• Clinical Research •

# Nanosilver eye patch for ocular surface trauma: a prospective randomised trial and review of the literature

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## Abstract

● **AIM:** To evaluate nanosilver eye patches versus Atrauman nanosilver dressings for ocular surface trauma.

● **METHODS:** This randomized non-inferiority trial (November 2024–April 2025) enrolled 60 patients assessed pre-treatment and on days 1, 7, and 14 post-treatment. The patients were then randomized into treatment (nanosilver eye patches) and control groups (Atrauman nanosilver dressings). Outcomes included wound healing, comfort (Ocular Comfort Index, OCI), and safety. Statistical analyses used *t*-tests, non-inferiority tests, and Chi-square tests.

● **RESULTS:** Patient baseline characteristics were comparable between groups, with a mean age of 60.633±10.934 in the treatment group versus 64.933±9.606 in controls, and similar gender distribution (20/10 *vs* 17/13 male/female). Both groups showed comparable baseline OCI scores (treatment group: 6.100±2.187 *vs* control group: 6.267±2.303, $P$=0.775). Following treatment, scores increased significantly at day 1 (treatment group: 9.367±2.251; control group: 9.067±2.212, both $P$<0.001 *vs* baseline). Marked improvement was observed by day 7 (treatment group: 4.067±1.929; control group: 3.900±1.918, $P$<0.001 *vs* baseline), with complete resolution at day 14 (0.467±0.860 *vs* 0.467±1.008, $P$<0.001). The non-inferiority criterion was met. The treatment group showed greater improvement in Grade A wound healing rates (76.67% to 93.33%) compared to controls (80.00% to 86.67%) between 1 and 7d post-treatment. By 14d post-treatment, all patients achieved Grade A healing in both groups, with no Grade C cases observed throughout the study period. No adverse events were reported.

● **CONCLUSION:** Nanosilver eye patches are non-inferior to Atrauman dressings, offering effective, safe emergency care for ocular trauma.

● **KEYWORDS:** silver nanoparticle; eye patch; ocular surface trauma; non-inferiority trial; clinical trial

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## INTRODUCTION

Ocular trauma is one of the leading causes of blindness, particularly in developing countries. It has been estimated that a total of 1.6 million cases of blindness and 2.3 million cases of low vision can be attributed to ocular traumas per year. The number of incident cases of ocular trauma increased by 24% from 48 220.83 thousand in 1990 to 59 933.29 thousand in 2019 worldwide[1]. According to the classification proposed by the International Society for Ocular Trauma, ocular injuries can be divided into mechanical and non-mechanical injuries, with mechanical injuries further subdivided into open- and closed-globe injuries[2]. Mechanical ocular surface trauma (*e.g.*, corneal abrasions, conjunctival lacerations)[3] poses unique risks due to the cornea's avascularity and high susceptibility to infection[4-6]. Without prompt intervention, such injuries may progress to microbial keratitis or scarring, resulting in irreversible vision loss[6-7].

In the US-Afghan War, rigid eye patches were used for ocular trauma, but they only served as a barrier and had very poor compliance[8]. Among the general population, current first-aid options (*e.g.*, antibiotic drops and ointments) face practical limitations: they require frequent reapplication, lack sustained antimicrobial coverage, and are often unavailable in pre-hospital settings. Moreover, ointments may blur vision, while liquid formulations are prone to rapid clearance from the ocular surface. These challenges underscore the need for a stable, easy-to-use intervention that can bridge the gap between injury and definitive care.

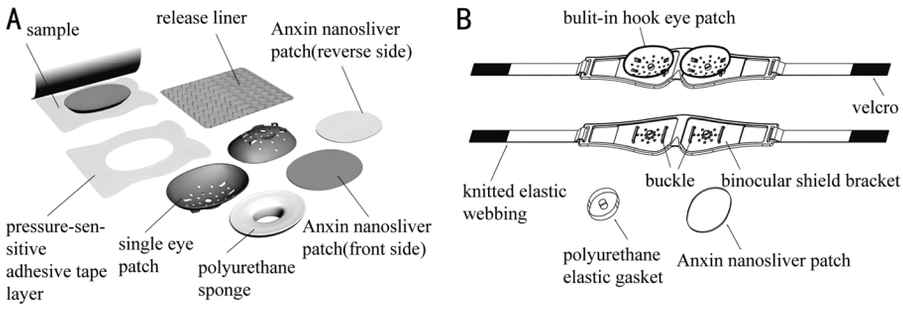


**Figure 1 Schematic diagram of Anxin monocular (A) and binocular (B) nanosilver eye patch.**

Silver has been used in wound care since the 16th century, with modern nanosilver dressings offering superior antimicrobial efficacy over ionic silver ($Ag^+$) due to their sustained release, reduced cytotoxicity, and resistance to inactivation by biological fluids[9-15]. However, a literature review revealed that nanosilver dressings have been used only for wound healing and antibacterial treatment of skin wounds, and there are no known applications of emergency nanosilver eye patches for ocular trauma.

With the support of the National Science and Technology Support Program Project "Research on On-Site First Aid Equipment for Lethal and Disabling Combat Trauma (2009BAI87B04)", we have developed a multifunctional nanosilver first aid eye patch in conjunction with Anxin Nano-Biotechnology (Zhuhai, China) Co., Ltd (Figures 1 and 2). The patches are designed to: 1) provide a physical barrier against further injury; 2) deliver prolonged antimicrobial activity; 3) enable immediate application in emergency scenarios. Open-globe injuries always need complex surgeries. Ocular surface trauma is relatively common both in peacetime and wartime, and is easier to observe. Therefore, this trial aimed to validate the clinical effectiveness of nanosilver eye patches in ocular surface trauma. The product is hypothesized to have a clinical cure rate that is not inferior to that of Atrauman nanosilver dressings from the German company B. Braun Melsungen AG.

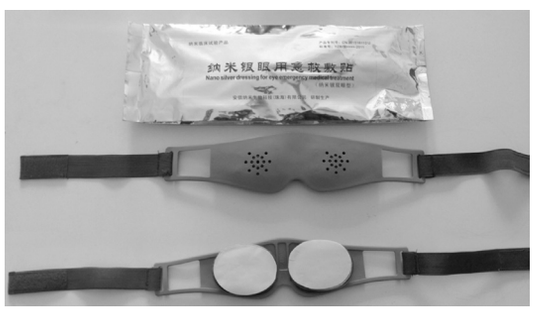

**Figure 2 Product appearance image of Anxin binocular nanosilver eye patch.**

## PARTICIPANTS AND METHODS

**Ethical Approval** This study was performed in accordance with the Declaration of Helsinki and was approved by Hainan Hospital of PLA General Hospital ethics committee (Ethic approval number: No.S2024-12). Written informed consent was obtained from all patients after a full explanation of the potential benefits and risks of the study. Clinical Registry: Chinese Clinical Trial Registry, ChiCTR2400091106, Registered on 21 October 2024.

**Trial Design** The study was designed as a non-inferiority trial. Non-inferiority trials aim to demonstrate that the treatment effect difference (experimental therapy minus control) is no worse than a non-inferiority margin. Non-inferiority is established if the lower bound of the confidence interval for this difference exceeds non-inferiority margin[16]. The treatment group and control group were arranged in a 1:1 ratio. Based on previous efficacy data for similar products and general statistical requirements, the parameters were: Type I error ($\alpha$)=0.05, power ($1-\beta$)=80%, non-inferiority margin $\delta$=15%, and average efficacy rate $P$=0.95. Clinically, the non-inferiority margin ($\delta$=15%), which means a loss of ≤15% efficacy, was deemed acceptable by expert consensus, as smaller differences would not outweigh the benefits of portability and ease of use in emergency settings[17]. A non-inferiority margin of 15% was prespecified based on a prior study[18], which reported a 27.3 percentage-point difference in wound area reduction favoring Atrauman Ag over Bactigras. This margin preserves more than 50% of the reference treatment effect. This aligns with Food and Drug Administration (FDA) guidelines recommending $\delta$≤50% of the standard therapy's effect to ensure clinical relevance[19]. Using the traditional calculation formula: $n=(Z_{1-\alpha}+Z_{1-\beta})^2\times 2P(1-P)/\delta^2$, we obtained $n$=26.11≈27 [$Z_{1-\alpha}$ means the (1-$\alpha$) percentile of the standard normal distribution]. This indicates that at least 27 effective cases in each group need to be completed. That is to say, when the first type of error is 0.05, each group needs to include at least 27 patients in order to ensure the expected result with an 80% confidence level. Considering a dropout rate of 10%, the sample size was increased, resulting in a requirement of 30 effective cases. For statistical convenience, we allocated 30 cases to the control group for symmetry. According to literature review[20] and expert discussion, the inferiority criterion was set as 1 score.

**Participants** This trial was conducted between November 2024 and April 2025. Sixty patients with ocular surface

**Table 1 Basic demographic characteristics of full analysis set**

| Characteristics | Treatment group | Control group | *P* |
|---|---|---|---|
| Age (y) | 60.633±10.934 (35-84) | 64.933±9.606 (38-84) | 0.111 |
| Sex (*n*) | 30 | 30 | 0.426 |
| Male | 20 | 17 | |
| Female | 10 | 13 | |

traumas in the Department of Ophthalmology of Hainan Hospital of PLA General Hospital were selected. All patients had 8-15 mm conjunctival lacerations accompanied by corneal epithelial injuries. A randomization table of 60 unique numbers was generated using SAS software (SAS Institute Inc., Cary, NC, USA), with a 1:1 allocation ratio. The first 30 numbers were assigned to the nanosilver eye patch group, and the remaining 30 to the Atrauman dressing group (control). Sequentially numbered, opaque, sealed envelopes were prepared, each containing a group assignment card. To ensure concealment, the envelopes were stored in a locked box accessible only to the study coordinator, who was not involved in patient recruitment or outcome assessment. After surgery, nurses (who were not involved in postoperative evaluations) opened the envelopes in sequential order based on patient enrollment time. Both the assigned patch and control dressing were repackaged in identical, unlabeled sterile packaging by an independent technician. Participant characteristics of the full analysis set were summarized in Table 1. There were no significant differences in sex and age between the two groups.

**Eligibility Criteria** The inclusion criteria were as follows: 1) volunteers for the trial who signed an informed consent form; 2) inpatients or outpatients between the ages of 18 and 85y who received initial treatment within 6h after ocular surface injury; 3) patients with clean, potentially contaminated, or contaminated ocular surface traumas; 4) women of childbearing age who agreed to take effective contraceptive measures during the study period.

The exclusion criteria were as follows: 1) individuals not consenting to participate in the trial; 2) participants with known allergies to any component of the product; 3) pregnant women; 4) patients with severe conditions that precluded definitive evaluations of the efficacy and safety; 5) patients deemed unsuitable for the experiment by other researchers.

The termination criteria were as follows: 1) participants with poor compliance who were unable to complete the trial according to the protocol; 2) occurrence of severe adverse events or significant laboratory abnormalities that required discontinuation of the product; 3) the reasons for termination should be recorded in detail, and adverse events should be included in the statistics of adverse events if they occur.

**Treatment** Upon admission, patients were evaluated for their overall health status and the extent of their injuries. If their health status was stable, further ophthalmic interventions were performed. The wound was irrigated with saline solution under topical or local anesthesia, followed by three rounds of povidone-iodine disinfection around the eye. Additionally, the wound was irrigated again with saline solution under microscopic observation. Foreign bodies were removed before suturing the conjunctival wounds. Postoperatively, a tobramycin-dexamethasone ointment was applied routinely for infection prophylaxis. According to the random number contained in the envelope taken by the nurse, the patients were then randomized into treatment (nanosilver eye patches) and control groups (Atrauman nanosilver dressings). The eye patches or dressings were replaced once on postoperative day 1, 3, 5, and 7, maintaining 10-hour nightly application by patient self-administration. Prior to hospital discharge, we provide thorough training to both patients and their caregivers on proper use of the eye patches or dressings, along with supplemental supplies to account for potential loss or handling errors. Patients and families are instructed to contact our team immediately if any discomfort occurs. Throughout all assessments, the clinicians remained completely blinded to patient group allocation, ensuring unbiased evaluation of outcomes. Patients and ophthalmologists were blinded to group allocation throughout the study.

**Observation Parameters** Four visits were made at different times, before the trial, on the first day, the seventh day, and the fourteenth day after the treatment, to document patient complaints and examination findings. As the duration of necessary treatment varies among patients, significant improvement was generally observed within fourteen days. The duration varied depending on the conditions. The treatment was considered ineffective if there was no significant recovery in two weeks.

Clinical trial case report forms were completed to accurately record the condition and treatment of each subject. The forms were provided to the patients in Chinese, which is their first language, to ensure clear understanding and accurate completion of the information. Researchers responsible for completing these forms received professional and standardized training to minimize the impact of patient subjectivity.

**Efficacy Determination** Efficacy was determined in two domains: wound healing and patient comfort.

**Table 2 Wound healing grading criteria**

| Healing grade | Descriptions |
|---|---|
| Grade A | Excellent initial healing with no adverse effects |
| Grade B | Poor healing, with inflammatory reactions at the healing site, such as redness, swelling, hardness, hematoma, effusion, but not purulent |
| Grade C | The incision is septic and requires incision and drainage |

**Table 3 Grading and scores for symptom severity**

| Grade | Descriptions | Score |
|---|---|---|
| None | No discomfort | 0 |
| Mild | Slight discomfort that can be ignored | 1 |
| Moderate | Noticeable discomfort that cannot be ignored | 2 |
| Severe | Serious discomfort that distracts concentration | 3 |
| Extreme | Intense discomfort that significantly disrupts normal activities | 4 |

**Wound healing assessment** Wound healing was classified according to the conventional healing classification system, which classifies wounds into three categories: grades A, B, and C (Table 2).

**Comfort assessment** Comfort assessment was based on the Ocular Comfort Index (OCI) and tailored to the specifics of ocular surface traumas. The evaluation protocol involved the following methodology: five primary symptoms were identified for assessment: ocular pain, photophobia, foreign-body sensation, itchiness, and discharge. The severity of each symptom was scored on a scale ranging from none to extreme, with classifications of none, mild, moderate, severe, and extreme. Each category was assigned a score (Table 3).

The frequency of each symptom was classified as none, occasional, sometimes, often, or constant, with the corresponding scores (Table 4). The baseline severity and frequency were assessed using the OCI questionnaire, which is a validated psychometric tool designed to address the limitations of clinical instrument detection, as per the study by Johnson and Murphy[21]. The OCI provides robust and reliable measurement results and correlates moderately with the Ocular Surface Disease Index. Case record forms recorded patient basic information, ophthalmic examination findings, eligibility criteria, adverse events, OCI scores, and wound healing status, among other details.

**Safety Determination** All adverse events were observed, and symptom descriptions, onset and end dates, severity, relation to the device, treatment, and outcomes were recorded. All adverse events, whether reported by the subject or observed by the investigator, were documented in the adverse event section of the case report form. Events related to adverse reactions to the device, illnesses occurring during the study, and exacerbations of preexisting diseases were recorded. In the event of a serious adverse event, such as a life-threatening, disabling occurrence or causing congenital anomalies, emergency measures were taken to protect the patient's interests, regardless of association with the trial, and reported to the medical device regulatory authorities, relevant units within 24h. The clinical symptoms that arose during treatment were promptly managed. If a symptom was determined to be unrelated to the product, the trial continued.

**Table 4 Grading and scores for symptom frequency**

| Grade | Duration | Score |
|---|---|---|
| None | | 0 |
| Occasional | <25% of the time | 1 |
| Sometimes | 25%–50% of the time | 2 |
| Often | 50%–100% of the time | 3 |
| Constant | 100% of the time | 4 |

**Evaluation of adverse reactions** Reactions were classified into five levels of association with the trial product: definitely related, probably related, possibly related, unlikely related, and unrelated. The first three were counted as the incidence of adverse reactions.

Related: the reaction occurs within a reasonable time sequence after using the product, matches known reactions to the product, disappears after discontinuation, and cannot be explained by the clinical presentation of the disease or other causes unrelated to the product.

Probably related: the reaction occurs in a reasonable time sequence after using the product, matches known reactions to the product, improves significantly after discontinuation, and cannot be explained by the clinical presentation of the disease or other causes not related to the product.

Possibly related: the reaction occurs in a reasonable time sequence after using the product, matches known reactions to the product, improves after dose reduction or discontinuation, and could also be caused by the clinical status of the disease or other treatments.

Unlikely related: the reaction does not occur in a reasonable time sequence after using the product, does not match known reactions to the product, improves after dose reduction or discontinuation, and improves with the disease or other measures.

**Table 5 Total OCI scores at four time points** mean±SD

| Parameters | Pre-treatment | 1d post-treatment | 7d post-treatment | 14d post-treatment |
|---|---|---|---|---|
| Treatment group | 6.100±2.187 | 9.367±2.251[c] | 4.067±1.929[c] | 0.467±0.860[c] |
| Control group | 6.267±2.303 | 9.067±2.212[c] | 3.900±1.918[c] | 0.467±1.008[c] |
| *P* | 0.775 | 0.605 | 0.738 | 1.000 |

[c]*P*<0.001 compared to pre-treatment (paired *t*-test). OCI: Ocular comfort index; SD: Standard deviation.

**Table 6 Severity of OCI subscale scores at four time points** mean±SD

| Parameters | Pre-treatment | 1d post-treatment | 7d post-treatment | 14d post-treatment |
|---|---|---|---|---|
| Treatment group | 2.967±1.189 | 4.067±1.230[c] | 2.033±0.964[c] | 0.233±0.430[c] |
| Control group | 3.067±1.202 | 4.033±1.426[c] | 1.900±0.960[c] | 0.233±0.504[c] |
| *P* | 0.747 | 0.923 | 0.593 | 1.000 |

[c]*P*<0.001 compared to pre-treatment (paired *t*-test). OCI: Ocular comfort index; SD: Standard deviation.

**Table 7 Frequency of OCI subscale scores at four time points** mean±SD

| Parameters | Pre-treatment | 1d post-treatment | 7d post-treatment | 14d post-treatment |
|---|---|---|---|---|
| Treatment group | 3.133±1.167 | 5.300±1.489[c] | 2.033±0.964[c] | 0.233±0.430[c] |
| Control group | 3.200±1.243 | 5.033±1.450[c] | 2.000±0.983[c] | 0.233±0.504[c] |
| *P* | 0.831 | 0.485 | 0.895 | 1.000 |

[c]*P*<0.001 compared to pre-treatment (paired *t*-test). OCI: Ocular comfort index; SD: Standard deviation.

Unrelated: the reaction does not occur within a reasonable time sequence after using the product, does not match known reactions to the product, and does not improve after dose reduction or discontinuation.

**Statistical Analysis** The IBM® SPSS® Statistics software (version 26.0 for Windows; SPSS Inc., Chicago, IL, USA) was utilized to conduct statistical analysis. The Shapiro-Wilk test was used to assess whether the data followed a normal distribution. For data demonstrating normal distribution, continuous variables were expressed as mean±standard deviation (SD). Between-group comparisons at specific time points were performed using unpaired *t*-tests, with non-inferiority testing implemented where appropriate using pre-specified margin thresholds. Within-group longitudinal comparisons were conducted using paired *t*-tests to evaluate changes over time. Comparisons of wound healing grade distributions between groups were analyzed using Pearson's Chi-square tests. If the data were not normally distributed, they were presented as M ($P_{25}$, $P_{75}$). Between-group analyses utilized Wilcoxon rank-sum tests, while within-group comparisons across multiple time points were assessed using Friedman tests.

## RESULTS

**Baseline Characteristics of Patients in Each Group Before Treatment** Before treatment, both groups were scored for the severity and frequency of ocular pain, photophobia, foreign body sensation, eye itchiness, and discharge. Results of the two groups were presented in Tables 5-7. At the pre-treatment baseline assessment, no statistically significant differences were found between the treatment and control groups in OCI total scores ($P$=0.775), OCI severity subscale scores ($P$=0.747), or OCI frequency subscale scores ($P$=0.831), demonstrating excellent baseline comparability between the two groups.

**Baseline Characteristics of Patients in Each Group After Treatment** One, seven and fourteen days after treatment, both groups were scored for the severity and frequency of comfort levels (ocular pain, photophobia, foreign body sensation, eye itchiness, and discharge). Statistical analysis demonstrated no significant between-group differences in OCI total scores at any measured timepoint (1-day post-treatment: $P$=0.605; 7-day post-treatment: $P$=0.738; 14-day post-treatment: $P$=1.000; Table 5). Non-inferiority was confirmed through confidence interval analysis using the formula:

$$CI_{\text{lower}} = (\overline{X}_1 - \overline{X}_2) - t_{\alpha/2} \times \sqrt{\frac{S_1^2}{n_1} + \frac{S_2^2}{n_2}}$$

with all lower bounds exceeding the predefined margin of -1 (1-day post-treatment: -0.663; 7-day post-treatment: -0.664; 14-day post-treatment: -0.405), thereby establishing non-inferiority at all post-treatment evaluations. No significant differences in both OCI severity subscale scores (Table 6) and frequency subscale scores (Table 7) were observed after treatment. Nanosilver eye patches are not inferior to Atrauman nanosilver dressings.

**Comparison of OCI Scores and Wound Healing Rates Between Groups After Treatment** The heatmap of OCI scores for both treatment (Figure 3A) and control (Figure 3B) groups before and after treatment revealed that ocular surface discomfort was primarily characterized by significant ocular pain and foreign body sensation prior to treatment. In the early

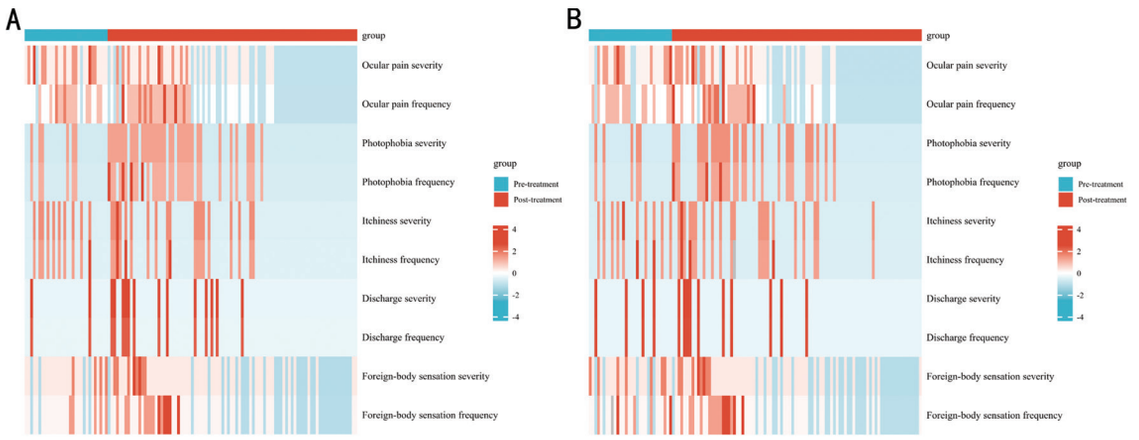


**Figure 3 The heatmap of OCI scores for both treatment (A) and control (B) groups before and after treatment** OCI: Ocular comfort index.

post-treatment phase, surgical suture irritation exacerbated these symptoms (ocular pain and foreign body sensation), accompanied by photophobia due to patients' reluctance to open their eyes. However, marked improvement was observed by post-treatment day 7, with near-complete resolution by day 14 except for mild residual foreign body sensation in a few patients. Itchiness and discharge remained mild throughout the treatment course.

Intragroup self-comparisons revealed that on post-treatment day 1, both the treatment and control groups showed significant increases in all three OCI parameters (total scores, severity subscale scores, and frequency subscale scores) compared to pre-treatment baseline levels (all $P<0.001$), indicating aggravated ocular surface symptoms during the early post-treatment period. By post-treatment day 7, both groups demonstrated significant reductions in all three measures relative to pre-treatment values (all $P<0.001$), reflecting marked symptomatic improvement. At post-treatment day 14, these parameters further decreased to near-normal levels, with statistically significant reductions maintained from baseline (all $P<0.001$). In summary, both patient groups exhibited a consistent trajectory of initial symptom exacerbation followed by progressive recovery, achieving near-complete resolution of ocular surface symptoms by postoperative day 14.

From day 1 to day 7 post-treatment, the treatment group demonstrated a more pronounced improvement in wound healing grades compared to controls. The proportion of Grade A healing wounds increased from 76.67% (23/30) to 93.33% (28/30) in the nanoscale silver group, whereas the control group showed a more modest increase from 80.00% (24/30) to 86.67% (26/30). By post-treatment day 14, all patients (100%, 30/30) in both groups achieved Grade A healing. No Grade C healing was observed in either group during the 14-day treatment period (Figure 4). At day 1 and 7 post-treatment, no statistically significant difference was observed in Grade A healing rates between the nanoscale silver group and the control group (1-day post-treatment: $P=1.000$; 7-day post-treatment: $P=0.381$). The results demonstrated that both Nanosilver eye patches and Atrauman nanosilver dressings promoted wound healing and prevented infection. Notably, Nanosilver eye patches demonstrated a higher rate of Grade A wound healing compared to Atrauman nanosilver dressings, suggesting potentially superior efficacy in enhancing ocular surface trauma recovery.

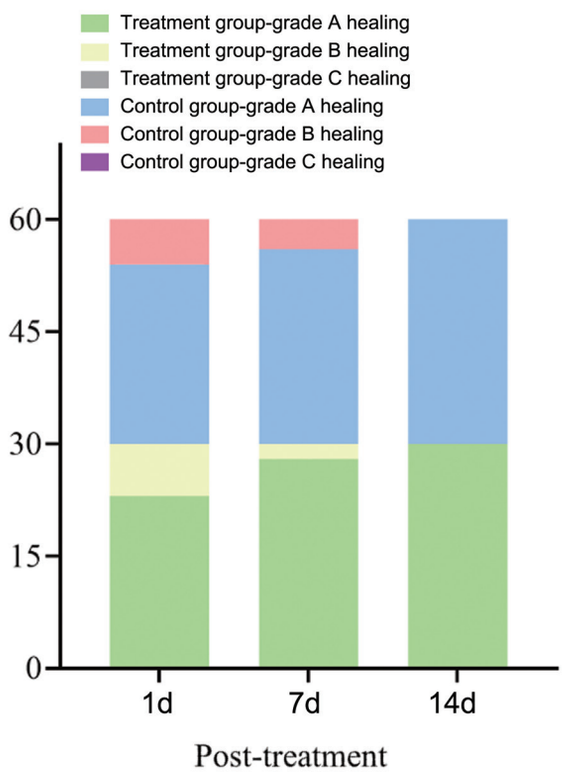


**Figure 4 Stacked bar graphs depicting the proportional distribution of wound healing grades (Grade A/B/C) in both treatment groups at each post-treatment time point.**

**Safety Determination After Treatment in Each Group** No adverse events were reported in either group after treatment.

## DISCUSSION

The ocular surface is a continuous epithelial structure

encompassing the cornea, conjunctiva, lacrimal apparatus as well as meibomian gland ducts[22]. The ocular surface barrier function helps maintain the immune-privileged nature of the cornea and the aqueous humor by providing the first line of defense against allergens and pathogens[23]. Disruption of this barrier function results in ocular surface discomfort, especially the cornea which contains a wealth of nerve endings[24]. According to the study by Taskiran Comez and Ozbas[25], conjunctival lacerations smaller than 10 mm typically heal within one week with medical therapy alone, and defects between 10 and 20 mm often respond adequately to 24-hour pressure patching with antibiotic ointment. However, surgical repair with sutures or fibrin glue is recommended when wound edge apposition is poor, the laceration is horizontally oriented, or blinking impedes spontaneous epithelialization. All patients in our study had 8–15 mm conjunctival lacerations accompanied by corneal epithelial injuries. Due to the presence of horizontally oriented or irregularly shaped wound edges that prevented adequate spontaneous apposition, all patients underwent suturing following debridement in the emergency setting. After repair, the different products were applied. Based on the expected healing time for sutured conjunctival wounds and standard clinical practice, the maximum duration of product application was set at 7d post-treatment, with clinical observations continued through day 14. The application of nanosilver technology to emergency eye patches for ocular surface trauma integrates the antimicrobial advantages of nanosilver with the convenience of eye patches. We selected Atrauman nanosilver dressings as the control group because they are well-researched, with substantial evidence supporting their wound healing and antimicrobial properties[26-27] as well as their safety[28]. Additionally, Atrauman nanosilver dressings are cost-effective, offering the lowest per square centimeter price among similar products [National Health Service Supply Chain Online Catalogue Pricing (https://my.supplychain.nhs.uk/catalogue)], making them a high-value choice for patients.

Our clinical trial demonstrated that nanosilver eye patches achieved non-inferiority to Atrauman nanosilver dressings in improving OCI scores for ocular surface trauma, with no statistically significant differences observed between the two treatments. Notably, both groups showed significant improvement in comfort scores from post-treatment day 1 to day 14, confirming their clinical utility in managing ocular surface trauma. Both the treatment and control groups showed increased proportions of Grade A healing wounds, with a more pronounced improvement observed in the treatment group. Neither group exhibited any Grade C healing outcomes. These findings demonstrate that both nanosilver eye patches and Atrauman dressings effectively promote wound healing, while the nanosilver patches may offer superior performance in achieving optimal (Grade A) healing. The absence of infection in both groups confirms that nanosilver eye patches and Atrauman dressings possess effective antimicrobial properties. No adverse events occurred in either group during the clinical trial, thus validating its safety. From a product usage perspective, compared to Atrauman nanosilver dressings, which need to be cut and fixed according to the location and size of the ocular trauma, nanosilver eye patches can conform to the shape of the eye. The eye patch can be stored separately from the layered dressing material and applied by sticking the dressing to the back of the eye patch.

In the comparative analysis of treatment options for ocular surface trauma, the amniotic membrane has been demonstrated to possess three therapeutic properties: anti-inflammatory (by promoting inflammatory cell apoptosis), anti-angiogenic, and anti-scarring effects [through inhibiting myofibroblast differentiation, reducing protease activity, and modulating transforming growth factor-beta (TGF-β) signaling pathways][29-30]. Emerging evidence also suggested potential antimicrobial capabilities. Currently developed derivatives such as amniotic membrane extracts and amniotic protein-incorporated hydrogels can further enhance wound healing rates[31-32]. However, this approach has significant limitations: it requires surgical transplantation in hospital settings and specialized procurement and storage protocols, making it unsuitable as first-line emergency treatment for ocular trauma. While conventional gauze dressings provide passive wound management through exudate absorption and facilitation of eschar formation, they are fundamentally limited by their lack of bioactive properties[33]. Compared to traditional treatments, the nanosilver eye patch demonstrates superior clinical utility by combining immediate injury source isolation (effective in both routine and combat environments) with active infection prevention and wound healing promotion, all packaged in a compact and user-friendly design.

Nanosilver dressings have emerged in the evolving field of trauma repair and anti-infection therapies. Silver nanoparticles (AgNPs) exhibit broad-spectrum inhibitory activity against nearly 650 types of microorganisms, including drug-resistant bacteria. Importantly, co-incubation experiments demonstrated suppression of biofilm formation, which is a critical property for practical wound dressing applications[34]. Nanosilver exerts antibacterial effects through multiple mechanisms. First, Nanosilver interacts with sulfur-containing biomolecules in bacterial membrane proteins, causing structural alterations and membrane damage[35-36]. Second, the reaction between nanosilver and protein thiol groups can induce reactive oxygen species generation, which subsequently inhibits respiratory enzymes and leads to cell death[37-38]. Additionally, $Ag^+$ released from nanosilver bind to negatively charged bacterial cell walls,

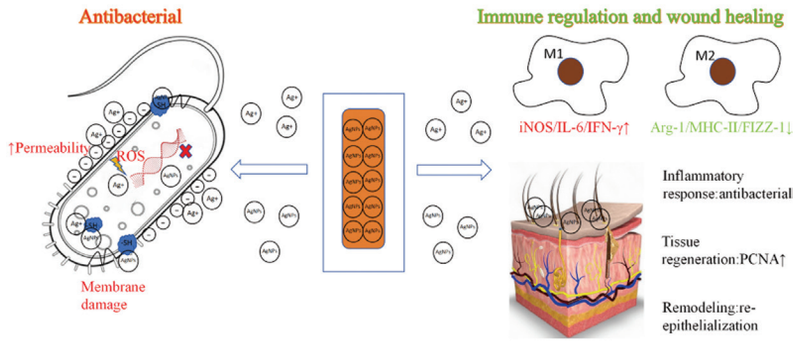


**Figure 5 Schematic illustration of the mechanism of silver nanoparticles (AgNPs)** ROS: Reactive oxygen species; iNOS: Inducible nitric oxide synthase; IL-6: Interleukin 6; IFN-γ: Interferon gamma; Arg-1: Arginase 1; MHC-II: Major histocompatibility complex class II; FIZZ-1: Found in inflammatory zone 1; PCNA: Proliferating cell nuclear antigen. Created with Microsoft PowerPoint.

increasing membrane permeability[39]. Both $Ag^+$ and AgNPs then penetrate the bacterial cells, where they disrupt thiol groups in proteins and severely interfere with DNA replication, ultimately causing cell death[40]. AgNPs demonstrate significant efficacy in promoting wound healing[41]. In a wound healing study following AgNPs hybrid collagen-chitosan scaffold implantation in rat dorsum, You *et al*[42] observed that AgNPs inhibited M1 macrophage activation and pro-inflammatory proteins (iNOS, IL-6, and IFN-γ), while promoting M2 macrophage polarization and tissue-repair markers (arginase-1, MHC-II, and FIZZ-1). This shift in macrophage phenotype contributed to suppressed foreign body responses and accelerated wound healing. Liu *et al*[34] discovered that wound dressings containing AgNPs significantly enhance the expression of proliferating cell nuclear antigen, which is a well-established marker of cellular proliferation, in keratinocytes. This upregulation promotes accelerated re-epithelialization and facilitates wound healing. Wound healing is a complex biological process involving three sequential phases: inflammatory response, tissue regeneration, and remodeling[43]. Active keratinocyte proliferation and rapid re-epithelialization are critical for successful tissue regeneration, whereas bacterial infection represents a primary cause of impaired healing[43-44]. Therefore, Nanosilver dressings can effectively prevent local bacterial infections while maintaining a conducive microenvironment for cellular proliferation and tissue regeneration, thereby promoting optimal wound healing[34] (Figure 5). Moreover, nanosilver dressings have been proven to be easy to use and improve patient comfort and have good breathability and fluid absorption capabilities[45].

The biocompatibility of AgNPs remains a critical concern. The toxicity profile appears to be determined by multiple factors: AgNP dimensions (size and shape)[46], tissue sensitivity, and silver release kinetics[47-48]. These parameters are further modulated by coating characteristics, material attributes, and local physiological conditions including pH and sweat components[49]. While smaller particles exhibit elevated toxicity due to enhanced cellular internalization[50], surface functionalization (*e.g.*, polyvinylpyrrolidone)[51] and low concentrations[52] can significantly improve biocompatibility profiles. Current research demonstrates that plant-derived AgNPs exhibit enhanced biocompatibility[53-54], while conjugation with biopolymers (*e.g.*, chitosan) significantly reduces their cytotoxic effects[20].

In this trial, all ocular surface injuries were related to the conjunctiva and cornea, and both the nanosilver eye patches and dressings were used outside the eyelid skin. AgNPs may need to penetrate the eyelid into the conjunctival and corneal tissues to exert their effects. However, current research does not indicate that AgNPs can penetrate full-thickness skin tissue directly into the underlying tissue[55-56]. *In vitro* skin penetration studies demonstrate limited transdermal absorption of AgNPs. Larese *et al*[57] applied 70 μg/cm$^2$ of polyvinylpyrrolidone-coated AgNPs (25±7.1 nm diameter) in synthetic sweat to human abdominal skin for 24h, detecting particles only in the deepest stratum corneum and outermost epidermal layers. Complementary work by Bianco *et al*[58] using smaller AgNPs (19±5 nm) on fresh human skin measured an extremely low silver flux rate of 0.2 ng/cm$^2$·h with an 8.2-hour lag time. These consistent findings across independent studies confirm that AgNPs, regardless of slight size variations (19-25 nm), exhibit minimal penetration through intact human skin, being predominantly retained in the epidermis' upper layers. The nanosilver eye patches used in the treatment group feature in situ-generated AgNPs on medical dressings, with all particles measuring <25 nm in diameter. Our clinical trial specifications indicate the mesh-structured nanofabric contains 0.25-0.28 g of nanosilver per 100 g of material. Based on the application duration of the nanosilver eye patch and the characteristics of AgNPs, we hypothesize that the AgNPs would not penetrate full-thickness skin during the observation period. The nanosilver eye patch likely functions through a dual mechanism: 1) forming a protective barrier to shield injured ocular surface tissues from bacterial infection; 2) creating a

pro-healing microenvironment. This combined action, which features localized antimicrobial activity coupled with tissue protection, represents a significant research direction for future ophthalmic wound management studies.

This study has potential limitations. First, comfort level scores are subjective patient reports, and while researchers filling out clinical trial case report forms have been professionally trained, there is potential for reporting bias and subjective interpretation bias. Second, we did not perform localized histological and hematological tests on the subjects. AgNPs have been employed in ophthalmic treatments since 1915, when Roe[59] first used colloidal silver ointments for corneal ulcers, burns, and ocular surface injuries. However, subsequent studies identified potential toxicity: AgNPs can accumulate in ocular connective tissues and basement membranes, causing conjunctival (particularly in the semilunar fold and caruncle) and eyelid discoloration, with deposits observed in the cornea, lens, vitreous, and retina[60]. Gallardo *et al*[61] reported three cases of ocular argyrosis resulting from over 10y of prolonged use of silver-containing eyelash dyes. This condition manifested as irreversible dark pigmentation of the eyelids and conjunctiva, along with diffuse gray-brown deposits in the corneal stroma and Descemet's membrane. Although silver deposits remained present within corneal and conjunctival cells, they typically did not cause any harmful cellular changes[61-62]. All observed adverse effects were associated with chronic exposure. Based on our experimental protocol with limited wearing duration and the pharmacokinetic profile of nanosilver, we conclude that AgNPs are unlikely to penetrate full-thickness eyelid tissues or induce significant toxic effects during short-term application in this study. Therefore, the relationship between the duration of use and the safety of nanosilver dressings on the eye may be a focus for future research.

In summary, in terms of wound comfort and promoting wound healing, nanosilver eye patches are not inferior to Atrauman nanosilver dressings. Both can have a certain level of safety and provide antibacterial treatment. The nanosilver eye patches demonstrate superior clinical value and optimized design for emergency management of ocular surface trauma in both military and civilian settings. Looking forward, the device requires further development and refinement. The key next step is to promote its application in larger, more diverse populations through multi-center clinical trials and real-world studies. This process of widespread use will be instrumental in gathering comprehensive data for gradual optimization, ultimately maximizing its therapeutic impact and adaptability.

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