Available online at www.sciencedirect.com
ScienceDirect
journal homepage: www.elsevier.com/locate/burns

Review

Human herpes viruses in burn patients: A systematic review

Paul Wurzer [a,b,*], Ashley Guillory [a], Daryousch Parvizi [b], Robert P. Clayton [a,c], Ludwik K. Branski [a,b], Lars-P. Kamolz [b], Celeste C. Finnerty [a,c], David N. Herndon [a], Jong O. Lee [a]

[a] Department of Surgery, University of Texas Medical Branch and Shriners Hospitals for Children, Galveston, TX, USA
[b] Division of Plastic, Aesthetic and Reconstructive Surgery, Department of Surgery, Medical University of Graz, Graz, Austria
[c] Sealy Center for Molecular Medicine and the Institute for Translational Sciences, University of Texas Medical Branch, Galveston, TX, USA

ARTICLE INFO

Article history:
Accepted 3 February 2016
Available online xxx

Keywords:
Human herpes virus
Herpes simplex virus
Varicella-zoster virus
Chickenpox
Cytomegalovirus
Burns

ABSTRACT

Objective: The contribution of human herpes viruses, including herpes simplex virus (HSV), cytomegalovirus (CMV), and varicella zoster virus (VZV) to morbidity and mortality after burns remains controversial. This systematic review was undertaken to assess evidence of herpes virus-related morbidity and mortality in burns.

Materials and methods: PubMed, Ovid, and Web of Science were searched to identify studies of HSV, CMV, or VZV infections in burn patients. Exclusion criteria included: A level of evidence (LoE) of IV or V; nonhuman *in vivo* studies; and non-English articles. There was no limitation by publication date.

Results: Fifty articles were subjected to full-text analysis. Of these, 18 had LoE between I–III and were included in the final review (2 LoE I, 16 LoE II–III). Eight had a prospective study design, 9 had a retrospective study design, and 1 included both.

Conclusions: No direct evidence linked CMV and HSV infection with increased morbidity and mortality in burns. Following burn, CMV reactivation was more common than a primary CMV infection. Active HSV infection impaired wound healing but was not directly correlated to mortality. Infections with VZV are rare after burns but when they occur, VZV infections were associated with severe complications including mortality. The therapeutic effect of antiviral agents administered after burns warrants investigation *via* prospective randomized controlled trials.

* *Corresponding author at:* Shriners Hospitals for Children, 815 Market Street, Galveston, TX 77550, USA. Tel.: +1 409 770 6974; fax: +1 409 770 6919.
E-mail address: wurzer_paul@gmx.at (P. Wurzer).

http://dx.doi.org/10.1016/j.burns.2016.02.003
0305-4179/

Contents

1. Introduction

Bacterial and viral infections such as cellulitis, pneumonia, wound infections, and septicemia are among the most common complications following burn [1]. An increased inflammatory response and overall immunosuppression occur following massive thermal injuries [2–4]. Burn-related phenotypic changes in T-cells contribute to burn immunosuppression [5]. Also, defective natural killer cell activity against virus-infected cells weakens the immune response of these severely injured patients [6]. As a result of these burn-induced changes, severely burned patients are more prone to infections and septicemia [7]. Studies have shown that sepsis and infections enhance the hypermetabolic response [2], which negatively affects the long-term outcomes of severely burned patients for up to 2 years after burn [4]. Along with bacterial infections, viral infections have been associated with increased morbidity and mortality in the severely burned [7–11]. Viral infections in burns are thought to promote bacterial and other infections [12]. Early treatment of sepsis and prevention of infections are a key component to reducing morbidity and improving the long-term outcome of burn victims.

The human herpes virus (HHV) family includes herpes simplex virus type 1 (HSV-1), herpes simplex virus type 2 (HSV-2), varicella zoster virus (VZV), cytomegalovirus (CMV), Epstein–Barr viruses (EBV), and human herpes virus 6 to 8 [13]. In immunosuppressed burn patients, primary infections or a reactivation of viral infections with HSV-1, HSV-2, or CMV are common complications during hospitalization. Primary infection or vaccination results in a seroprevalence of immunoglobulin G (IgG) antibodies against the virus. Of note, the overall HSV-2 seroprevalence rate in the U.S. is 21.9% according to an analysis of more than 13,000 serum samples [14]. In Australia, a study showed a seroprevalence of 75% for HSV-1 and 12% for HSV-2 in the adult population [15]. Seroprevalence for CMV was found to be 50.4% [16]. In contrast to natural immunity against other HHV, that against VZV is being replaced by vaccine-induced immunity in many countries to protect against herpes zoster infections in older individuals who did not receive immunity during chickenpox infection [17]. However, about 95% of adults have acquired immunity against VZV infections owing to chickenpox exposure in childhood [13,18].

In order for HSV to be transmitted, there must be contact between a virus-shedding person and a susceptible host. The primary infection can cause symptoms ranging from fever, characteristic vesicles with erythematous base, on to viremia and visceral dissemination [13]. Severe HSV infections promotes bacterial infections in burns and prolongs the burn recovery process [12], and thus, HSV infections can be associated with a higher mortality [9,19].

In a review of CMV in burns, Rennekampff and Hamprecht concluded that allografts and blood transfusions can be sources of infections [20]. They showed that there is no direct evidence that CMV infections directly increase morbidity and mortality of severely burned patients [21,22]. Furthermore, antiviral therapy for CMV infections in burns is still controversial [23,24].

Infections with VZV in burns are rare, although burn wound colonization with VZV has been well described [25–27]. VZV immunity, imparted by childhood chickenpox infections or VZV vaccination, seems to prevent burn-induced VZV infections [28].

HSV, CMV, and VZV infections are believed to play a pivotal role in morbidity and mortality in burns. Thus far, there is no existing systematic review (citing Level III evidence or higher) describing the contributions of these viruses to poor burn outcomes or concurrent infections. The aim of this review is to delineate the clinical differences between these human herpes virus subtypes, to outline established therapy approaches, and to evaluate evidence for virus-related morbidity and mortality in burns.

2. Methods

The review protocol was registered in the clinicaltrials.gov database (#SHC-G-SR-HHV). This systematic review was created according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines and checklist [29].

Please cite this article in press as: Wurzer P, et al. Human herpes viruses in burn patients: A systematic review. Burns (2016), http://dx.doi.org/10.1016/j.burns.2016.02.003