Saudi Journal of Biological Sciences 25 (2018) 797–800

Contents lists available at ScienceDirect

Saudi Journal of Biological Sciences

journal homepage: www.sciencedirect.com

Original article

Effect of nano-silver hydrogel coating film on deep partial thickness scald model of rabbit

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ARTICLE INFO

Article history:
Received 20 June 2017
Revised 16 September 2017
Accepted 17 September 2017
Available online 19 September 2017

Keywords:
Nano-silver hydrogel coating film
Deep degree burns
Topical
Rabbits

ABSTRACT

Objective: Observing the effect of nano-silver hydrogel coating film on deep partial thickness scald model of rabbit.
Method: We prepared boiling water scalded rabbits with deep II degree scald models and applied high, medium and low doses of nano-silver hydrogel coating film for different time and area. Then we compared the difference of burned paper weight before administration and after administration model burns, burn local skin irritation points infection, skin crusting and scabs from the time, and the impact of local skin tissue morphology.
Result: Rabbits deep II degree burn model successful modeling; on day 12, 18, high, medium and low doses of nano-silver hydrogel coating film significantly reduced skin irritation of rabbits infected with the integral value ($P < 0.01$, $P < 0.05$); high, medium and low doses of nano-silver hydrogel coating film group significantly decreased skin irritation, infection integral value ($P < 0.01$, $P < 0.05$); high, medium and low doses of nano-silver hydrogel coating film significantly reduced film rabbits' scalded skin crusting time ($P < 0.01$), significantly shortened the rabbit skin burns from the scab time ($P < 0.01$), and significantly improved the treatment of skin diseases in rabbits scald model change ($P < 0.01$, $P < 0.05$).
Conclusion: The nano-silver hydrogel coating film on the deep partial thickness burns has a significant therapeutic effect; external use has a significant role in wound healing.

1. Introduction

Burn and scald is common damage, which is caused by many factors such as physics, chemistry, radiation and so on. It is an extremely complex and traumatic disease (Deng et al., 2011; Muhammad et al., 2017; Rashid et al., 2017). Burn wound management is an important part of the treatment. In addition to surgical treatment, most of the wound dressing needs treatment. Rational topical wound healing period can directly affect the overall treatment of deep degree burn wounds course and outcome. The nano-silver particle has a broad-spectrum antimicrobial effect lasting, easy to produce drug resistance and other characteristics. The nano silver gel in clinical application is particularly widespread. It can be divided into different categories according to different process. Nano silver gel can treat cervicitis, vaginitis, hemorrhoids, rhinitis and other effects (Zhou et al., 2011; Yang et al., 2014). This observation of nano-silver - hydrogel composite film antibacterial therapeutic effect on rabbits was degree burn model to evaluate the value of nano silver in the treatment of burn wounds.

2. Material

2.1. Experimental animals

Japanese rabbits of general level, provided by Henan Kangda experimental animal Co., animal certificate number: 1005365.

2.2. Drugs and reagents

Nano silver hydrogel wound film, provided by Henan Province Academy of Sciences Tongweisuo Research Institute Co., Ltd., batch number 20120712-7; Jingwanhong ointment for scald, Jingwanhong Tianjin Darentang Pharmaceutical Co. Ltd., batch number

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Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

https://doi.org/10.1016/j.sjbs.2017.09.002
1319-562X/

211793; Sulfuric acid paper, Zhejiang Minfeng Special Paper Co., Ltd., batch number 20121218; Ethyl carbamate (urethane), recovery of Tianjin Institute of Fine Chemicals, batch number 20120401; Claudel depilatory creams, Guangzhou Yibai Ya Cosmetics Co., Ltd., batch number 20110321; Medical absorbent gauze bag, Henan day and sanitary materials Co., Ltd., batch number 20120603; HL-R-A medical plaster, Xuzhou Hongli sanitary materials Co. Ltd. batch number 20121022; Sodium Chloride Injection, Chen Xin Pharmaceutical Co. Ltd., batch number 1208308201; Formaldehyde solution, Yantai shuangshuang Chemical Co. Ltd., batch number 20121012.

3. Methods

3.1. Model

We take healthy Japanese rabbits 36, 2.0–2.5 kg, male and female. After both sides shaved back of rabbits with clever Claudel hair removal cream, we remove the rabbit's hair of an area of approximately 20 cm × 15 cm; the next day to take 30 for modeling, with ear vein injection of 20% urethane (1 g/kg) anesthesia, and their limbs in prone position. They are fixed on the operating table with a rubber band. We put a cotton pad (18 floors) package of 200 g in weight and 1.8 cm in diameter in 100 Celsius degree boiling water for infiltration. After boiling, we immediately placed them on the left and right side of the spine skin preparation area, each pressurized 20 s, from front to back on each side of each hot three circular wounds, resulting in a total of 6 wounds per animal. The wound's diameter is 1.8 cm, with an area of about 2.54 cm^2, making a deep II degree burn model (biopsy confirmed). Immediately after that, we have intraperitoneal injection of sterile saline 20 mL/only in ot those models (Wu et al., 2011; Miao et al., 2016; Wang et al., 2016; Razali and Said, 2017).

3.2. Grouping and administration

The next day after the burn with sulfuric acid paper drawing of the graphics area of skin burns, we observe the quality of drawings, which was taken from the burn area on an electronic scale to indicate the quality of burn on the skin area (Miao et al., 2012; Mi et al., 2014). Animals' burn area varies due to difference in the operation so we divided them into groups, namely, model group, Jingwanhong group and large, medium and small doses of nano-silver hydrogel coating film groups, six in total. The other six form a control group. After modeling, each group of rabbits will be given the appropriate drugs. Large, medium and small doses of nano-silver hydrogel film are applied topical for each dose group. Jingwanhong group applied Jingwanhong burn cream (thickness 2 mm). Control group, model group, liberally saline in each group after administration of the above are covered with plastic wrap and taped securely, with uninterrupted regular dosing to maintain the drug in contact with skin for 6 h per day and with continuous medication for18 days.

3.3. Experimental index

Experimental indicators: local infection in burns, the overall situation, and pathology. Burn area: sulfuric acid to burn the paper cover to the first 1, 6, 12, 18 d ulcers along the wound edge tracings. We weighed the drawing of the burned skin area. The change of the weight shows the change in skin burns. We use the weight of the sheet before the administration to subtract that after treatment for evaluation to assess the effect of the test drug (Wang et al., 2014; Shamsudin et al., 2017; Zaheer et al., 2017). Burn local tissue pathology: the next day after the last dose, conducting drawn histopathological examinations, clipping burn parts of the skin, fixing them in 10% formalin solution and cutting into paraffin-embedded sections. Its staining was observed to compare each group of rabbits' burns for the observance of the healing degree of the skin.

3.4. Methods statistical analysis

Data were analyzed by using windows statistical software SPSS 17.0. The differences of measurement data between groups were analyzed by using ANOVA.

4. Results

4.1. Effect of nano-silver hydrogel coating film on rabbit scalded model ($\overline{x} \pm s$)

As can be seen from Table 1, compared with the blank group, the area of skin paper weight difference on the model group was significant ($P < 0.01$), which shows that burns rabbit model is successful. Compared with model group, on the day 6, high and low doses of nano-silver hydrogel coating burns groups and Jingwanhong rabbits skin area paper weight difference was significantly increased ($P < 0.05$); on the day 12, medium dose of nano-silver hydrogel coating film group and Jingwanhong rabbits burn the skin area of the paper weight difference was significantly increased ($P < 0.05$); on the day 18, medium dose of nano-silver hydrogel coating film group rabbits rabbit skin area burned paper weight difference was significantly increased ($P < 0.05$).

4.2. Nano-silver hydrogel film was scalded local skin irritation in rabbits infected points

As can be seen from Table 2, on the day 3, high, medium and low doses of nano-silver hydrogel coating film group and Jingwanhong rabbits infected skin irritation integration value decreased significantly ($P < 0.05$); On day 6, high dose of nano-silver hydrogel coating film group significantly reduced skin irritation rabbits infected with the integral value ($P < 0.01$), the dose nano-silver hydrogel coating significantly reduced skin irritation rabbits infected integral value ($P < 0.05$); on the 12th and 18th day of treatment, each group rabbit skin irritation infection disappeared.

4.3. Effect of nano silver hydrogel coated on rabbit scald skin scar and scab time

As can be seen from Table 3, the skin in the blank group and the normal, the model group appeared scab, scab time; compared with the model group, high medium and low dose of nano-silver hydrogel coating film group and Jingwanhong group can significantly shorten the scalded rabbits skin scab time ($P < 0.01$); high, medium and low dose of nano-silver hydrogel coating film group and Jingwanhong group can significantly shorten the scalded rabbits skin scab time ($P < 0.01$).

4.4. Effect of nano silver hydrogel coated on local tissue morphology of rabbit's skin scald

As can be seen from Table 4, after *Ridit* test, compared with the blank group, significant pathological changes in the skin of model group rabbits. Compared with the model group, high and medium doses of nano-silver hydrogel coating film group can significantly improve the skin pathological changes in the model of burn ($P < 0.01$).

Table 1
Effect of nano-silver hydrogel coating film on rabbit scalded model.

Group	n	The burn area of different time after treatment and the weight difference of the former paper (mg)		
		Day 6	Day 12	Day 18
Blank group	6	0 ± 0**	0 ± 0**	0 ± 0**
Model group	6	31.90 ± 27.13	82.05 ± 29.71	137.52 ± 26.03
Jingwanhonggroup	6	69.68 ± 33.56*	124.55 ± 35.16*	164.62 ± 35.38
High dose of nano-silver hydrogel coating film group	6	63.55 ± 25.67*	108.92 ± 30.45	147.97 ± 13.90
Medium dose of nano-silver hydrogel coating film group	6	69.08 ± 37.21	118.33 ± 18.16*	166.50 ± 20.46*
Low dose of nano-silver hydrogel coating film group	6	68.52 ± 11.06*	107.17 ± 7.18	158.73 ± 18.69

Note: compared with the model control group.
** P < 0.01.
* P < 0.05.

Table 2
Nano silver hydrogel coated on rabbit scald erythroderma infection points ($\bar{x} \pm i$).

Group	n	Infection of skin redness and swelling after administration					
		Day 1	Day 2	Day 3	Day 6	Day 12	Day 18
Blank group	6	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Model group	6	1 ± 0	1.33 ± 0.52	1.50 ± 0.55	1.00 ± 0.63	0.17 ± 0.41	0.17 ± 0.41
Jingwanhonggroup	6	1 ± 0	1 ± 0	1 ± 0*	0.50 ± 0.55	0 ± 0	0 ± 0
High dose of nano-silver hydrogel coating film group	6	1 ± 0	1 ± 0	1 ± 0*	0 ± 0**	0 ± 0	0 ± 0
Medium dose of nano-silver hydrogel coating film group	6	1 ± 0	1 ± 0	1 ± 0*	0.17 ± 0.41*	0 ± 0	0 ± 0
Low dose of nano-silver hydrogel coating film group	6	1 ± 0	1 ± 0	1 ± 0*	0.50 ± 0.55	0 ± 0	0 ± 0

Note: compared with the model control group.
** P < 0.01.
* P < 0.05.

Table 3
Effect of Nano silver hydrogel coated on rabbit scald skin scar and scab time ($\bar{x} \pm$ Ef).

Group	n	Scabby time (d)	Callus time (d)
Blank group	6	0 ± 0**	0 ± 0**
Model group	6	5.00 ± 0.63	8.83 ± 0.75
Jingwanhonggroup	6	2.67 ± 0.81**	6.67 ± 0.82**
High dose of nano-silver hydrogel coating film group	6	2.83 ± 0.75**	6.67 ± 0.52**
Medium dose of nano-silver hydrogel coating film group	6	3.00 ± 0.63**	7.00 ± 0.63**
Low dose of nano-silver hydrogel coating film group	6	3.33 ± 0.52**	7.33 ± 1.03**

Note: compared with the model control group.
*P < 0.05.
** P < 0.01.

Each group of rabbits back burn local tissue morphology results appendix: control group animals horny layer of epithelial tissue and squamous epithelial cells intact and thin subcutaneous tissue and hair follicles of the hair follicles and sebaceous glands were normal, both subcutaneous normally, see photo 1; experimental animal model group horny layer of epithelial tissue, squamous epithelium completely denatured, subcutaneous tissue, hair follicles and sebaceous glands and hair follicles are denatured and disappeared. Subcutaneous tissue is replaced by a large amount of granulation tissue, see photo 2; In Jingwanhong group, some experimental animal epithelial tissue layer thickening keratosis, squamous epithelial hyperplasia and inflammatory cells significantly exudation, subcutaneous tissue of the hair follicles, sebaceous glands and hair follicles are phosphate; the horny layer of some animal epithelial tissues disappear. Squamous epithelial hyperplasia and hair follicle completely denatured. Subcutaneous tissue, hair follicles and sebaceous glands disappear. Subcutaneous tissue is replaced by a large amount of granulation tissue, see photo 3; large doses of Nano-silver hydrogel coating film animal experiments keratinized epithelial tissue layer is leaking. Large amounts of inflammatory cells are replaced by squamous epithelium hyperplasia somewhat. Subcutaneous tissue hair follicles, sebaceous glands and hair follicles epithelial cells disappear, and are replaced by a large amount of granulation tissue, see photo 4; horny layer of the epithelium covered Nano-silver hydrogel dose group animals. Squamous epithelium is replaced by the

Table 4
Effect of Nano silver hydrogel coated on local tissue morphology of rabbit's skin scald.

Group	n	–	+	++	+++	*P*
Blank group	6	6	0	0	0	<0.01
Model group	6	0	0	0	6	
Jingwanhong group	6	0	0	6	0	
High dose of nano-silver hydrogel coating film group	6	0	4	2	0	<0.01
Medium dose of nano-silver hydrogel coating film group	6	0	2	4	0	<0.01
Low dose of nano-silver hydrogel coating film group	6	0	0	2	4	

"–": Keratosis, squamous epithelium, hair follicle, hair follicle glands, sebaceous glands, and subcutaneous tissues were normal; "+": cornified layer thinner, slightly squamous epithelial hyperplasia, follicular small partially denatured gland follicles, sebaceous cell proliferation slightly, subcutaneous tissue, normal; "++": thickening of the horny layer and a small amount of exudation of inflammatory cells, squamous epithelial hyperplasia, partially denatured hair follicle, the hair follicle glands, sebaceous glands phosphate, granulation tissue is subcutaneous replaced; "+++": horny layer thickening and exudation of inflammatory cells, squamous epithelial proliferation significantly, the hair follicle degeneration, follicular glands, sebaceous glands disappear, subcutaneous tissue is replaced by a large amount of granulation tissue.

disappearance of many inflammatory cells and degeneration of tissue, subcutaneous tissue, hair follicles, sebaceous glands and hair follicles disappeared, Subcutaneous tissue is replaced by a large amount of granulation tissue, see photo 5; Nano-silver hydrogel small dose group animals were covered by horny layer of the epithelium. Squamous epithelium disappears; many inflammatory exudate and tissue cell degeneration replaced the subcutaneous tissue of hair follicles. Sebaceous glands and hair follicles disappear. Subcutaneous tissue was replaced by large amounts of granulation tissue, see photo 6.

5. Conclusions

Burn wounds are more open wounds, and can be easily contaminated by reproductive bacteria. Antibiotics are often for clinical use. With the expanding variety of clinical abuse of antibiotics and resistant strains on skin and sore wound, using a simple antibiotic therapy has been difficult to achieve the desired results. Methods for addressing topical burn wound are various, but how to control the use of wound infection on burn treatment in a reasonable and effective way, is still under heated discussion so far (Li et al., 2016). Modern medicine holds that, after burn damage, local skin tissue functions, resulting in local wound microcirculation, insufficient blood supply, stasis edema and necrosis, and because the skin barrier function has been damaged, various inflammatory exudate increases. This easily leads to bacterial infections. And the use of Nano-silver particles and bacterial protein thiol groups (-SH) binding, causing their degeneration, so sulfhydryl enzyme inactivation play its broad-spectrum antimicrobial effect, while Nano-silver wound matrix metalloproteinase has inhibiting effect. This advantage contributes greatly to wound healing (Shi et al., 2014; Gao et al., 2017). Nano silver is a new generation of natural non-antibiotic fungicides, with stable physical and chemical properties and potent broad-spectrum bactericidal capacity (Liu et al., 2009; Liu, 2016). Strong permeability Nano-silver, can rapidly penetrate the skin pores, killing a variety of bacteria, fungi, mycoplasma, chlamydia and other bacteria within several minutes, and bacterial resistance to silver is extremely rare, thus obtaining the medical biology a wide range of applications.

Experiment selected local burn skin area paper weight difference as the main appearance index, because it is visible; histopathological changes reflect impaired organization the layers of the skin lesion and healing. Choosing local pathological tissue as the objective index can help us better estimate scald model modeling degree (Li et al., 2013; Liang et al., 2013). The above indexes respectively from two aspects of disease and quality, providing a comprehensive evaluation of curative effect of Nano silver hydrogel composite external application on scalded rabbits model.

The experimental results are shown, and small dose of Nano silver gel is coated group could reduce the scalded rabbit's area and avoid the scald edema and infection. Local burn skin scab time was significantly shortened. Nano silver gel can significantly improve the skin pathological changes of scalded rabbits site, suggesting that it has a certain therapeutic effect on the scalded skin. So, this experiment using Nano silver gel film for treating scald and clinical burn proves to be a simple, effective, and controllable treatment method.

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