Konuralp Medical Journal
Konuralp Tıp Dergisi
2026;18(1):43-48.
https://doi.org/10.18521/ktd.1788811
e-ISSN: 1309-3878
https://dergipark.org.tr/en/pub/ktd



Research Article

Protective Effects of N-Acetylcysteine, Carvedilol, and Paricalcitol in a Rat Model of Peritoneal Fibrosis

Kürşad Öneç[1*], Özgür Ekinci[2], Özge Tuğçe Paşaoğlu[3], Kadriye Altok[4]

[1] Duzce University, Faculty of Medicine, Department of Nephrology, Duzce, Türkiye. ror.org/04175wc52

[2] Gazi University, Faculty of Medicine, Department of Medical Pathology, Ankara, Türkiye. ror.org/054xkpr46

[3] Gazi University, Faculty of Medicine, Department of Biochemistry, Ankara, Türkiye. ror.org/054xkpr46

[4] Gazi University, Faculty of Medicine, Department of Nephrology, Ankara, Türkiye. ror.org/054xkpr46

*Corresponding author: kursadonec@gmail.com

Received: 22.09.2025
Revision: 22.12.2025
Accepted: 06.02.2026
Online: 24.03.2026

ABSTRACT

Aim: This study aimed to evaluate the potential protective effects of paricalcitol, N-acetylcysteine (NAC), and carvedilol in a rat model of chlorhexidine gluconate–induced peritoneal fibrosis.

Material and Methods: Thirty-six female Wistar albino rats were randomized into six groups (n=6 each). Peritoneal fibrosis was induced with daily intraperitoneal chlorhexidine gluconate injections for 21 days. Treatment groups received paricalcitol, NAC, or carvedilol, alone or in combination. Serum TGF-β1 levels and histopathological parameters (peritoneal thickness, fibrosis, inflammation, vascularization) were assessed.

Results: Serum TGF-β1 was significantly higher in the chlorhexidine group compared to controls (58.29 ± 4.40 vs. 49.06 ± 2.35 ng/mL, $p<0.05$). NAC significantly reduced TGF-β1 compared to chlorhexidine alone (46.76 ± 4.79 ng/mL, $p<0.05$). Peritoneal thickness was markedly increased in the chlorhexidine group (245 ± 27.3 µm vs. 22.3 ± 2.6 µm in controls, $p<0.01$) but attenuated by NAC (169.8 ± 30.8 µm, $p<0.01$) and carvedilol (146.5 ± 43.1 µm, $p<0.01$). Fibrosis and inflammation scores were also reduced in NAC and carvedilol groups (all $p<0.05$). Paricalcitol alone showed only partial and non-significant effects.

Conclusions: NAC demonstrated consistent antifibrotic and anti-inflammatory effects, while carvedilol provided moderate benefit and paricalcitol had limited efficacy. These findings suggest that antioxidant therapy, particularly NAC, may represent a potential strategy for preserving peritoneal membrane integrity, though further studies are warranted.

Keywords: Peritoneal fibrosis, peritoneal dialysis, n-acetylcysteine, carvedilol, paricalcitol.

INTRODUCTION

End-stage renal disease (ESRD) remains a major global health challenge with rising prevalence, high mortality, and substantial morbidity (1). Renal transplantation is considered the gold standard treatment; however, the scarcity of suitable donors necessitates dialysis as a long-term renal replacement therapy for many patients (2,3). Peritoneal dialysis (PD) is widely used as an effective and feasible modality for ESRD, yet long-term exposure to high-glucose dialysate solutions, recurrent peritonitis, and bio-incompatible fluids result in progressive structural alterations of the peritoneal membrane, the most critical of which is peritoneal fibrosis (PF) (4,5).

Peritoneal fibrosis is characterized by thickening of the submesothelial zone, extracellular matrix (ECM) accumulation, angiogenesis, and chronic inflammation, ultimately leading to ultrafiltration failure and reduced dialysis efficiency (6). In severe cases, this process culminates in encapsulating peritoneal sclerosis, a rare but life-threatening complication associated with bowel obstruction and significant morbidity (7). Despite its clinical significance, reliable biomarkers for early prediction of PF are limited, and no established pharmacological therapies are currently available to reverse advanced fibrosis (8). Therefore, preventive and disease-modifying strategies remain a major unmet need.

Among molecular mediators, transforming growth factor-beta 1 (TGF-β1) plays a central role in fibrogenesis through fibroblast activation, myofibroblast differentiation, and promotion of ECM deposition. Experimental approaches targeting the TGF-β1 pathway, as well as agents with anti-inflammatory and antioxidant properties, have been investigated in models of PF. Angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, immunosuppressants, and various antifibrotic molecules have shown promise, but their clinical applicability is often limited by safety concerns or insufficient long-term efficacy (9).

In this context, several agents already in clinical use for other indications have attracted attention for their potential antifibrotic properties. N-acetylcysteine (NAC), a precursor of intracellular glutathione, exerts potent antioxidant activity and has been shown to inhibit TGF-β1-mediated profibrotic signaling. Carvedilol, a non-selective β-blocker with additional α1-adrenergic blocking and antioxidant properties, has demonstrated protective effects against fibrosis in cardiac, hepatic, and renal experimental models (10,11). Paricalcitol, a selective vitamin D receptor activator widely prescribed for mineral and bone disorders in ESRD, has been reported to attenuate renal and cardiac fibrosis through modulation of TGF-β1 and related pathways (12,13).

Given these promising preclinical findings, the present study was designed to investigate the protective effects of

Cite as: Öneç K, Ekinci Ö, Paşaoğlu ÖT, Altok K. Protective effects of N-Acetylcysteine, carvedilol, and paricalcitol in a rat model of peritoneal fibrosis. Konuralp Med J. 2026;18(1):43-48. doi:10.18521/ktd.1788811.

This is an open access paper distributed under the terms and conditions of the Creative Commons Attribution-NonCommercial 4.0 International License.

paricalcitol, NAC, and carvedilol, alone or in combination, in a rat model of chlorhexidine gluconate–induced peritoneal fibrosis. Understanding the potential of these well-established agents may provide new insights into preventive strategies and translational opportunities for preserving peritoneal membrane function in patients undergoing long-term PD.

MATERIAL AND METHODS

Study Design and Ethical Approval

This study was conducted as a prospective, randomized, and controlled experimental investigation. Ethical approval was obtained from the Gazi University Animal Research Ethics Committee (Project No: 12081, Date: 25/09/2012, Approval Code: 141-18973). All procedures complied with the ARRIVE guidelines, and every effort was made to minimize animal suffering throughout the experiment.

Animals and Housing

Thirty-six female Wistar albino rats, six weeks old and weighing an average of 240 ± 13 g, were used. The animals were housed in polycarbonate cages under controlled conditions with a room temperature of 22–25 °C, relative humidity of 55 ± 10%, and a 12-hour light/dark cycle. Standard chow and water were provided ad libitum. Daily monitoring included health status and body weight assessment to ensure welfare and consistency across the study.

Experimental Groups and Interventions

The rats were randomly divided into six groups, each consisting of six animals, and followed for 21 days. Peritoneal fibrosis was induced by daily intraperitoneal injections of 0.1% chlorhexidine gluconate at a dose of 10 ml/kg dissolved in 15% ethanol. Group 1 received chlorhexidine gluconate alone. Group 2 received chlorhexidine gluconate together with paricalcitol at a dose of 0.2 µg/kg/day administered subcutaneously. Group 3 was treated with the same paricalcitol regimen combined with N-acetylcysteine at a dose of 450 mg/kg/day delivered in drinking water. Group 4 received chlorhexidine gluconate together with N-acetylcysteine alone, while Group 5 was treated with chlorhexidine gluconate and carvedilol at a dose of 10 mg/kg/day by oral gavage. Group 6, serving as the control, was administered physiological saline at 2 ml/day intraperitoneally. At the macroscopic level, the peritoneum of control rats appeared smooth, thin, and translucent, while the chlorhexidine group displayed marked thickening and opacification (Figure 1).

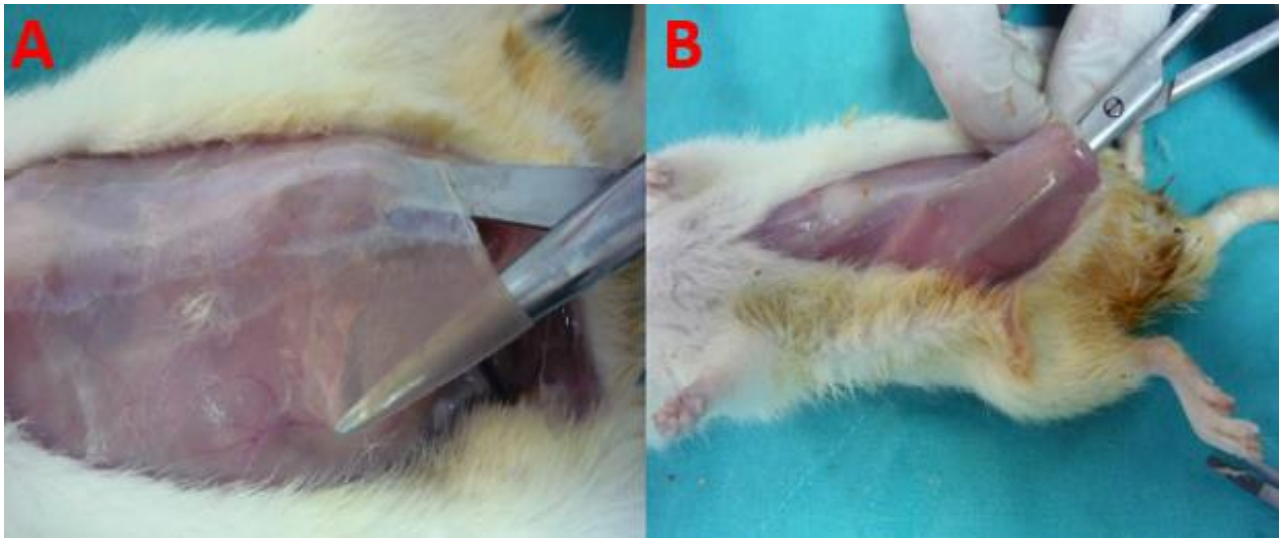


Figure 1. Macroscopic appearance of the parietal peritoneum in rats. (A) Control group; (B) Chlorhexidine gluconate (CG) group.

Sacrifice and Sample Collection

On day 21, all animals were anesthetized with ketamine (50 mg/kg) and xylazine (10 mg/kg) and euthanized by cardiac puncture. Blood samples were collected and centrifuged, and serum was stored at –20 °C for subsequent analysis of TGF-β1 levels using an ELISA kit (eBioscience, BMS632/2). Following sacrifice, parietal peritoneal samples were excised via midline laparotomy, fixed in 10% neutral-buffered formalin, embedded in paraffin, and cut into 4-µm sections for histological evaluation.

Histopathological Evaluation

Sections were stained with hematoxylin-eosin and Masson's trichrome and examined under a light microscope by a pathologist blinded to the study groups. Semi-quantitative scoring systems were applied to assess inflammation, fibrosis, and vascularization on a scale from 0 to 3 (0 = none, 1 = mild, 2 = moderate, 3 = severe) (14). Peritoneal membrane thickness was assessed morphometrically using an Olympus BX51 microscope equipped with a DP72 imaging system. Representative histological image of the peritoneal membrane showing the morphometric measurement is presented in Figure 2 (Hematoxylin–Eosin stain, ×200 magnification).

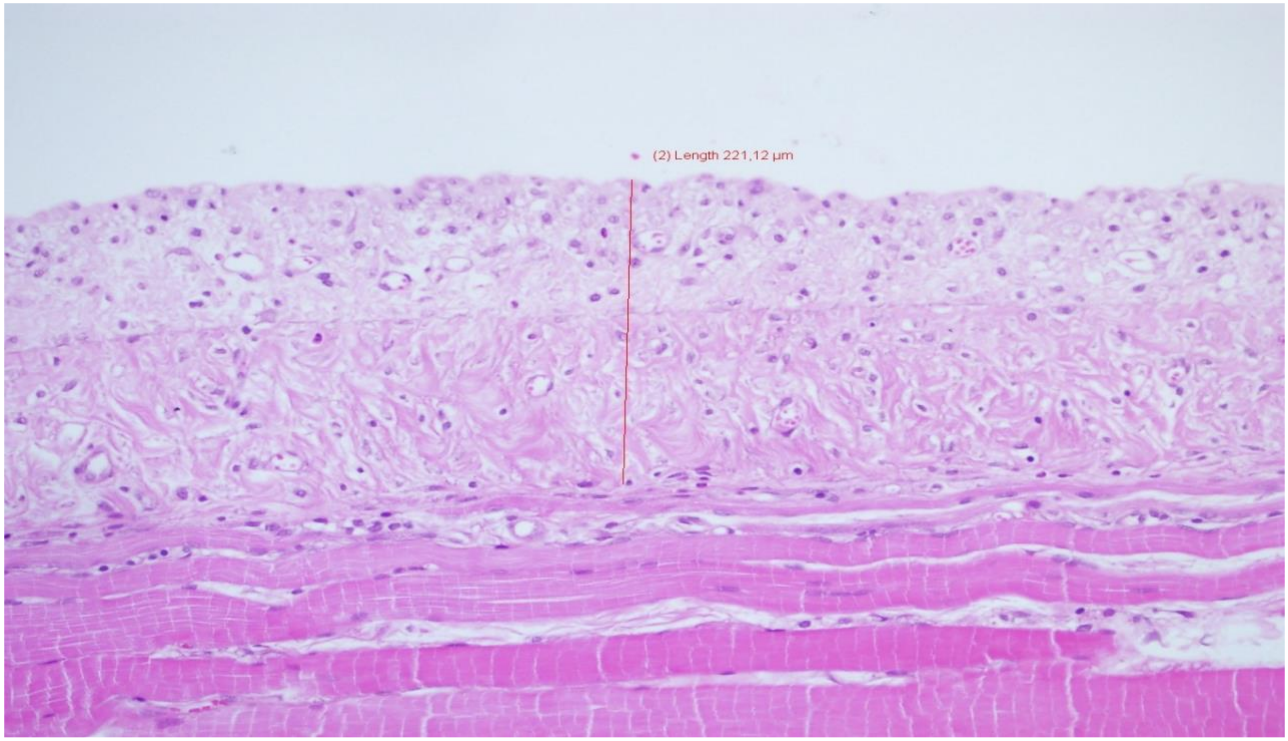


Figure 2. Morphometric measurement of peritoneal membrane thickness shown in the center of the image.

Statistical Analysis

All statistical analyses were performed using SPSS version 16.0 (Chicago, IL, USA). Normality of data distribution was tested with the Kolmogorov–Smirnov test. Parametric variables were expressed as mean ± standard deviation and compared using one-way ANOVA, followed by Tukey HSD or Tamhane's T2 tests depending on variance homogeneity. Non-parametric variables were presented as median (min–max) and analyzed with the Kruskal–Wallis test, with pairwise comparisons performed using the Mann–Whitney U test. Categorical variables were compared using the chi-square test. A p-value <0.05 was considered statistically significant.

RESULTS

According to Table 1, serum TGF-β1 levels were significantly higher in the CG group compared with the control group (58.29 ± 4.40 vs. 49.06 ± 2.35 ng/mL, $p < 0.05$). In Group 4 (CG+NAC), TGF-β1 levels were significantly lower compared with the CG group (46.76 ± 4.79 vs. 58.29 ± 4.40 ng/mL, $p < 0.05$). No statistically significant differences were observed in Groups 2 (CG+Paricalcitol), 3 (CG+Paricalcitol+NAC), and 5 (CG+Carvedilol) compared with the CG group ($p > 0.05$).

Table 1. Serum TGF-β1 levels across experimental groups

Group	TGF-β1 (ng/mL)
Group 1: CG	58.29 ± 4.40
Group 2: CG + Paricalcitol	58.65 ± 12.40
Group 3: CG + Paricalcitol + NAC	58.12 ± 10.48
Group 4: CG + NAC	46.76 ± 4.79 a
Group 5: CG + Carvedilol	56.73 ± 5.86
Group 6: Control	49.06 ± 2.35 a

*Values are mean ± standard deviation. a: $p < 0.05$ vs. Group 1 (CG).

According to Table 2, peritoneal membrane thickness was significantly higher in the CG group compared with the control group (245 ± 27.35 vs. 22.3 ± 2.58 µm, $p < 0.01$). Thickness was significantly lower in Groups 4 (169.8 ± 30.82 µm) and 5 (146.5 ± 43.05 µm) compared with the CG group ($p < 0.01$). Fibrosis scores were significantly lower in Groups 4 (1.33 ± 0.51) and 5 (1.17 ± 0.40) compared with the CG group (2.17 ± 0.75, $p < 0.05$). Inflammation scores were significantly lower in Group 4 (0.83 ± 0.40) compared with the CG group (2.00 ± 0.63, $p < 0.01$). Vascularisation scores were significantly lower in Group 4 (1.33 ± 0.51) compared with the CG group (2.00 ± 0.00, $p < 0.05$).

Table 2. Peritoneal membrane thickness and histopathological scores among groups

Parameter	G1: CG	G2: CG+P	G3: CG+P+NAC	G4: CG+NAC	G5: CG+C	G6: Control	p-value
Thickness (µm)	245 ± 27.35	191.3 ± 60.4	176.5 ± 65.2	169.8 ± 30.82[a]	146.5 ± 43.05[a]	22.3 ± 2.58	<0.01
Fibrosis score	2.17 ± 0.75[b]	1.33 ± 0.51	1.33 ± 0.51	1.33 ± 0.51	1.17 ± 0.40[b]	0	<0.01
Inflammation score	2.00 ± 0.63	1.83 ± 0.75[d]	1.33 ± 0.51	0.83 ± 0.40[c]	1.50 ± 0.54[d]	0	<0.01
Vascularisation score	2.00 ± 0.00[e]	2.00 ± 0.63	1.67 ± 0.51	1.33 ± 0.51[e]	1.50 ± 0.54	0	<0.01

*G1: Chlorhexidine gluconate (CG); G2: CG+Paricalcitol; G3: CG+Paricalcitol+NAC; G4: CG+NAC; G5: CG+Carvedilol; G6: Control. a: $p < 0.01$ vs. Group 1; b, c, d, e: $p < 0.05$ vs. Group 1.

DISCUSSION

In this experimental study, we investigated the effects of N-acetylcysteine (NAC), carvedilol, and paricalcitol on chlorhexidine gluconate–induced peritoneal fibrosis in rats. As expected, the CG group exhibited significant increases in peritoneal membrane thickness, fibrosis, inflammation, vascularization scores, and serum TGF-β1 levels, confirming the successful induction of fibrosis. These findings are consistent with the established pathophysiology of peritoneal membrane injury, where persistent inflammation and oxidative stress promote fibroblast activation, extracellular matrix deposition, and angiogenesis.

The observed elevation of TGF-β1 in the CG group highlights its central role as a master regulator of fibrogenesis through the Smad signaling cascade, stimulating fibroblast proliferation and collagen deposition. Treatment with NAC significantly attenuated TGF-β1 levels, supporting the notion that antioxidant therapy can suppress TGF-β1 expression and mitigate fibrotic signaling (15,16). Previous reports have shown that NAC reduces oxidative stress and inflammatory activation in renal and peritoneal fibrosis models, which aligns with our findings. In contrast, carvedilol and paricalcitol induced less pronounced changes in TGF-β1, suggesting that their mechanisms may act indirectly or require longer treatment durations to exert full antifibrotic effects (17,18).

Histopathological analysis further demonstrated that NAC and carvedilol markedly reduced peritoneal membrane thickening, whereas paricalcitol achieved only partial attenuation without statistical significance. This reduction is likely mediated by the inhibition of fibroblast activation and collagen accumulation, consistent with earlier evidence indicating that oxidative stress and chronic inflammation accelerate submesothelial thickening in peritoneal dialysis–related injury. Fibrosis scores followed a similar pattern, with NAC showing the strongest protective effect, carvedilol providing moderate benefit, and paricalcitol exhibiting limited efficacy. The superior performance of NAC may be attributed to its ability to replenish intracellular glutathione levels, thereby enhancing cellular resilience against oxidative and inflammatory stressors (19,20).

With respect to inflammation, NAC significantly reduced inflammatory scores, while carvedilol conferred partial benefit. These results correspond to NAC's well-documented inhibition of the NF-κB pathway, which limits proinflammatory cytokine release. Furthermore, vascularization scores were notably decreased in the NAC group, reflecting suppression of TGF-β1–driven angiogenesis and oxidative stress–mediated vascular proliferation. Taken together, these outcomes reinforce the concept that inflammation and angiogenesis are critical contributors to peritoneal fibrogenesis and that their modulation is essential for membrane preservation (21,22).

Overall, NAC demonstrated the most consistent antifibrotic efficacy across biochemical and histopathological parameters, while carvedilol showed moderate protection and paricalcitol exerted only minor effects (23). These results underscore the predominant role of oxidative stress and inflammation in peritoneal fibrosis and highlight the translational potential of antioxidant therapy, particularly NAC, in preventing structural and functional deterioration of the peritoneal membrane. Current literature increasingly supports antioxidant and anti-inflammatory strategies as promising adjuncts in prolonging peritoneal dialysis viability, and our findings are in line with this perspective (24,25).

Interestingly, the combination of paricalcitol and NAC did not result in a greater reduction in peritoneal thickness compared with NAC alone. This finding suggests that the antifibrotic effects of NAC may predominate under the experimental conditions used. NAC primarily exerts its protective role through antioxidant mechanisms and suppression of oxidative stress–driven TGF-β signaling, whereas paricalcitol modulates fibrosis via vitamin D receptor–dependent transcriptional pathways. It is possible that overlapping downstream signaling targets or pharmacodynamic interactions limited the additive benefit of combined therapy. Additionally, the fixed dosing regimen and relatively short treatment duration may not have been sufficient to reveal potential synergistic effects. Further studies exploring different dose combinations, longer exposure periods, and molecular pathway analyses are warranted to clarify these interactions.

Limitations

Nevertheless, several limitations must be acknowledged. The use of an animal model may not fully capture the complexity of human peritoneal tissue. Only a single dose and limited treatment duration were tested, leaving the dose–response relationship and long-term effects unexplored. In addition, potential pharmacodynamic interactions between NAC and paricalcitol were not specifically investigated, and the fixed dosing regimen may have limited the detection of possible synergistic effects. Molecular pathways such as Smad2/3 activation, VEGF expression, and oxidative enzyme activity were not evaluated, limiting mechanistic insights. Finally, functional outcomes such as ultrafiltration capacity were not assessed, restricting the translational interpretation of histological and biochemical results.

CONCLUSION

In conclusion, NAC exhibited robust protective effects against peritoneal fibrosis by reducing TGF-β1 levels, peritoneal thickening, fibrosis, inflammation, and vascularization. Carvedilol conferred moderate benefit, while paricalcitol showed limited impact under the conditions tested. These findings suggest that targeting oxidative stress and inflammatory pathways may represent an effective therapeutic strategy to preserve peritoneal membrane integrity. Further preclinical and clinical studies are warranted to confirm these effects and to optimize dosing and treatment regimens for clinical translation.

DECLARATIONS

Acknowledgements: The authors do not wish to acknowledge any individual or institution.

Author Contributions: Conceptualization, K.Ö.; Methodology, K.Ö. and Ö.E.; Validation, Ö.E. and K.A.; Formal Analysis, Ö.T.P.; Investigation, K.Ö. and Ö.T.P.; Resources, K.A.; Data Curation, Ö.T.P.; Writing—Original Draft, K.Ö.; Writing—Review & Editing, Ö.E. and K.A.; Visualization, Ö.T.P.; Supervision, Ö.E.; Project

Administration, K.Ö. All authors have read and approved the final version of the manuscript.

Conflict of Interest: The authors declare no conflict of interest.

Supporting Institutions: This research received no external funding.

Ethical Approval: Ethical Approval: This study was conducted as a prospective, randomized, and controlled experimental investigation. Ethical approval was obtained from the Gazi University Animal Research Ethics Committee (Project No: 12081, Date: 25 September 2012, Approval Code: 141-18973). All procedures were performed in accordance with the ARRIVE guidelines, and every effort was made to minimize animal suffering throughout the experiment.

Plagiarism Statement: The manuscript was evaluated for plagiarism using appropriate software, and no instances of plagiarism were detected.

Use of AI Tools: The authors declare that AI-based tools were used solely for language editing and improving readability, and the authors take full responsibility for the scientific content of the manuscript.

REFERENCES

1. Xie K, Cao H, Ling S, Zhong J, Chen H, Chen P, et al. Global, regional, and national burden of chronic kidney disease, 1990-2021: a systematic analysis for the global burden of disease study 2021. Front Endocrinol (Lausanne). 2025;16:1526482. doi:10.3389/fendo.2025.1526482.
2. Abecassis M, Bartlett ST, Collins AJ, Davis CL, Delmonico FL, Friedewald JJ, et al. Kidney transplantation as primary therapy for end-stage renal disease: a National Kidney Foundation/Kidney Disease Outcomes Quality Initiative (NKF/KDOQITM) conference. Clin J Am Soc Nephrol. 2008;3(2):471-80. doi:10.2215/CJN.05021107.
3. Nardelli L, Scalamogna A, Messa P, Gallieni M. Peritoneal dialysis for Potential Kidney Transplant Recipients: pride or Prejudice? Medicina (Kaunas) 2022;58(2):214. doi:10.3390/medicina58020214.
4. Roumeliotis S, Dounousi E, Salmas M, Eleftheriadis T, Liakopoulos V. Unfavorable Effects of Peritoneal Dialysis Solutions on the Peritoneal Membrane: The Role of Oxidative Stress. Biomolecules. 2020;10(5):768. doi:10.3390/biom10050768.
5. Saxena R. Pathogenesis and treatment of peritoneal membrane failure. Pediatr Nephrol. 2008;23(5):695-703. doi:10.1007/s00467-007-0580-5.
6. Terri M, Trionfetti F, Montaldo C, Cordani M, Tripodi M, Lopez-Cabrera M, et al. Mechanisms of Peritoneal Fibrosis: Focus on Immune Cells-Peritoneal Stroma Interactions. Front Immunol. 2021;12:607204. doi:10.3389/fimmu.2021.607204.
7. Moinuddin Z, Summers A, Van Dellen D, Augustine T, Herrick SE. Encapsulating peritoneal sclerosis-a rare but devastating peritoneal disease. Front Physiol. 2014;5:470. doi:10.3389/fphys.2014.00470.
8. Nallagangula KS, Nagaraj SK, Venkataswamy L, Chandrappa M. Liver fibrosis: a compilation on the biomarkers status and their significance during disease progression. Future Sci OA. 2017;4(1):FSO250. doi:10.4155/fsoa-2017-0083.
9. Frangogiannis N. Transforming growth factor-β in tissue fibrosis. J Exp Med. 2020;217(3):e20190103. doi:10.1084/jem.20190103.
10. Tenório MCDS, Graciliano NG, Moura FA, Oliveira ACM, Goulart MOF. N-Acetylcysteine (NAC): impacts on human health. Antioxidants (Basel). 2021;10(6):967. doi:10.3390/antiox10060967.
11. Rushworth GF, Megson IL. Existing and potential therapeutic uses for N-acetylcysteine: the need for conversion to intracellular glutathione for antioxidant benefits. Pharmacol Ther. 2014;141(2):150-9. doi:10.1016/j.pharmthera.2013.09.006.
12. Duplancic D, Cesarik M, Poljak NK, Radman M, Kovacic V, Radic J, et al. The influence of selective vitamin D receptor activator paricalcitol on cardiovascular system and cardiorenal protection. Clin Interv Aging. 2013;8:149-56. doi:10.2147/CIA.S38349.
13. Donate-Correa J, Domínguez-Pimentel V, Muros-de-Fuentes M, Mora-Fernández C, Martín-Núñez E, Cazaña-Pérez V, et al. Beneficial effects of selective vitamin D receptor activation by paricalcitol in chronic kidney disease. Curr Drug Targets. 2014;15(7):703-9. doi:10.2174/1389450115666140417120902.
14. Huo MH, Troiano NW, Pelker RR, Gundberg CM, Friedlaender GE. The influence of ibuprofen on fracture repair: biomechanical, biochemical, histologic, and histomorphometric parameters in rats. J Orthop Res. 1991;9(3):383-90. doi:10.1002/jor.1100090310.
15. Zhang X, Ma Y, You T, Tian X, Zhang H, Zhu Q, et al. Roles of TGF-β/Smad signaling pathway in pathogenesis and development of gluteal muscle contracture. Connect Tissue Res. 2015;56(1):9-17. doi:10.3109/03008207.2014.964400.
16. Evans RA, Tian YC, Steadman R, Phillips AO. TGF-beta1-mediated fibroblast-myofibroblast terminal differentiation-the role of Smad proteins. Exp Cell Res. 2003;282(2):90-100. doi:10.1016/s0014-4827(02)00015-0.
17. Ozaydin M, Peker T, Akcay S, Uysal BA, Yucel H, Icli A, et al. Addition of N-acetyl cysteine to carvedilol decreases the incidence of acute renal injury after cardiac surgery. Clin Cardiol. 2014;37(2):108-14. doi:10.1002/clc.22227.
18. Baba D, Çam K, Şenoğlu Y, Yüksel A, Erdem H, Başaran E. The Efficacy of N-acetylcysteine against renal oxidative stress after extracorporeal shock wave treatment: an experimental rat model. J Urol Surg. 2020;7(1):8-15. doi:10.4274/jus.galenos.2019.2941.
19. Zakaria AY, Badawi R, Osama H, Abdelrahman MA, El-Kalaawy AM. A comparative study of N-Acetyl Cysteine, Rosuvastatin, and Vitamin E in the management of patients with Non-Alcoholic Steatohepatitis: a randomized controlled trial. Pharmaceuticals (Basel). 2025;18(5):650. doi:10.3390/ph18050650.
20. Pereira-Filho G, Ferreira C, Schwengber A, Marroni C, Zettler C, Marroni N. Role of N-acetylcysteine on fibrosis and oxidative stress in cirrhotic rats. Arq Gastroenterol. 2008;45(2):156-62. doi:10.1590/s0004-28032008000200013.
21. Sztolsztener K, Bzdęga W, Hodun K, Chabowski A. N-acetylcysteine decreases myocardial content of inflammatory mediators preventing the development of inflammation state and oxidative stress in rats subjected to a high-fat diet. Int J Inflam. 2023;2023:5480199. doi:10.1155/2023/5480199.
22. Singh M, Kim A, Young A, Nguyen D, Monroe CL, Ding T, et al. The mechanism and inflammatory markers involved in the potential use of N-acetylcysteine in chronic pain management. Life (Basel). 2024;14(11):1361. doi:10.3390/life14111361.
23. Hamdy N, El-Demerdash E. New therapeutic aspect for carvedilol: antifibrotic effects of carvedilol in chronic carbon tetrachloride-induced liver damage. Toxicol Appl Pharmacol. 2012;261(3):292-9. doi:10.1016/j.taap.2012.04.012.

24. Lee OYA, Wong ANN, Ho CY, Tse KW, Chan AZ, Leung GP, et al. Potentials of natural antioxidants in reducing inflammation and oxidative stress in Chronic Kidney Disease. Antioxidants (Basel). 2024;13(6):751. doi:10.3390/antiox13060751.
25. Liakopoulos V, Roumeliotis S, Gorny X, Eleftheriadis T, Mertens PR. Oxidative stress in patients undergoing peritoneal dialysis: a current review of the literature. Oxid Med Cell Longev. 2017;2017:3494867. doi:10.1155/2017/3494867.