Available online at www.sciencedirect.com

SciVerse ScienceDirect

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

The impact of oxandrolone on length of stay following major burn injury: A clinical practice evaluation

Amalia Cochran [a,*], *Wiley Thuet* [b], *Brennen Holt* [c], *Iris Faraklas* [c], *Randall J. Smout* [d], *Susan D. Horn* [e]

[a] *University of Utah, Department of Surgery, Burn Center at the University of Utah, United States*
[b] *Wake Forest University, Department of Emergency Medicine, United States*
[c] *University of Utah, Department of Surgery, United States*
[d] *ISIS/ICOR, United States*
[e] *ISIS/ICOR, University of Utah, Department of Biomedical Informatics, United States*

ARTICLE INFO

Article history:
Accepted 1 April 2013

Keywords:
Oxandrolone
Severity of illness
Clinical practice improvement
Burns
Length of stay

ABSTRACT

Introduction: The anabolic agent oxandrolone (OX) has been found to decrease length of stay (LOS) following 20–60% total body surface area (TBSA) burn injury. This study uses the Comprehensive Severity Index (CSI) to control for severity of illness and explores the relationship between OX and LOS in a more broadly selected sample of burn patients and a natural practice setting.

Methods: A practice-based evidence study was conducted at a single regional burn center. Maximum severity of illness (MCSIC) was measured using a burn-specific version of CSI. Data on 167 consecutive surviving patients with TBSA $\geq$ 15% were analyzed using case-control matching for MCSIC, TBSA, and age. Thirty-eight patients received OX.

Results: Median patient age for the entire patient sample was 42.7 years. Using a 1:1 match based upon MCSIC, TBSA, then age, mean LOS for patients who received OX was 33.6 days, as opposed to 43.4 days for those who were not managed with OX ($p = 0.03$). If patients were matched >1:1 for controls: cases, mean LOS was 40.9 days (controls) versus 31.6 days (cases).

Conclusions: OX is associated with shorter LOS after controlling for MCSIC, TBSA, and age. Future comparative effectiveness studies should better define which patients derive the greatest benefits from receipt of OX during their recovery from major burn injury.

1. Introduction

Severe burns lead to a physiologic hypermetabolic response. This response is associated with increased energy expenditure, increased protein consumption, and ultimately catabolic lean muscle mass wasting and decreased wound healing that may persist for a year or more following major burn injury [1]. Numerous studies have aimed to determine pharmacologic methods of counteracting this hypermetabolism in adult burn patients. Most notably the use of oxandrolone (OX) has come into favor as an oral synthetic testosterone analog to decrease the catabolic loss of lean body mass and speed up wound healing. In turn, it is expected that these improvements in catabolism and wound healing will result in a decreased length of stay (LOS) associated with severe burns. Two studies have supported this hypothesis, demonstrating that LOS was significantly shorter with the administration of OX in the

* *Corresponding author at*: 30 North 1900 East, SOM 3B313, Salt Lake City, UT 84132, United States. Tel.: +1 801 581 7508; fax: +1 801 585 6005.
E-mail address: amalia.cochran@hsc.utah.edu (A. Cochran).
0305-4179/$36.00
http://dx.doi.org/10.1016/j.burns.2013.04.002

setting of acute burns [2,3]. More recently it has come into question as to whether OX truly decreases LOS in severely burned patients. In one multicenter study that identified multiple benefits associated with OX use in burn patients including decreased mortality, LOS remained unchanged [4].

Because of the unclear influence of oxandrolone on LOS following major burn injury, our goal was to evaluate its impact in a natural practice setting. The aim of this study was to clarify the relationship between LOS in severely burned patients with the use of OX in the acute stages of burn. We conducted a retrospective study that utilized a practice-based evidence (PBE) research method to control for severity of illness and explore the relationship between oxandrolone and LOS in adults with major burn injury.

2. Methods

A retrospective practice-based evidence (PBE) study with the goal of identifying process measures associated with shorter LOS following burn injury was conducted at a regional burn center located within an academic health science center. The goal of PBE studies is to optimize both outcomes and costs of care; the formal definition states that a PBE study is ''an analysis of the content and timing of the individual steps of a medical care process to produce superior medical outcomes for the least necessary cost over the continuum of a patient's care'' [5]. The design of PBE studies enables the clinician to establish if differences in outcomes are due to differences in care process or differences in severity of illness, and does so in a natural practice environment. This stands in contrast to randomized controlled trials, which often have strict enrollment criteria that are not always consistent with the characteristics of the ''typical'' patient.

The incorporation of Comprehensive Severity Index (CSI) into a PBE study protocol provides a covariate that balances clinical conditions besides those under study. CSI is a physiologic indexing system that is age- and disease-specific and can be used to control for differences in acuity at the individual patient level. CSI has been validated in many care settings over the last 25 years, and has been used in two major general surgery PBE studies and other clinical areas such as stroke, spinal cord, and traumatic brain injury, and nursing homes [6–8]. Most importantly, CSI accounts for the complex interaction between all diseases that are present, their severity, and the relationships between the diseases; use of CSI in this study accounts for differences in TBSA and severity of illness. A burn-specific CSI was used in this analysis as a covariate for balancing the impact of co-morbid and co-occurring conditions on severity of illness in burn patients (Table 1); CSI stratifies patient severity of illness as mild, moderate, severe, or catastrophic. This use of CSI allows for detection of differences that might otherwise be hidden or ''washed out'' by the effect of overall injury severity.

Clinical use of oxandrolone was at practitioner discretion. Patients were considered candidates for oxandrolone if they had total body surface area (TBSA) burn injury ≥15%. Oxandrolone could be started at any time during the hospital course and was never started prior to completion of initial burn shock resuscitation. Oxandrolone was only stopped during hospitalization if a patient had a worsening hepatic function profile or if their volume status management became unusually complicated.

Using previously described techniques the clinical components of the CSI module data were used to calculate severity scores for each patient [9,10]. Severity scores were captured at three different time windows during patient hospitalization: within 24 h of admission, within 24 h of discharge, and maximum (any time during admission with highest scores). In most medical conditions, maximum CSI (MCSIC) > 60 indicates that the patient is very severely ill, catastrophic, or life threatening. Although the intent of the CSI system as developed was not to explain specific outcomes such as costs, length of stay, or mortality, CSI scores were highly correlated with these outcomes in multiple studies [11–16].

All adult patients with ≥15% TBSA burn injury admitted as inpatients to a regional ABA-verified burn center between January 1, 2005 and April 30, 2009 were included. Patients meeting inclusion criteria were identified using the center's ABA/TRACS™ registry. Data collection from chart review included demographics, calculation of the Baux index, and abstraction of data for the burn CSI data module. Trained personnel (WT, BH) abstracted data from the patient's medical chart after hospital discharge. Accuracy of data abstraction was verified after each data abstractor entered data from five patients.

2.1. Statistical analysis

The initial plan for data analysis was to use least squares regression to identify patient and treatment variables associated with LOS. However, careful review of those patients who received oxandrolone versus those who did not clearly demonstrated that the treatment was not evenly distributed between these two groups; propensity scoring could not be used because the OX patients had much longer LOS, meaning many non-OX patients with short LOS could not be matched. Because of the bias at our center for treatment of the sickest patients with OX, Student's *t*-test was used to compare LOS between treatment groups using MCSIC, TBSA, and age, in that order for manual matching. Coarsened matching was used to select MCSIC within 10, age within 10 years, and TBSA within 10% TBSA. While most matches were 1:1 matches control: case, if more than one control matched a case then the multiple controls were included in the analysis. SAS 9.2 was used for all analyses.

3. Results

3.1. Patients demographics and injury characteristics

Between January 1, 2005 and April 30, 2009, 198 patients with ≥15% TBSA injury were admitted to the regional burn center. Of these patients, 55 had burn size between 15 and 20% TBSA, 93 were between 20 and 40% TBSA, 50 were >40% TBSA, and 8 of these had >60% TBSA. The mortality rate in this patient cohort was 15% (N = 29). Two patients were excluded due to insufficient data in their medical chart; therefore data from