et al.*, 2020). The CT scan demonstrated positive effects in reducing adhesion development when uncomplicated. Computed tomography is the preferred imaging modality for the diagnosis of small-bowel obstruction (SBO) and postoperative intra-abdominal adhesions (PIA). Adhesions are probable when CT verifies the existence of SBO and does not identify a reason (Delabrousse *et al.*, 2009; Gremillet *et al.*, 2022). Differentiating PIA leading to SBO from functional ileus, commonly observed post-abdominal surgery. Therefore, CT may be advantageous in confirming adhesive obstruction while also identifying other mechanical obstruction causes and localizing the obstruction's site and level (Angle *et al.*, 1963; Mak *et al.*, 2006; Ong *et al.*, 2020). The extensive utilization of CT and recognition of the elevated prevalence of PIA-induced SBO can assist surgeons in identifying early postoperative SBOs and formulating suitable treatment strategies, particularly when the evident causes of mechanical SBOs remain unknown in patients with a surgical history (Ong *et al.*, 2020). In comparison to many human research (Attard and MacLean, 2007). Consequently, in our investigation, the topical application of NAC to the intestinal incision and during CT imaging did not reveal adhesions, representing a principal strategy to prevent PIA, which can lead to SBO Majeed *et al.* (2021).

Conclusion

1. The results indicate that NAC has shown promising effectiveness in reducing the rate of postoperative intestinal adhesions.
2. NAC accelerates the healing process compared with other methods.

Acknowledgments

The University of Basra Veterinary Medicine staff provided assistance with the surgical procedures, for which the authors are grateful. We also thank the laboratory staff for their assistance in processing and analysing the tissue samples.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

The authors received no financial support for the research, authorship, and publication of this article.

Authors' contributions

Abdulrazaq, A. W.: Conceptualization, surgical procedures, and original draft preparation. Rafid M. Naeem: Methodology, supervision, and formal analysis of the manuscript. Ali W. Sadeq: Data

curation, histopathological sample preparation, and software development. Alaa A. Ibrahim and Hiba M Abdulrahman: I have read and agreed to the published version of the manuscript.

Data availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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