



Case series

Efficacy of tilapia skin xenograft compared to paraffin-impregnated gauze as a full-thickness burn dressing after excisional debridement: A case series

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ABSTRACT

Introduction and importance: Due to its high collagen, good adherence to wound bed, and great wound healing properties, Tilapia (*Oreochromis niloticus*) skin has been studied as a biomaterial in regenerative medicine, including as a burn dressing. This paper evaluated the efficacy of tilapia skin xenograft as a temporary full-thickness burn dressing.

Methods: Four acute burn patients aged 23–48 years old with total body surface area ranging from 27.5 to 37% with a similar burn area on both sides of the limbs were included. Each limb was dressed in tilapia skin or paraffin-impregnated gauze. Two subjects passed away due to septic shock. All limbs treated with tilapia skin xenograft required fewer dressing changes compared to the limbs treated with paraffin-impregnated gauze. All remaining subjects underwent skin autograft transplantation surgery on the eleventh day after the debridement surgery. No allergic reaction was found in any of the subjects.

Outcomes: The tilapia xenograft performed better in controlling and containing the exudates compared to the paraffin-impregnated gauze, as reflected in the fewer dressing changes needed. The cause of death of the two patients was questionable as both of them have severe pneumonia and COVID-19 still could not be ruled out yet.

Conclusion: The tilapia skin xenograft was not inferior to the standard paraffin-impregnated gauze for full-thickness burn dressing in terms of time needed for wound bed preparation for autograft surgery.

1. Introduction

Currently, the treatment for burns has shifted from early excision and skin grafting to staged excision and temporary coverage with xenograft or allograft [1,2]. However, both xenograft and allograft are currently unavailable in Indonesia for several reasons, including strict cultural and religious preferences [3,4]. Due to its high collagen, good adherence to wound bed, and great wound healing properties, Tilapia (*Oreochromis niloticus*) skin has been studied as a temporary burn dressing [5]. To provide better burn care in Indonesia, this paper evaluated the efficacy of tilapia skin xenograft as a full-thickness burn dressing.

2. Methods

This prospective case series was conducted in the Burn Unit, Dr Cipto Mangunkusumo Hospital, a public academic hospital in Jakarta,

Indonesia, from August to October 2020. The samples were adult acute burn patients, aged 18–60 years old, with 20–40% of total body surface area with a similar full-thickness burn on both sides of their upper or lower limbs, who underwent excisional debridement on ≤ 96 h post-burn. The exclusion criteria were patients with infected burns, comorbidity, severe allergic reaction, and a positive result of the COVID-19 PCR swab test which was taken on the admission day. Subjects were recruited consecutively. This study compared tilapia skin xenograft to paraffin-impregnated gauze, the standard care in our burn unit, for wound bed preparation before autograft surgery. The outcomes evaluated were the time needed for wound bed preparation and the frequency of dressing changes.

This study protocol was approved by the ethical committee of the Faculty of Medicine Universitas Indonesia (No.KET-760/UN2.F1/ETIK/PPM.00.02/2020, Protocol Number: 20-05-0539) and conducted according to the principles of the Declaration of Helsinki. This study has

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also been registered publicly on [researchregistry.com](https://www.researchregistry.com) (Unique Identifying Number: researchregistry7916) [6]. Written informed consent was obtained for the publication of this paper and accompanying images.

The tilapia (*Oreochromis niloticus*) xenograft production was conducted as follows. First, the skin is separated from the muscle and washed with tap water. Second, the fish skin is cut into 20 cm × 10 cm pieces, rinsed with 0.9% of saline, and soaked in 2% chlorhexidine gluconate in a sealed container for 60 min. Third, it was rinsed with 0.9% saline and soaked in a mixture of 75% glycerol and 25% saline solution in a sterile sealed container for an hour. Fourth, the skin is rinsed again with sterile 0.9% saline and moved to another sealed sterile container filled with 100% glycerol, in which it is massaged for 5 min and kept soaked for 3 h. Fifth, the skin is packed in sealed plastic envelopes and stored at 4 degrees Celsius. Last, the fish skin is irradiated with gamma rays on a Cobalt 60 multipurpose irradiator at 30 kGy in Indonesia’s national nuclear energy agency (BATAN). Random samples of the xenograft were checked through several bacterial and fungal culture tests to ensure sterility.

Before the surgery, all patients were stabilized first, the mean arterial pressure must be more than 65, normal axillary temperature (36.0–37.5 °C), and administered an empirical antibiotic (Ampicillin-sulbactam 1.5 g IV every 6 h) starting from the first day of hospitalization. All patients underwent excisional debridement of a maximum of 20% of TBSA under general anesthesia by an experienced plastic surgeon with a subspecialty in burn (with >5 years of experience in the burn unit). Then, each limb was dressed in either tilapia skin or paraffin impregnated gauze according to the randomization result. A family member of the patient chose an envelope containing either “right” or “left” and the chosen side would be treated with tilapia xenograft, while the other side was dressed with paraffin gauze. Then, each wound was covered with dry sterile gauze, then with an elastic bandage.

The dressing was changed every 2–3 days for the paraffin gauze group and every 5 days for the tilapia skin xenograft group. Additional dressing changes would be done if the dressing looked saturated. Two experienced burn surgeons (with >5 years of experience in the burn unit) independently evaluated the wound with Bates-Jensen Wound Assessment Tool (BWAT). The BWAT score was calculated every time the dressing on both groups was changed simultaneously, which was every five days after the surgery. The split-thickness skin graft (STSG) procedure was done the following day after both surgeons scored less than 20 on BWAT. Patients were monitored until the wounds are ready for the STSG procedure. If any allergic reaction was shown, the dressing would be immediately removed and changed to tulle dressing as the standard burn dressing. This case series has been reported in line with the PROCESS Guideline [5].

3. Results

Fifty tilapia skin graft patches were produced over four weeks, measuring 20 cm × 10 cm on average. Besides the labor and transportation cost, each patch only cost around \$1. Four patients were recruited with a total of 7 pairs of limbs as samples, patients’ characteristics were described in Table 1. Two out of four patients passed away due to septic shock (Clavien-Dindo grade V) and the deaths were reported to the local ethics committee. No allergic reaction was observed in both groups, either clinically or from laboratory examinations. The remaining surviving subjects commented that the side treated with

Table 1
Characteristics of included subjects.

Subject number	Age	Gender	% total body surface area	Length of stay
1	44	Male	27.5	31
2	48	Female	28	20
3	23	Male	37	5
4	36	Female	31.5	8

tilapia skin xenograft was less painful compared to the other side. There were no changes in the interventions during the course of the case series.

The BWAT score of both groups on the fifth and tenth days have normal distribution based on the Shapiro-Wilk test. The mean BWAT score on the fifth day was identical in the control [30.5 (±3.1)] and xenograft [30.5 (±2.5)] groups. On day ten, the mean BWAT score was also similar in the control [18.75 (±0.9)] and xenograft [18.75 (±1.25)] groups. None of the patients need additional debridement surgery.

The burn wound progress of the first and second subjects can be seen in Figs. 1 and 2, respectively. The partial-thickness burns on the right upper limb of subject number 1 which was treated with the tilapia xenograft have completely epithelialized on the fifth day, as seen in Fig. 1.

None of the patients in both groups needed extra dressing changes besides the regular schedule. In the control group, exudates were seeping through the elastic bandages as early as the next day after debridement. In comparison, no leakage was observed in the tilapia xenograft group, even on the fifth and tenth days. Therefore, over ten days period, all subjects in the xenograft group required two fewer dressing changes compared to the paraffin gauze group.

4. Discussion

Tilapia skin has non-infectious microbiota, a high level of moisture, and is mainly composed of collagen type 1, which is morphologically similar to human skin. Due to its composition, tilapia skin has a high resistance and tensile extension at break property [5]. Recent studies showed that tilapia skin adheres well to the wound bed. Moreover, tilapia xenograft improved wound healing rate in rats by promoting cell adhesion, proliferation, and differentiation [7–9].

This is the first study on the efficacy of tilapia skin xenograft compared to paraffin-impregnated gauze as a full-thickness burn dressing. There were two case reports on the use of tilapia skin as xenograft on partial-thickness burns, one of which was for a pediatric patient [7,10].

The production of tilapia skin xenograft only needed a few days, making it an accessible choice as a burn dressing. It was also affordable as a 20 cm × 10 cm xenograft only cost about \$1 besides the transportation and labor cost. Tilapia skin xenograft also needed fewer dressing changes which makes it even more cost-effective. However, further research is needed on the storage life of this tilapia xenograft. In our trial, all xenografts were used within a week after being produced.

This study showed that tilapia skin xenograft was not inferior to paraffin-impregnated gauze in terms of time needed for wound bed preparation for STSG surgery. BWAT score was used to standardize the readiness for autografting. The BWAT score on days five and ten after excisional debridement surgery were similar between groups. All wounds underwent STSG on the eleventh day, thus no re-debridement surgery was needed. Costa et al. [7] and Lima et al. [10] used tilapia skin xenograft for partial-thickness burns and complete epithelialization was achieved within 10–17 days. In our study, the first subject has partial-thickness burns on the area covered by the tilapia skin xenograft and it was completely re-epithelialized on the first dressing change (on the fifth day).

The only difference between groups was the dressing change frequency. Over ten days period, all subjects in the xenograft group required two fewer dressing changes compared to the paraffin gauze group. Therefore, tilapia xenograft was superior in controlling and containing the exudates compared to paraffin gauze. The use of tilapia xenograft on burns was also safe as there was no allergic reaction observed. Other studies which utilized tilapia skin xenograft for second-degree burn in humans also reported no side effects [7–10].

4.1. Limitations

The limitations of this study were the small number of participants



Fig. 1. The burn wounds on the right upper limbs of subject number one (A) on the day of the accident, (B) after excisional debridement and xenograft surgery, (C) fifth day after surgery, and (D) tenth day after surgery in which the wound has been completely epithelialized.



Fig. 2. The burn wounds on the left upper limbs of subject number two (A) on the day of the accident, (B) after the excisional debridement and xenograft surgery, and (C) fifth day after surgery.

(only four patients) and the high percentage of serious adverse events which might be caused by the intervention. Two patients passed away a few days after the first surgery due to severe septic shock. Both of them have severe pneumonia and COVID-19 still could not be ruled out yet.

4.2. Recommendations

Due to the high mortality rate in the treatment group, future larger RCT studies should be focused on improving the sterilization process and contaminants testing, also maintaining the sterile condition until transplantation. The maximum shelf life of the tilapia skin xenograft should also be found. Patients’ subjective complaints i.e., pain and pruritus should also be observed in upcoming studies.

5. Conclusions

This case series highlighted that tilapia skin xenograft was not inferior to paraffin-impregnated gauze for wound bed preparation in full-thickness burns. Despite the high rate of serious adverse events, the fish skin xenograft performed better in controlling and containing the burn exudates compared to the standard paraffin-impregnated gauze. Larger prospective studies on the production, efficacy, and shelf life of

the tilapia skin xenograft as burn dressing are encouraged and the xenograft production have to be strictly regulated and monitored.

Patient perspective

Two out of the four patients mentioned that the side treated with tilapia skin xenograft was less painful compared to the other side. However, one participant told that the appearance of the xenograft was slightly disturbing.

Informed consent

The scan of written informed consent is available if requested by the journal.

Disclosure

This case series has never been presented at any conference or regional meeting.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

This study protocol was approved by the ethical committee of the Faculty of Medicine Universitas Indonesia (No.KET-760/UN2.F1/ETIK/PPM.00.02/2020, Protocol Number: 20-05-0539). The study was performed following the Good Clinical Practice.

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Guarantor

Aditya Wardhana and Nandita Melati Putri.

Research registration number

This study has been publicly registered on [researchregistry.com](https://www.researchregistry.com) (Unique Identifying Number: researchregistry7916, link: <https://www.researchregistry.com/browse-the-registry#home/registrationdetails/6282941c8eaa85001e31d5cc/>).

CRediT authorship contribution statement

N.M.P.: conceptualization, methodology, formal analysis, investigation, data curation, writing original draft, visualization, project administration, funding acquisition.

P.K.: methodology, validation, resources, writing original draft, supervision, funding acquisition.

A.N.S.: software, validation, investigation, resources, writing review and editing.

G.A.D.: conceptualization, methodology, formal analysis, investigation, data curation, writing original draft, writing review and editing, visualization.

N.J.: software, formal analysis, data curation, visualization, writing review and editing.

A.W.: conceptualization, methodology, validation, investigation, writing review and editing, supervision.

Declaration of competing interest

The authors declare no conflict of interest.

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