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Research Article

Analysis of Chitosan-Based Nanosilver Composites for the Repair of Umbilical Cord Wounds in Newborns

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The study aim reports a new umbilical cord wound repair material based on modified chitosan-based nanosilver (CS-HDH/Ag NPs). The repair of umbilical cord wound has always been the focus of neonatal departments. The study method chitosan, which is famous for its "biological glue," is used as a modifier to compound silver nanoparticles with strong coordination and adsorption capacity of chitosan. It is worth noting that CS-HDH/Ag NPs has a significant inhibitory effect on common bacterial infection and reduces the incidence of umbilical cord wound inflammation. The study problem wound bleeding and stump shedding and other factors make the periumbilical cord vulnerable to bacterial infection. For study results, the porous and lamellar structure endows the repair material with breathable properties and excellent antiadhesion, which greatly reduces the number of dressing changes and effectively protects the skin of newborns. CS-HDH/Ag NPs provides a new model for efficient neonatal health management.

1. Introduction

As the link between the fetus and the mother, the umbilical cord provides an important channel for the fetus to absorb nutrients and for the transfer of oxygen and blood [1, 2]. However, the umbilical cord needs to be cut after birth to prevent jaundice or erythrocytosis from affecting the health of the newborn. Previous clinical reports reveal that the period between the cutting of the umbilical cord and its natural detachment is a high incidence of umbilical bacterial infections in newborns, which will lead to redness and swelling of the umbilical cord or surrounding skin tissues or will cause peritonitis or sepsis, which poses a great threat to the life of the newborn [3–6] (Figure 1). For this reason, the prevention and treatment of umbilical cord wound infection in neonates have attracted the attention of many scholars in the medical field.

Clinicians utilize iodine tincture or methyl violet solution to prevent and treat newborn umbilical cord wound infections. However, concentrated tincture of iodine is highly irritating, and methyl violet solution is not bactericidal against certain gram-negative and acid-resistant bacteria, reducing therapy efficacy. In view of this, researchers considered the application of medical dressings to promote the healing of umbilical cord wounds in newborns. After a long phase of exploration, medical practitioners worldwide have a more complete understanding of medical dressings [7–10]. Modern medicine believes that an ideal sterile dressing should have the following characteristics [11–14]: one is nontoxic to the body, two is able to create a sterile environment to isolate dust and microorganisms from the external environment to infect the wound, three has a hemostatic effect to accelerate wound healing, four is to absorb wound exudate to avoid its infection of the tissue around the

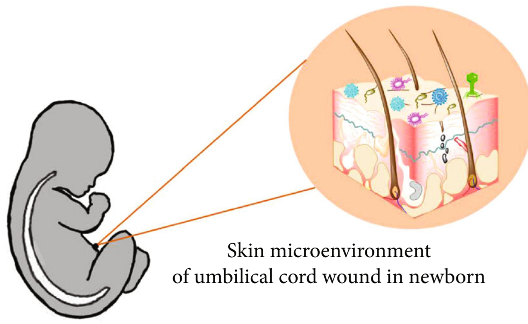

FIGURE 1: Schematic diagram of skin microenvironment around neonatal umbilical cord wound.

wound, and five has low adhesion to avoid secondary injury to the wound during dressing change. The second injury was caused by changing dressing. Traditional antimicrobial dressings are mainly made of medical skimmed cotton, which is inexpensive and simple to prepare. However, traditional antimicrobial dressings also exhibit many limitations, including the inability to absorb excess wound exudate, severe adhesion to tissue, and poor microbial isolation [15, 16]. Therefore, plans to develop new dressings are urgently needed [17–19].

The rapid development of biotechnology has provided new opportunities for researchers to design dressings with superior performance. Chitosan (CS) is a natural polymeric biomaterial, and studies have confirmed the outstanding effects of CS in antibacterial, hemostatic, analgesic, and wound healing, as well as its good biocompatibility and biodegradability, which makes CS valuable as a raw material for medical dressing applications [20–23]. In the in-depth study of CS, researchers also found that the active hydroxyl and amino groups within the molecular structure of CS have strong chemical properties, which makes CS have good modifying properties. Based on this excellent property, many scholars aspire to design composite multifunctional dressings.

As an abundant metallic element in nature, silver (Ag) has stable physicochemical properties and broad-spectrum antibacterial effects, and it is widely used in multiple fields. The development of nanotechnology has reduced the particle size of metallic silver to the nanoscale, which has greatly expanded the scope of Ag applications in various fields [24–27]. Distinct from the sterilization mechanism of silver, nanosilver materials increase the relative specific surface area of silver particles, and their electrostatic adsorption of bacteria, inhibition of bacterial respiration, and sterilization are more effective.

The umbilical cord connects the fetus to the mother and offers a pathway for nutrition, oxygen, and blood flow. Umbilical cord wound infections in neonates are treated with strong iodine or methyl violet solution. The fast advancement of biotechnology has opened new doors for researchers to create improved dressings.

The study contribution chitosan modified nanosilver was used as a raw material to prepare composites to design medical antimicrobial dressings, which were also applied to the repair treatment of umbilical cord wounds in newborns. The aim of this work is to investigate the specific application effects of chitosan-based nanosilver composites and to evaluate their potential value. The study is reported below.

2. Materials and Methods

2.1. Clinical Data. Ninety-two neonates, 39 males and 51 females, born in the pediatric department of the Second Hospital of Shaoyang College from August to November 2020, were selected for this study. They were divided into control group and CS-HDH/Ag NPs group according to random assignment, with 46 cases in each group. Inclusion criteria included neonates delivered at term, normal weight, and no signs of potential intrauterine infection during delivery, and all subjects participating in this study had their families sign an informed consent form. Exclusion criteria were neonates requiring admission to an intensive care center or undergoing asphyxia resuscitation. The differences in general information between the two groups of neonates were not statistically significant and were comparable, as shown in Table 1.

2.2. Materials and Apparatus. Chitosan was provided by Qingdao Honghai Biotechnology Co., Ltd. (Shandong, China). Acetic acid was provided by Hubei Yihang Biotechnology Co., Ltd. (Hubei, China). 1-Hydroxymethyl-5,5-dimethylhydantoin was provided by Jiangsu Aikang Biopharmaceutical R&D Co., Ltd. (Jiangsu, China). Acetone solvent was provided by Beijing Zhongnuo Taian Technology Co., Ltd. (Beijing, China). Ethanol was provided by Shandong Juhe Biotechnology Co., Ltd. (Shandong, China). Acetic acid solution was provided by Xi'an Qiyue Biotechnology Co., Ltd. (Shanxi, China). Silver nitrate was provided by Shanghai Aladdin Biochemical Technology Co., Ltd. (Shanghai, China). Borohydronium was provided by Shanghai Yilang Chemical Co., Ltd. (Shanghai, China). Sterile gauze and cotton swabs were provided by Henan Piaoan Group Co., Ltd. (Henan, China). Blood agar plate was provided by Shanghai Qiyuan Biotechnology Co., Ltd. (Shanghai, China).

BC-6800 series fully automated hematocrit analyzer was provided by Shenzhen Myriad Biomedical Electronics Co., Ltd. (Guangdong, China). Field Emission Scanning Electron Microscope was provided by Funa Scientific Instruments Co., Ltd. (Shanghai, China).

2.3. Preparation of Chitosan-Based Silver Nanocomposites. 0.1 mol of chitosan powder was dissolved in a solution of acetic acid with a volume fraction of 1%. An equimolar mass of 1-hydroxymethyl-5,5-dimethylhydantoin (HDH) was continued to be added to the mixed solution, and the reaction was stirred well under the condition of heating at 100°C in an oil bath for 1 d. After the reaction was continued, the solution was cooled to room temperature. The solvent was removed by centrifugation, and the obtained viscous product was added to the acetone solution; the mixed liquid was stirred until milky white, and the flocculent product was removed. After the above steps were repeated three times, the solid product of modified chitosan (CS-HDH) was then washed and dried by ethanol. The synthesized CS-HDH was dissolved in acetic acid solution, and 0.05 mol/L silver nitrate solution was added dropwise to the solution with magnetic stirring for 20 min. 0.3 mol/L sodium borohydride solution was added dropwise, and the reaction was left for 1.5 h to obtain CS-HDH/Ag NPs solution. Finally, the CS-HDH/Ag NPs thin film material

Table 1: Clinical information.

Parameter		Group	
		Control ($n = 46$)	CS-HDH/Ag NPs ($n = 46$)
Sex	Male	20 (43.48%)	19 (41.30%)
	Female	26 (55.52%)	27 (58.70%)
Gestational age (week)		39.46 ± 1.13	39.65 ± 1.22
Weight (kg)		3.41 ± 0.32	3.27 ± 0.39
Hospital stay (d)		5.91 ± 0.55	5.88 ± 0.62

was prepared by gel precipitation film casting-volatilization method.

2.4. Repair of Umbilical Cord Wounds in Newborns. After the birth of the newborn, the fetal umbilical cord was cut, the blood stains at the cord were cleaned, and the cord was ligated in the usual way. After the newborns were bathed for the first time, 75% ethanol was used to disinfect the umbilical cord section. In the control group, the stump of the umbilical cord was covered with sterile gauze and then bandaged daily, while in the CS-HDH/Ag NPs group, CS-HDH/Ag NPs film material was applied to the umbilical cord section and then bandaged with sterile gauze, which was changed every 24 h. The umbilical cord wound should be wrapped in such a way that it does not affect its blood circulation function, and the gauze should not rotate or fall off easily.

2.5. Observed Indicators of Umbilical Cord Wound Repair

2.5.1. Stopping Bleeding and Detachment of Umbilical Cord Stump. After cutting the umbilical cord of newborns, observe the time of stopping bleeding and the time of drying and shedding of the umbilical cord stump in both groups.

2.5.2. Bacterial Infection. After the neonates in both groups received umbilical cord wound repair, the secretions from the umbilical cord sections of each group were taken for bacterial culture experiments. Briefly, saline was used to wash around the umbilical cord of the newborns, and then, a sterile cotton swab was used to collect secretions from the crusted part of the wound into a test tube for backup. The collection of secretions from the wound is done in strict adherence to aseptic guidelines. The secretions were transferred to a blood agar plate at 35°C and incubated for 36 h. Suspected colonies were picked and identified using a fully automated bacterial identifier. The identified bacteria included Staphylococcus aureus (*Sa.*), Escherichia coli (*E. coli*), Group B hemolytic streptococci (*GBS*), and Pseudomonas aeruginosa (*Pa.*).

2.5.3. Indicators of Inflammation. Improperly treated umbilical cord wounds in newborns can lead to bacterial invasion and multiplication of the umbilical stump and cause umbilicitis. Therefore, after using the CS-HDH/Ag NPs film material, blood was collected from the newborns for routine blood tests and the inflammation assessment indicators specifically included white blood cells (WBC), neutrophils, C-reactive protein (CRP), and calcitonin gene (PCT).

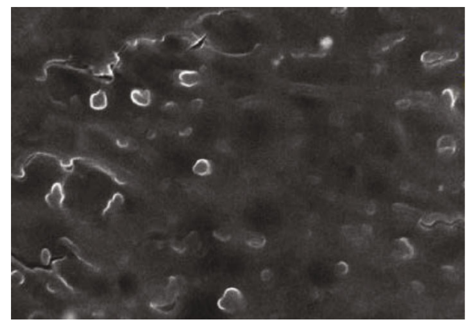

Figure 2: Scanning electron microscope (SEM) images of chitosan-based nanosilver thin film materials (CS-HDH/Ag NPs).

2.5.4. Periumbilical Skin Condition. During daily dressing changes, the skin condition around the umbilical cord was observed, and a distinction was made between normal newborns, patients with minor infections, and patients with severe infections. Among them, a little clear or yellowish mucus exuded from the umbilical cord wound, but no odor indicated that the newborn returned to normal. A mildly red and swollen umbilical chakra and periumbilical skin with a little pus visible in the umbilical fossa along with a slight odor is judged as a mild infection. If the skin around the umbilicus is obviously red, swollen, and hard, with a foul odor, the infection is considered severe.

2.6. Statistical Analysis. The experimental data collected in this study were statistically analyzed by the SPSS 25.0 statistical software. Continuous data were expressed as mean ± standard deviation, and discontinuous data were expressed as percentage (%).

3. Results and Discussion

3.1. Characterization of CS-HDH/Ag NPs Thin Film Material. The characterization images of CS-HDH/Ag NPs thin film materials under scanning electron microscopy (SEM) are shown in Figure 2. The dried composite film material has excellent network formation, and the silver nanoparticles are uniformly dispersed within the chitosan without obvious agglomeration due to the chelation between the silver ions and the lone pair of electrons within the chitosan.

3.2. Hemostasis and Detachment of the Umbilical Cord Stump. The hemostasis, stopping time of bleeding and drying, and detachment time of the umbilical cord stump in neonates with

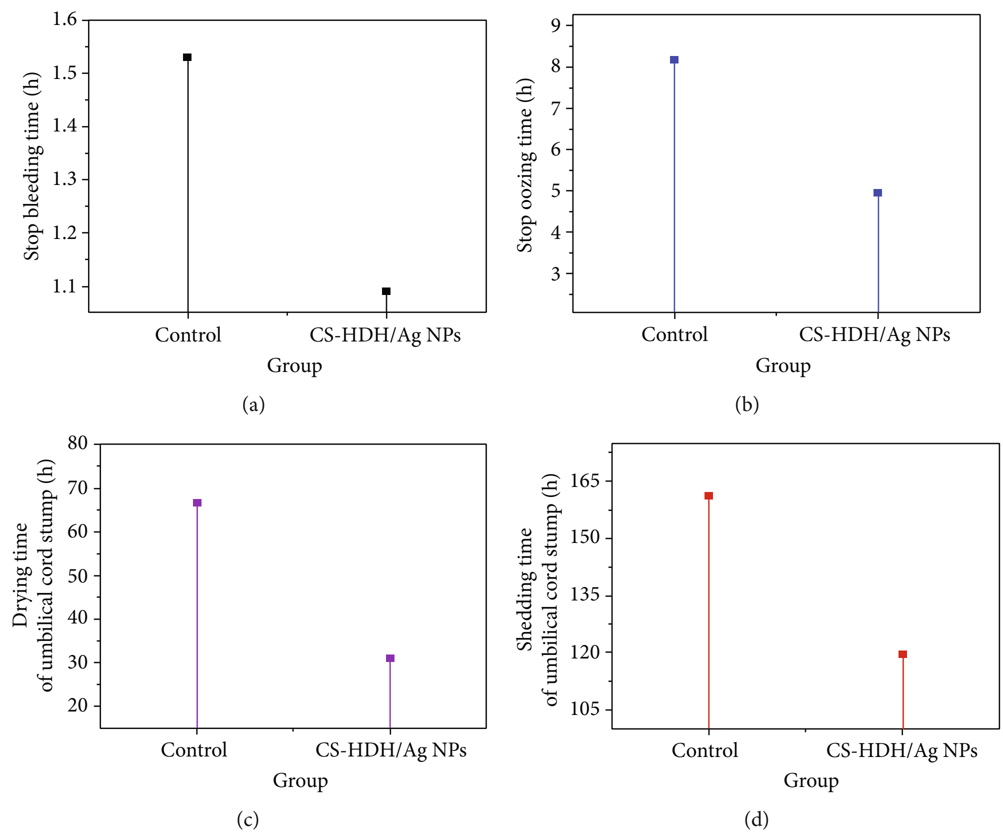

Figure 3: Comparison of hemostasis and shedding time of umbilical cord stump: (a) stop bleeding time; (b) stop oozing time; (c) drying time of umbilical cord stump; (d) shedding time of umbilical cord stump.

cut umbilical cord were observed, and the results are shown in Figure 3. The time to stop bleeding from the umbilical cord incision in the CS-HDH/Ag NPs group was 1.09 h, which was significantly lower than that of the control group, which was 1.53 h (Figure 3(a)). The time to stop bleeding from the umbilical cord incision in the CS-HDH/Ag NPs group was 4.96 h, which was shorter than that of the control group, which was 8.18 h (Figure 3(b)). The drying time of the umbilical cord stump was 31.09 h in the CS-HDH/Ag NPs group and 66.58 h in the control group, which was shorter in the CS-HDH/Ag NPs group (Figure 3(c)). There was also a significant difference in the detachment time of the umbilical cord stump between the two groups (Figure 3(d)), with a shorter time for the CS-HDH/Ag NPs group (119.64 h) than the control group (161.16 h). The results indicated that the experimentally prepared CS-HDH/Ag NPs composites could accelerate the repair time of umbilical cord wounds in neonates.

3.3. Bacterial Infection. The results of the bacterial culture at the umbilical cord wound of the newborn are shown in Figure 4. A total of 27 pathogenic strains were isolated from the control group, and the bacterial detection rate was 58.70% (Figure 4(a)). Among them, 9 strains (19.57%) of *Sa.*, 8 strains (17.39%) of *E. coli*, 4 strains (8.70%) of *GBS*, and 6 strains (13.04%) of *Pa.* were isolated from the CS-HDH/Ag NPs group, with a bacterial detection rate of 15.22% (Figure 4(b)). Among them, *Sa.* was 2 strains (4.35%), *E. coli* was 3 strains (6.52%), *GBS* was 1 strain (2.17%), and *Pa.* was 1 strain (2.17%). The data showed that the chitosan-based nanosilver composites had good antibacterial property and significantly improved bacterial infections in neonates after cutting the umbilical cord.

3.4. Inflammatory Indicators. Clinical cutting of the umbilical cord is often associated with the invasion of pathogens such as bacteria, leading to umbilical cord inflammation. In view of this, regular testing of inflammation-related indicators is helpful for health care workers to respond quickly and accurately to neonatal-related diseases. In this work, WBC, neutrophil, CRP, and PCT were quantified in newborns from 3 to 11 days of age, and the results are shown in Figure 5. In the control group, the WBC index showed an increasing trend from 18.33×10^9 cells/L to 21.98×10^9 cells/L. In the CS-HDH/Ag NPs group, the WBC index was 17.91×10^9 cells/L at 3 days after birth, and then, it fluctuated up and down, and at day 11, the WBC index was 18.19×10^9 cells/L on day 11 (Figure 5(a)). In the control group, the neutrophil index increased from 11.21×10^9 cells/L to 13.75×10^9 cells/L, whereas in the CS-HDH/Ag NPs group, the neutrophil index was 10.98×10^9 cells/L on the third day after birth and fluctuated in the following days to 11.10×10^9 cells/L on the 11th day. The neutrophil count was 11.10×10^9 cells/L at day 11 (Figure 5(b)). There was a significant difference in the changes of CRP index between the two groups of neonates (Figure 5(c)), where the CRP

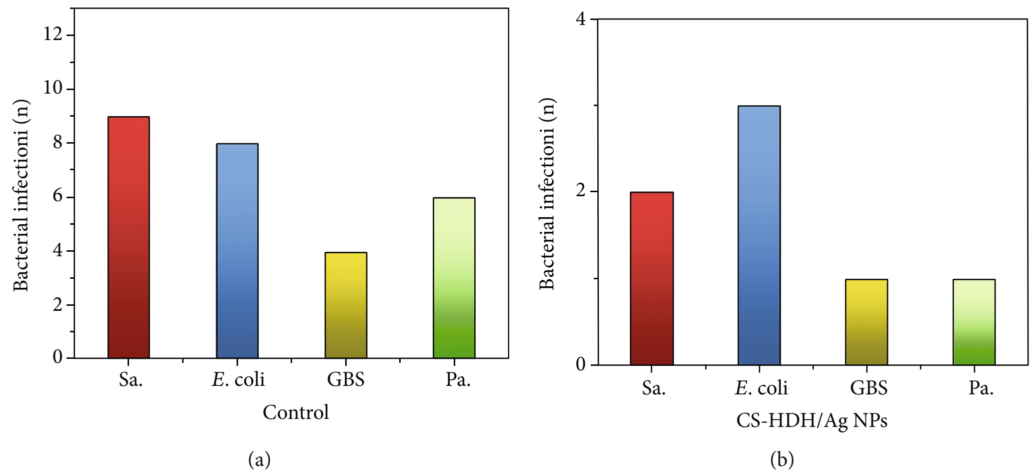

FIGURE 4: Analysis of bacterial infection: (a) control group; (b) CS-HDH/Ag NPs group.

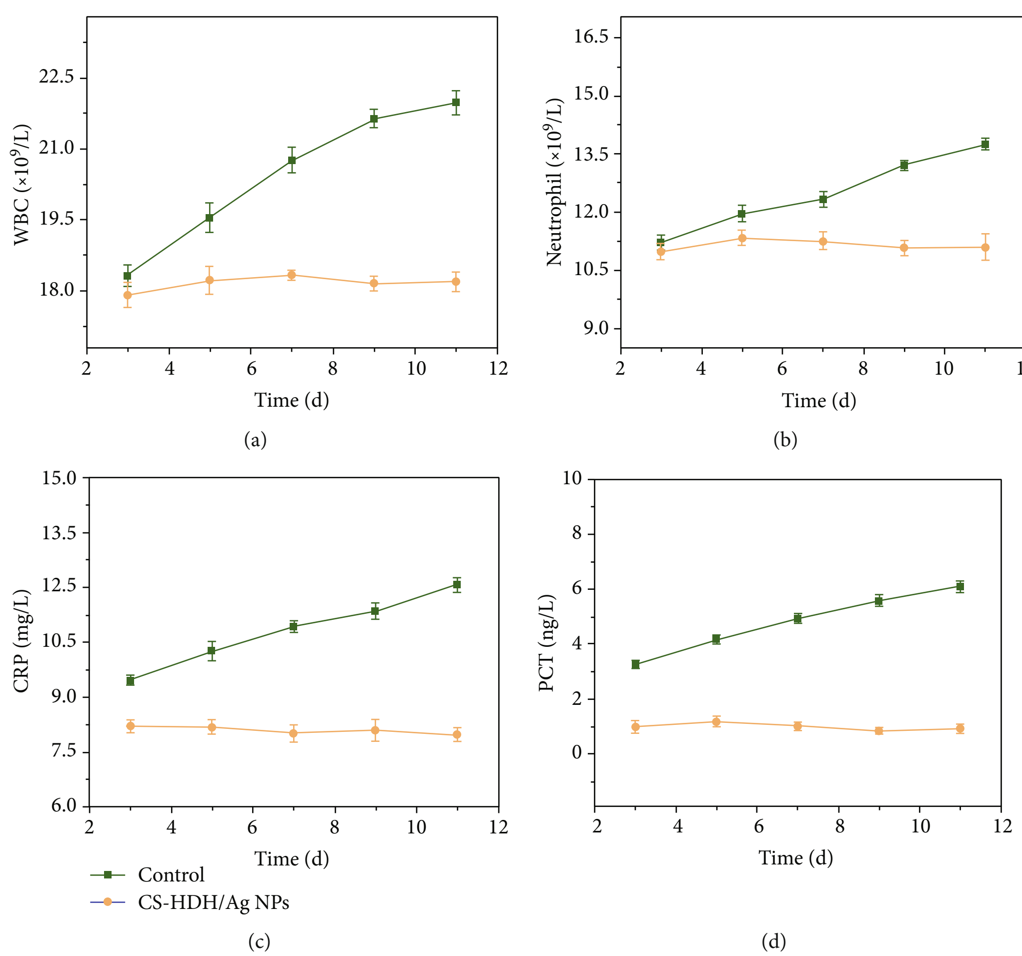

FIGURE 5: Inflammatory markers: (a) white blood cell; (b) neutrophils; (c) C-reactive protein; (d) procalcitonin.

concentration was 9.46 ± 0.14 mg/L in the control neonates on day 3 of life and 12.07 ± 0.21 mg/L on day 11, with a significant increase in CRP levels. In contrast, the CRP index of neonates in the CS-HDH/Ag NPs group decreased from 8.22 ± 0.17 mg/L to 7.97 ± 0.18 mg/L. Comparing the PCT index of neonates in both groups (Figure 5(d)), the PCT index in the control group increased from 3.25 ± 0.15 ng/mL to 6.09 ± 0.21 ng/mL, whereas the PCT index of the

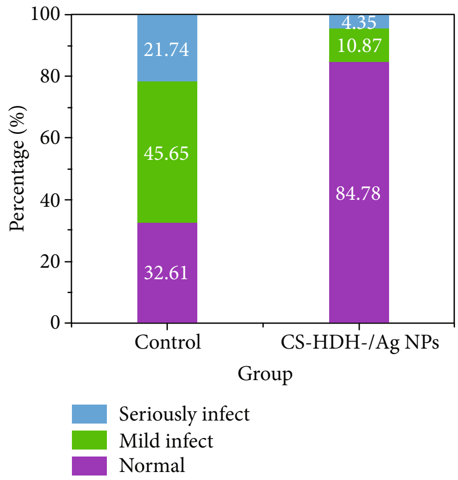

Figure 6: Skin condition around umbilicus of newborn.

CS-HDH/Ag NPs group fluctuated between 0.83 ± 0.12 ng/mL and 1.18 ± 0.19 ng/mL. The experimental results showed that the CS-HDH/Ag NPs film material for neonatal umbilical cord wound repair was effective in antimicrobial activity, suppressing inflammatory indexes and alleviating neonatal inflammation.

3.5. Periumbilical Skin Condition. The periumbilical skin condition of the newborns was observed during daily dressing changes to assess the effectiveness of the repair of the neonatal cord wounds, and the results are shown in Figure 6. Among them, 15 cases (32.61%) had normal periumbilical skin condition in the control group. Twenty-one cases (45.65%) were slightly infected. The 10 cases with severe infection accounted for 21.74%. In the CS-HDH/Ag NPs group, there were 39 neonates with normal periumbilical skin condition, accounting for 84.78%. Five cases (10.87%) were slightly infected. Two cases, or 4.35%, were severely infected. The data showed that the application of CS-HDH/Ag NPs film material significantly improved the problems of periumbilical skin redness and hardness and accelerated the repair of umbilical cord wounds in newborns.

3.6. Discussion. The umbilical cord is the link of material exchange between the mother and the fetus, transporting oxygen, energy, and nutrients to the developing fetus, and this stage is from the birth of the fetus up to the time when the umbilical cord of the newborn needs to be cut. After the umbilical cord is cut, the newborn's wounds exposed to the external environment are open wounds, and skin colonies are formed within a few hours. Therefore, improper repair of the umbilical cord wound will pose a threat to the health of the newborn.

Silver is a broad-spectrum antibacterial material that is useful in preventing wound infection and promoting wound drying, crusting, and healing. Meanwhile, chitosan, as a natural antibacterial material, gains a lot in long-lasting bactericidal effect. In view of this, a chitosan-based nanosilver composite was prepared in this work to achieve the management of umbilical cord wounds in neonates.

Clinical observations revealed that CS-HDH/Ag NPs film material can effectively shorten the cessation time of bleeding and drying time and detachment time of umbilical cord stump in neonates due to the unique surface effect of nanosilver with bacteria. Nanosilver can bind to the -SH base of bacterial metabolic enzymes and inhibit bacterial metabolism, while achieving enhanced bacterial inactivation by binding to DNA bases of pathogenic bacteria [28–30]. This conclusion is consistent with the results of bacterial infection experiments in the present study. Given the combined antibacterial effect of nanosilver and chitosan, this experiment also achieved control of umbilical cord inflammation and accelerated the repair of umbilical cord wounds in newborns.

In conclusion, the CS-HDH/Ag NPs composite was effective in repairing umbilical cord wounds in neonates. Compared with traditional gauze, the composite material has excellent antiadhesion effect and can improve clinical efficiency. The application of this material provides a simpler option for neonatal units and deserves to be widely promoted.

4. Conclusion

The nanosilver composite film material (CS-HDH/Ag NPs) based on modified chitosan (CS-HDH) plays an important role in the repair of umbilical cord wounds in newborns, as it can effectively inhibit the infection of umbilical cord wounds and suppress the inflammation of umbilical cord while maintaining a good skin environment, and it provides a new raw material for neonatal units, according to the findings.

Data Availability

The data underlying the results presented in the study are available within the manuscript.

Ethical Approval

Research experiments conducted in this article with human were approved by the Medical Ethics Committee of Second Affiliated Hospital of Shaoyang University following all guidelines, regulations, legal, and ethical standards as required for animals.

Conflicts of Interest

There is no potential conflict of interest in our paper,

Authors' Contributions

All authors have seen the manuscript and approved to submit to your journal.

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