

**Tilapia allograft and tilapia xenograft in the treatment of pediatric 2nd degree burns***Aloinjerto de tilapia y xenoinjerto de tilapia en el tratamiento de quemaduras pediátricas de 2º grado**Aloenxertia e xenoenxertia de tilápia no tratamento de queimaduras pediátricas de 2º grau***Ana Beatriz Rebouças de Azevedo Marques<sup>1</sup>**

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**Submission:** 03-29-2021**Approval:** 04-08-2021**Abstract**

The aim of this study was to study the use of tilapia allograft and tilapia xenograft in pediatric second-degree burns in terms of therapeutics and clinical-surgical results. This is a narrative literature review carried out through a survey of articles in the MEDLINE databases via PubMed, Cochrane Library, VIA ELSEVIER, BVS, LILACS, Scopus. Allograft is indicated for covering full-thickness wounds, healing partial-thickness wounds, as well as preparing the bed for subsequent self-grafting. This option, however, becomes limited by the insufficient skin banks in Brazil. Xenograft can be considered a therapeutic and socioeconomic solution. The use of Nile tilapia skin has benefits in the treatment of burns, and, in Brazil, the large production of this fish allows access to its skin due to the disposal of this by-product. Its use represents the progress of clinical and surgical management by analyzing its benefits, possible complications, and socioeconomic impacts, in addition to the need to explore new therapeutic methods for the best treatment based on available resources.

**Descriptors:** Burns; Pediatrics; Allografts; Heterografts; Cichlids.**Resumen**

El objetivo de este estudio fue estudiar el uso de aloinjerto de tilapia y xenoinjerto de tilapia en quemaduras de segundo grado pediátricas en términos de terapéutica y resultados clínico-quirúrgicos. Se trata de una revisión de la literatura narrativa realizada a través de una encuesta de artículos en las bases de datos de MEDLINE a través de PubMed, Cochrane Library, VIA ELSEVIER, BVS, LILACS, Scopus. El aloinjerto está indicado para cubrir lesiones de espesor total, cicatrizar heridas de espesor parcial, así como preparar el lecho para el posterior autoinjerto. Esta opción, sin embargo, se ve limitada por la insuficiencia de los bancos de piel en Brasil. El xenoinjerto puede considerarse una solución terapéutica y socioeconómica. El uso de piel de tilapia del Nilo tiene beneficios en el tratamiento de quemaduras y, en Brasil, la gran producción de este pescado permite el acceso a su piel debido a la eliminación de este subproducto. Su uso representa el avance del manejo clínico y quirúrgico al analizar sus beneficios, posibles complicaciones e impactos socioeconómicos, además de la necesidad de explorar nuevos métodos terapéuticos para el mejor tratamiento en base a los recursos disponibles.

**Descriptores:** Quemaduras; Pediatría; Aloinjertos; Xenoinjertos; Cíclidos.**Resumo**

Objetivou-se estudar o uso da aloenxertia e xenoenxertia de tilápia nas queimaduras pediátricas de 2º grau quanto às terapêuticas e resultados clínico-cirúrgicos. Trata-se de uma revisão narrativa de literatura realizada através de levantamento de artigos nas bases de dados MEDLINE via PubMed, Cochrane Library, VIA ELSEVIER, BVS, LILACS, Scopus. A aloenxertia é indicada para a cobertura de lesões de espessura total, cicatrização de feridas de espessura parcial, assim como a preparação do leito para uma posterior autoenxertia. Essa opção, entretanto, torna-se limitada pelos insuficientes bancos de pele no Brasil. O xenoenxerto pode ser considerado uma solução no âmbito terapêutico e socioeconômico. O uso da pele da tilápia do Nilo apresenta benefícios no tratamento de queimaduras e, no Brasil, a grande produção desse peixe viabiliza o acesso à sua pele devido ao descarte deste subproduto. Seu uso representa o progresso do manejo clínico e cirúrgico ao analisar seus benefícios, possíveis complicações e impactos socioeconômicos, além da necessidade de explorar novos métodos terapêuticos para o melhor tratamento a partir de recursos disponíveis.

**Descritores:** Queimaduras; Pediatría; Aloenxertos; Xenoenxertos; Tilápia do Nilo.

## Introduction

Burns are defined as traumatic injuries to the lining of the body, from the epidermis to deeper tissues. They can be caused by contact with chemical substances, radiation, direct flame, electrical energy, thermal and flammable agents. The severity of the damage is associated with both the causal factor and the depth of the burn, the time and area of exposure. This type of injury portrays a serious scenario for public health, mainly because it is the second most frequent cause of accidents in childhood, as well as having the highest morbidity and mortality rate in trauma accidents. Children are in a situation of greater vulnerability to death compared to adults, due to their still immature musculoskeletal and immune systems. Likewise, due to more sensitive skin, your burns can progress to deeper levels with a consequent drop in general condition<sup>1-4</sup>.

With the beginning of the COVID-19 pandemic at the beginning of 2020 in Brazil, together with the need for the population to adapt to the new reality of social distance, hygiene habits and, consequently, a longer period for children at home, the Brazilian Society of Pediatrics published a warning note which evidenced an increase in the incidence of burns in children during quarantine, mainly related to the use of alcohol gel. Pediatric burns have been shown to increase by 25% since the onset of the pandemic<sup>5,6</sup>.

Most cases occur in children under 5 years of age, an age group in which the neuropsychomotor development is not complete, which, added to socioeconomic factors and failure in surveillance by parents or guardians, leads to the occurrence of burns<sup>2</sup>. Studies indicate males as the most affected and situations involving hot liquids as predominant in all pediatric phases. Inhalation injuries can also occur, such as in fires in closed places and burns close to the face, which increases the mortality rate, and its main cause is carbon monoxide poisoning<sup>7</sup>. Regarding the location of the lesions, in Brazil a prevalence in the trunk region was indicated<sup>3</sup>.

Second-degree burns are subdivided into superficial partial thickness, which is characterized by reaching the epidermis and the papillary portion of the dermis, manifesting blister formation due to the detachment of the epidermal layer and the exudate of the capillaries remaining in the deep layer of the dermis, as well as intense hyperemia, edema, pain and tenderness, indicating that the cutaneous adnexa were not reached, which will be responsible for spontaneous regeneration within 21 days; and deep partial thickness, which affects the epidermis and both the papillary and reticular dermis, thus, as a result of the great destruction of the vascular plexus, hyperemia and exudate are smaller, but the appearance of blisters is still possible. From the few remaining dermal attachments, regeneration can occur, however it will be accompanied by scarring. For the same reason, this lesion is less painful than the superficial one and has a greater possibility of infection and evolution to full thickness<sup>7,8</sup>.

The burned body surface (SCQ) can be calculated according to the "Rule of Nines", which divides the body into segments that are multiplied by the number nine. However, for children, the use of the Lund-Browder diagram is the choice for a more accurate calculation, due to the different

proportions in which the body is subdivided<sup>9,10</sup>. The indications for hospitalization of children take into account this calculation and the depth of the lesions, as in 2nd degree burns affecting more than 10% of the body surface, 3rd degree burns affecting more than 5%, and 2nd or 3rd degree burns on the face, genitals and perineum. In addition to chemical and electrical burns and burns associated with concomitant trauma, child victimization or lack of conditions for home management, underlying chronic diseases or young infants, inhalation injury and circumferential burns<sup>7</sup>.

This trauma provokes a local, metabolic, and systemic response, with loss of body fluid homeostasis. Immediately, vasoactive mediators are released and promote an increase in vascular permeability, with displacement of fluids from the intravascular environment to the interstitium, which results in hypovolemia and edema in the burned region. Edema usually progresses within 24 hours, at which time repair of the vascular endothelium begins, and in large burns it can originate in unburned tissue due to exacerbated hypoproteinemia<sup>7,11,12</sup>.

When regulating temperature, it is necessary to pay attention to children, who are more prone to hypothermia<sup>7</sup>. There is also a greater concentration of counterregulatory hormones, which makes the support of early enteral nutrition extremely important, as evidenced in a study that can provide shorter hospital stays, reduce the occurrence of bacterial translocation and the possibility of infectious complications, with considering that the high rate of infant mortality in burns is due to infection, systemic inflammatory response syndrome and sepsis<sup>1,3,9,11</sup>.

In the management of burn patients, it is essential to re-establish the permeability of the airways, ventilation, circulation, fluid resuscitation, urinary output and analgesia, according to the trauma protocol for treating burns, the therapy continues with the attention focused on the wound, and extends to the restitution phase and healing approach<sup>2,7,12</sup>. The proper treatment to be applied is one of the most important aspects, due to the high morbidity and mortality caused by this trauma<sup>9</sup>. The first step is to irrigate the wound, in which any clot present in the wound is disarranged, allowing bleeding to start. Hemostasis can be done through direct pressure or through vascular repair if a surgical approach is needed<sup>10</sup>.

Wound debridement is necessary when there is devitalization, to remove necrotic tissue and minimize bacterial infections. Depending on the urgency and stability of the patient, this process can occur at the bedside, however conventional surgical debridement is the gold standard. The form of total excision removes all necrotic tissue, but it can result in deformities, whereas in tangential excision, the removal is done in layers until vitalized tissue is found. This technique presents better aesthetic results and for future reconstructions, but allows for the risk of bleeding, uneven depth, and incomplete removal of the devitalized tissue<sup>10</sup>. Debridement of deep 2nd degree and 3rd degree burns is essential, and usually then requires grafting<sup>13</sup>. This process often presents several challenges for Medicine, from its availability to its application stages.



Tilapia skin allograft and xenograft are two options that should be increasingly explored. Thus, the study aims to analyze the use of tilapia allograft and xenograft of tilapia in pediatric second-degree burns in terms of therapeutic and clinical-surgical results, highlighting the benefits of its use to improve the management of burns based on available resources, complications and cost-effectiveness, which is extremely important for literary enrichment in the departments of Pediatrics and Plastic Surgery.

### Methodology

Narrative literature review from MEDLINE search via PubMed, Cochrane Library - Cochrane Central Register of Controlled Trial (CENTRAL), based on VIA ELSEVIER, BVS, LILACS, Scopus, using keywords and synonyms about tilapia allograft and tilapia xenograft in children with second-degree burns, with the aim of adapting the research requirements to each database. Finally, the Snowballing technique was used to expand the search based on the references of the included studies.

To find relevant articles for this review, the majority selected were those published between 2016 and 2020, except for those that include concepts that are still up-to-date, and descriptors available on the Health Sciences Descriptors (DeCS) platform were used: Burns; Pediatrics; Allografts; Xenografts; Nile Tilapia. Any publications on tilapia allografts and xenografts in children who had second-degree burns were considered, except for protocols, and any outcome that has been evaluated and reported by the authors of the publications. All pediatric patients, regardless of gender, who had second-degree burns were also included in the selection. There were no restrictions regarding the causal factor of burns.

### Results and Discussion

Grafts are skin fragments taken from a donor area and moved to the recipient area, which will provide the blood supply. There are several types of grafts in relation to their thickness, such as total, partial, and composite skin grafts: and in relation to its origin as the autograft, coming from the patient, the isograft, from one identical twin to the other, the allograft, between individuals of the same species, and the xenograft, between different species. Another way to fill the wound is through flaps, which, unlike grafts, have their own vascularization through the vessels of a pedicle that communicate between the flap and the receiving bed. To be performed, there must be skin leftovers and mobility in the donor region, so that the pedicle is not pulled with the positioning of the flap<sup>14</sup>.

The allograft can be used in children with a large, burned body surface, when autologous grafting is not possible, and with the purpose of alleviating pain, reducing the risk of infections, and contributing to re-epithelialization. Second-degree burns often require constant dressing changes, causing the injury to deepen and causing wound infection and pain, which highlights the possible benefits of using this technique. Allografts favor wound healing, reduce the loss of body fluids, and promote early and temporary coverage. Rejection occurs after a few days or weeks due to

genetic differences between donor and recipient, for this reason, when possible, grafting from a first-degree relative is preferred so that rejection can be postponed<sup>12,15</sup>.

Allograft is indicated for covering full-thickness lesions, healing partial-thickness wounds, as well as preparing the bed for subsequent self-grafting. For some pediatric patients it is still a better alternative to autografting, as it does not cause major clinical complications of homeostatic decompensation, resulting from a new injury from autograft collection, especially in the acute phase of the burn, in which children are susceptible to electrolyte losses and shock. In these cases, allograft enables early wound excision<sup>15</sup>.

A study carried out at the Jawaharlal Institute for Graduate Medical Education and Research showed that allografts, when compared to synthetic dermal substitutes, have more advantages and fewer disadvantages. Among the options for synthetic dermal substitutes, collagen is usually the most available and has properties like those of allografts, but its cost is higher, and its absorption takes place between 3 and 6 days, which makes it necessary for more of exchanges. The allograft remains in the wound for 2-3 weeks; thus, it is considered more effective in reducing pain and controlling infections.<sup>15</sup>

The allograft option, however, becomes limited by the insufficient number of skin banks in Brazil. In this scenario, xenograft can be considered a solution both from a therapeutic and socioeconomic point of view. The use of Nile tilapia skin (*Oreochromis niloticus*) has been increasingly studied and has several benefits in the treatment of burns. In Brazil, the large production of this fish allows access to its skin due to the disposal of this by-product. Histological studies have shown effectiveness in the adhesion of lesions, ability to retain moisture, high strength and extension when subjected to traction, and morphological structure like humans, which limits immune responses in relation to it<sup>16,19</sup>.

Tilapia xenograft has a high concentration of collagen type I and antimicrobial, anti-inflammatory, antioxidant, antihypertensive, nerve protective, and granulation tissue stimulation activities due to its diverse amino acid content. Based on these peptide properties, it could express epithelial and fibroblast growth factors, which induce cell differentiation, re-epithelialization, and proliferation, according to its hydrophilic characteristics. The components of your colony indicate a normal and non-infectious microbiota, and it also undergoes chemical steps of skin preparation, cleaning, decontamination, dehydration and radiosterilization, before being used as a graft<sup>18,20,21</sup>.

Research carried out at the Dr. José Frota Institute (IJF), a public hospital in Fortaleza, in stage 2 of the clinical trial on the use of tilapia in the grafting of superficial and deep second-degree burns, showed results such as excellent adhesion to the wound, which served as protective factor against infections and fluid loss, decrease in pain and costs. It was also observed that the graft remained until healing in superficial second-degree lesions, not requiring its replacement, which was also demonstrated in a case report described in Fortaleza, and used as a comparison in a study



carried out at Hospital São Marcos in Pernambuco, with the use of hydrofiber with Aquacel Ag® silver in superficial and deep second-degree burns, in which the use of tilapia xenograft demonstrated the lowest occurrence of dressing replacement<sup>16,19,20</sup>.

Edmar Maciel Lima et al. demonstrates the use of Tilapia skin as a xenograft in the case report of a patient with deep second-degree burns involving mainly the inguinal and genital regions after thermal injury by fire flames. The patient had 13.5% of her body surface burned. With the use of tilapia, a period of 16 days was necessary for the re-epithelialization of the burns, whereas if conventional treatment had been used, it would have taken around 3 weeks for complete healing. In addition, the use of this xenograft showed results such as the absence of side effects, antigenicity, and toxicity, in addition to benefits such as flexibility, adherence, moisture conservation, a reduction factor in the entry of microorganisms and a reduction in dressing changes. Furthermore, it was possible to observe good results with tilapia skin, including in areas of the body

that were little explored after this treatment, such as the genital and inguinal region, even with the need for skin replacement as in the case report<sup>22</sup>.

### Conclusion

The study of allografts and xenografts through tilapia skin, in pediatric burns, portrays the progress of clinical and surgical management by comparing their benefits, possible complications and socioeconomic impacts, and the enrichment of literary research on the subject. Considering that the number of studies is still scarce, this research represents a necessary basis for future work. The use of tilapia is an alternative to the demand of unmet skin banks and demonstrates good adhesion to the wound bed, less need for dressing change, and greater availability potential when compared to allograft, and reflects the need to explore new therapeutic methods for the optimal treatment of the patient based on available, effective and cost-effective resources.

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