Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/burns

# The use of porcine xenografts in patients with toxic epidermal necrolysis☆

Jason B. Young[a], Stephen P. Gondek[a], Maria Troche[a], J. Blair Summitt[a], Lisa Rae[a], Wesley P. Thayer[a], Steven A. Kahn[b,*]

[a] Department of Surgery, Division of Trauma and Surgical Critical Care, Vanderbilt University Medical Center, 1211 21st Ave South, 404 Medical Arts Building, Nashville, TN 37212, United States

[b] Department of Surgery, Division of Trauma, Burns, and Surgical Critical Care, University of South Alabama Medical Center, 2451 Fillingim Street, Suite 10-I, Mobile, AL 36617, United States

ARTICLE INFO

*Article history:*
Accepted 2 June 2016

*Keywords:*
Xenograft
Stevens-Johnson Syndrome
Toxic epidermal necrolysis

ABSTRACT

*Introduction:* Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) can be challenging to treat due to pain with wound care and ongoing fluid loss. The purpose of this study is to determine the role of porcine xenograft as a modality for wound coverage.

*Material and Methods:* A retrospective review from 2006 to 2014 was performed at a regional burn center on all patients admitted with the diagnosis of SJS (<10% TBSA involvement), SJS/TEN overlap (10–30% TBSA involvement), and TEN (>30% TBSA involvement). Patients who received porcine xenograft had physiologic and biochemical parameters compared in the 24 h before and after graft placement. In addition, xenograft patients were compared to historical controls that received traditional wound care which included silver impregnated dressings. Outcomes and variables collected included intravenous fluid given, urine output, pain scores (1–10), pain medication for wound care, biochemical markers, skin infections, hospital length of stay, and mortality.

*Results:* Eight patients had placement of a porcine xenograft. Median age was 50 years (IQR 41, 66) and 2 were male. Median % TBSA affected was 76 (IQR 64, 80). The median amount of fluid (ml/kg/day/%TBSA) administered decreased from 1.45 (IQR 1.03, 1.78) to 0.9 (IQR 0.65, 1.08) after xenograft placement ($p = 0.02$). The median amount of intravenous fluid (ml/kg/day/%TBSA) administered in the treatment group and historical control group was 0.9 (IQR 0.65, 1.08) and 0.8 (IQR 0.7, 1.47) respectively ($p = 0.72$). The median amount of urine output (ml/kg/day) in the treatment group and historical control group was 34.2 (IQR 22, 44.38) and 22 (IQR 11.25, 38.13) respectively ($p = 0.17$). Pain scores significantly decreased from 5.5 (IQR 2.5, 8.25) pre-xenograft to 2.8 (IQR 0.75, 4) post-xenograft placement ($p = 0.03$). There was a significant difference in pain scores between the treatment group and historical control group, 2.8 (IQR 0.75, 4) and 6 (IQR 5, 8) respectively ($p = 0.02$). Each study patient underwent moderate sedation for wound care prior to xenograft placement and one study patient required one moderate sedation for wound care after xenograft placement. One patient in the xenograft placement group was diagnosed with a cutaneous infection compared to 4 patients in the historical control group ($p = 0.63$). The mortality was 12.5% in each group.

☆ Presented at the 47th Annual Meeting of the American Burn Association, poster session, April 21–24, 2015, Hilton, Chicago, IL.

* *Corresponding author at*: Arnold Luterman Regional Burn Center; Burn Intensive Care Unit, Division of Trauma, Burns, and Surgical Critical Care; Department of Surgery-College of Medicine, University of South Alabama Medical Center, 2451 Fillingim Street, Suite 10-I, Mobile, AL 36617, United States.

E-mail address: skahn@health.southalabama.edu (S.A. Kahn).

http://dx.doi.org/10.1016/j.burns.2016.06.003

*Conclusions:* Placement of a porcine xenograft in patients with SJS, SJS/TEN overlap, or TEN is associated with a significant reduction in intravenous fluid use, pain scores, and pain medication. Further study with larger sample sizes is warranted to evaluate for statistically significant differences in outcomes after porcine xenograft placement for SJS, SJS/TEN overlap or TEN.



## 1. Introduction

Stevens-Johnson syndrome (SJS), first described by Stevens and Johnson in 1922, and toxic epidermal necrolysis (TEN), described by Lyell in 1956, involve a spectrum of immune-mediated mucocutaneous exfoliative disorders that involve sloughing of the skin at the dermal-epidermal junction [1,2]. From a pathogenesis standpoint, there is supportive evidence in the role of the death receptor Fas and its Fas ligand as well as CD8+ cytotoxic T cells in keratinocyte apoptosis [3–5]. SJS is defined as less than 10% total body surface area (TBSA) involvement, whereas TEN is defined as greater than 30% TBSA involvement, and SJS/TEN overlap syndrome involves 10–30% TBSA [6]. Drug induced hypersensitivity reactions cause the majority of cases (80%) of SJS and TEN [7]. The incidence of SJS or TEN is 0.4 to 1.2 cases per million with a 20–35% mortality rate [8]. There are some studies that report the mortality rate as high as 60% [9].

Treatment of SJS and TEN can be challenging due to pain with wound care and ongoing fluid loss. Pharmacologic options for the treatment of SJS and TEN have included corticosteroids, intravenous immunoglobulin (IVIG), and cyclosporine. Corticosteroids were prescribed routinely for SJS and TEN some years ago, however they have recently fallen out of favor as there is lacking evidence to support their benefit [7,10]. In patients with thermal injury, a number of skin substitutes have been used to help reduce pain, decrease the number of dressing changes, decrease fluid given, improve mobilization, and decrease infection [11–18]. After debridement of the affected areas, the wound may be covered with cryopreserved cutaneous allografts, amnion based skin substitutes, collagen based skin substitutes, biosynthetic skin material, silver impregnated dressings, and porcine cutaneous xenografts.

The purpose of this study is to determine the role of porcine xenograft as a modality for wound coverage with SJS, SJS/TEN overlap, or TEN, with a hypothesis that xenograft coverage reduces fluid use and pain scores compared to historical controls.

## 2. Material and methods

An IRB-approved retrospective review from 2006 to 2014 was performed at a regional burn center on all adult patients greater than or equal to 18 years of age admitted with the diagnosis of SJS, SJS/TEN overlap, or TEN.

Patients with >19% TBSA cutaneous involvement were included in the study. From 2012 onwards, all patients with >20% TBSA involvement underwent debridement with moderate sedation in the hydrotherapy room, with placement of porcine xenograft over the affected areas. There were no differences in the typical sedation protocol during the length of the study. The decision to place a silver impregnated dressing over the xenograft, versus overlying gauze dressing along, as well as the frequency of dressing changes, was at the treating physician's discretion. Previously, the decision to place a porcine xenograft for wound coverage was at the treating physician's discretion. Patients with SJS were excluded from the analysis portion of the study. Intravenous fluid use, urine output, pain scores (1–10), pain medication for wound care, and biochemical markers were compared in the treatment group 24 h prior to and 24 h post-porcine xenograft placement. Additional outcomes measured included skin infections, hospital length of stay, and mortality. Baseline characteristics included age, gender, weight, medical comorbidities, % TBSA involvement, and etiology of disorder. Outcomes and demographics for porcine xenograft patients were also compared to historical control patients (with a 2:1 historical control:xenograft patient ratio) that received traditional wound care which included silver impregnated dressings. The decision regarding frequency of wound care in the hydrotherapy room, whether or not the xenograft or just the overlying dressings were changed, and replacement of xenograft if separation between changes was noted, was at the treating physician's discretion. Given that the median time (hospital day) to placement of porcine xenograft in the treatment group was 3 days (IQR 2, 3), data points in the historical control group at hospital day 2 and 4 were used in the analysis. Data points used in the analysis between the treatment group and historical control group were at 24 h after-porcine xenograft placement and hospital day 4 respectively.

Values were reported as median [interquartile range (IQR)]. Continuous outcomes in the pre and post-porcine xenograft placement groups were analyzed with the Wilcoxon signed-rank test. Continuous outcomes in the porcine xenograft placement group and historical control group were analyzed with the Mann–Whitney *U* test. Dichotomous outcomes were analyzed with the Fisher's exact test. A $p$ value $<0.05$ was considered statistically significant. Statistical analyses were performed using Microsoft Excel 2013.

## 3. Results

From 2006 to 2014, a total of 90 patients with the diagnosis of SJS, overlap, or TENs were identified. Eight patients with