Coc Cer Derg/Turkish J Ped Surg 2022;36(2): 34-36
doi: 10.29228/JTAPS.58181

Research Article

Çocuk Cerrahisi Dergisi
Turkish Journal of Pediatric Surgery
Volum 36 Number 2 2022

The efficacy of clostiridial collagenase coated with antimicrobial agents on burn patients

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ABSTRACT

Objective: Burn eschar treatment delays the healing period and usually needs surgical intervention. Alternatively, enzymatic debridement materials are widely used and effective. However, these agents are bacteria originated and this limits antimicrobial agent use.
In this study we aimed to evaluate the efficacy of collagenase used with antimicrobial agents observing changes in systemic inflamatory symptoms .
Materials and Methods: Superficial and deep second degree burn patients between 2011-2013 were examined retrospectively.78 patients were divided into 2 groups : Only collagenase group, and collagenase with antimicrobial agents (Patch method) group. Demographics and recovery data were recorded and statiscally analyzed.
Results: Surgical intervention ratios for Collagenase and Patch groups were 29.2 % , 46.7 % respectively. Mean escharolysis time in The Collagenase and The Patch groups were 7.2 ± 3.3 , 9,6± 2.8 days respectively. Mean time of epithelization start in Collagenase and Patch groups were 12.3 ± 5.8, 13.4 ± 4.8 days respectively. Systemic inflammatory symptoms ratio in The Collagenase and the Patch group were 27.1% and 43.3% respectively. The only statistically significant difference was on the time of escharolysis.
Conclusion: The Patch method delays escharolysis period, but does not inhibit it. So it can be used safely.

Keywords: Enzymatic debridement, clostridial collagenase

Received / Geliş: 23.03.2022
Accepted / Kabul: 07.07.2022
Published Date: 01.08.2022

Cite as:Görkem Bulut, Ülküm Zafer Dökümcü, Emre Divarcı, Ahmet Çelik, Geylani Özok. The Effıccacy of Clostiridial Colleganase Coated With Antımıcrobıal Agents On Burn Patients. Coc Cer Derg/Turkish J Ped Surg 2022;36(2): 34-36. doi: 10.29228/JTAPS.58181

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This study was produced from the doctoral thesis done in Ege University Faculty of Medicine, Department of Pediatric Surgery in 2015.

Introduction

Eschar formation caused by burns, is more frequent in children than adults because their epidermis is thinner [1] . The most common method of eschar treatment is surgery, but there is a risk of dermal loss , thus need for a skin graft . Moreover most children do not have sufficiently large skin area to harvest. Thankfully methods like enzymatic debridement are becoming more popular [2-7].

Collagenase clostiridopeptidase A is a metalloproteinase enzyme which is produced from clostridium histolyticum. It hydrolizes the tri-helix zones of collagen [8-10]. Due to released peptides and not having antimicrobial effect these materials can cause bacterial colonization thus increasing systemic inflammatory response [11]. An antimicrobial agent use is considered, however it is widely known

In the USA several clinical findings have shown that these materials can be used together effectively and safely [12].

Hypothesis

1. Using collagenase with antimicrobial agents may not inhibit escharolysis and epithelization.
2. Using collagenase with antimicrobial agents may lower systemic inflammatory responses.

Materials and Methods

We restrospectively examined only 2nd degree deep burn patients hospitalized in our tertiary burn center between 2011 and 2013 . Patients were divided into two groups . First group was treated with only collagenase , while the second group was treated with collagenase and antibacterial agent together using a method we called *Patch*. This method entails using topical antimicrobial agents over collagenase scrubbing separately (Fig. 1-5). The demographic data of patients, the amount of time elapsed with the applications , need for surgeries, time of escharolysis and epithelization were calculated with mean values. To avoid bias, other time values like hospitalization and treatment duration were calculated with median values. First day of burn trauma was considered as day zero. Surgery was required in patients who were unresponsive to enzymatic debridement .In case of eschar persistence secondary excisions were needed and due to dermal loss some needed grafting. Autologous skin grafts were used for the procedures. We considered the epithelization start as total healing.

Systemic inflammatory responses are consisted of tachypnea, tachycardia, fever, leukocytosis, trombositopenia. Wound antibiograms were tested at least once a week.

The study was approved by Ege University Ethical Commitee of Clinical Research (B.30.2.EGE.0.20.05.00/OY/1271/613).

Statistical analysis

SPSS 22.0 for Windows is used with the help of Ege University Faculty of Medicine Department of Biostatistics for statistical analysis. $P < 0.05$ is considered significant.

Differences and similarities between groups were evaluated by T-test and Chi-square test , and Mann Whitney –u test.

Results

A. Demographics

The study contained 78 patients (41 male ,37 female) There were 48 patients in collagenase group and 30 in Patch group . Male contribution in collagenase group was 70.7 % . Female contribution in collagenase group was 51.4% . Mean age was calculated as months (47,5 ± 49,3 months) (p=0,079). In collagenase group mean age was 49,33 ± 51,37 months, in Patch group it was 44,57 ± 46,26 months (p=0,680). 80.8 % of burns occured of scalding followed by fire and electricity. The reason of burn contribution was similar between groups.

No statistically significant differences were found between groups in demographic data .(p>0,05)

B. Treatment application findings

Mean burnt area ratios in collagenase and Patch group were 6.1% and 8.1% ,respectively (p= 0,057) In collagenase group median time of treatment start and duration were 3.6±2.5 days and 4.2±2.8 days respectively. In Patch group median times for the mentioned feature were 3.6±2.1 days for start and 5.3±2.2 days till the end of treatment (p= 0,895 for start ; p= 0,082 for duration). Median hospitalization time till discharge was 11(min 3- max 26) days in collagenase and 13 days (min 5- max 23) in patch group (p=0,270).

There were no statistically significant differences between the groups in treated burn areas and treatment times. (Graphics 1-3)

C. Treatment end findings

Mean eschar lysis times in collagenase and Patch group were 7.2 and 9.6 days respectively (p=0.002). Epithelization occurrence times in collagenase and Patch group were 12.3 and 13.4 days respectively (p=0,395). Only eschar lysis time difference was statistically significant (Graphic 4)

28 (14 in collagenase, 14 in Patch group) patients had undergone surgery due to unresponsiveness of enzymatic debridement after 7 days mean. Grafting ratio was 16.6% in patch group(5 patients), 16.6% in collagenase group (8 patients). 4 patients of Patch group needed a secondary attempts for excision or grafting while in collagenase group 6 patients needed a secondary procedure. Ratio of total surgical intervention needed were 29.2 % and 46.7 % in collagenase and Patch group respectively. (p=0.535) (Graphic 5) .

Mean period of surgical escharectomy needed in the collagenase and Patch groups were 6.7±3, 7.5±4.1 days respectively (p=1,000).

Systemic inflammatory responses are shown in table 1 (p=0,139) .There were 12 patients in collagenase and 10 in Patch group who had positive results on antibiograms at wound sites (p=0,295). We have found that there is less diversity of bacteria in Patch group (Graphic 3 ,4) .There were no significant differences between groups.

Discussion

Even 2nd degree childhood burns can cause eschar formation more easily than adults due to their thinner epidermis layers. Eschar formation is a suitable base for pathogenic germs and delays the healing [1,13]. Removing the eschar is also a vital step to avoid post-healing scars.

In accordance to that many studies assert early tangential excision of eschar , which was first described by Janzekovic [4] . Although surgical excision is still widely used it can be a reason of dermal loss because of thin epidermis layers of children. It is known that epidermis can be derived from a healthy dermis. As

a result of deep excision skin grafts could be needed. In addition children do not have as sufficient graft area as adults. There are of course many dermal replacement materials . However these have many disadvantages like costs, graft versus host disease and applying difficulties. Invention of enzymatic debridement agents had many advantages against surgical excision [9,10,14-17] .
Clostridial collagenase was produced from filtrates of clostridium histolyticum by Altemeier [8]. Howes et al had used this for eschar lysis [3] .
The disadvantages of using collagenase are that it takes longer time than surgery and it makes the patient vulnerable to wound infections. Because these products are not indicated use with antimicrobial agents. Also Dökümcü et al has found that using collagenase indirectly increased systemic inflammatory responses [11] .
In our study we used collagenase ointment with antimicrobial agents by patching one on the other. Thus we called this as *Patch*. Although it's not common, we can see examples of it in the USA and in studies of Soroff and Sasvary [12] .
The demographic results, burn area ratios, treatment times between groups showed no statistically significance . This indicates that groups were divided homogenously to avoid bias. Albeit, hospitalization time range width may falsely indicate heterogenity due to one patient with too small electricity burn areas who could be discharged in 3 days and followed up as an outpatient in a daily basis.
We have observed eschar lysis could be safely done with Patch method which was our study's main goal. Also we found no significant difference in necessity of surgical intervention.The only statistically significant difference was that it took longer to diminish eschar formation in Patch group. But eventually epithelization has been observed in both groups without any significant difference. These results meant that using Patch method did inhibit escharolysis and epithelization in disconcordance to general beliefs and some studies [3,6,11,17] . Thanks to this no additional surgery was required except those unresponsive to enzymatic debridement. This shows our first hypothesis was true. Patch method did not obsolete the effect of collagenase in contrast to the general opinions.
Systemic inflammatory symptoms, results and number of positive tissue cultures did not vary significantly between groups. However we have observed that in Patch group there were far less bacterial species variety. Because of accepting systemic inflammatroy responses with tissue culture positiveness as real burn wound infection ,diversity of bacteria have no effect for our second hypothesis. Thus our second hypothesis was found as false. Contingently a more potent and wide spectrum antimicrobial product might have had a considerable effect on this.

Conclusion

Despite the fact that Patch method takes longer time to eliminate eschar formation it does not inhibit collagenase and thus eschar formation can be diminished safely and effectively. Although decreasing the species diversity of bacteria , patch method did not make a significant effect on sysytemic inflammatory responses.

Declaration of interest
None.

Acknowledgements
Thanks to Lecturer Mr. Ufuk Bilki (Celal Bayar University School of Foreign Languages Manisa/TÜRKİYE) for language help and proof reading.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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