Why we need a new therapeutical approach to analgesic strategy in burn patients and what is the way forward?

J. Bartková¹, L. Kubíčková², A. Príbojová¹, Ch. Tsagkaris³, Z. Haghani-Dogahe⁴, A. Rábová³, M. Joukal², B. Bakalář⁵, B. Lipový⁵

¹ Department of Burns and Plastic Surgery, Faculty of Medicine, Masaryk University Brno, and University Hospital Brno, Brno, Czech Republic

² Department of Anatomy, Cellular and Molecular Neurobiology Research Group, Faculty of Medicine, Masaryk University, Brno, Czech Republic ³ European Student Think Tank, Public Health and Policy Working Group, Amsterdam, Netherlands

⁴ Burn and Regenerative Medicine Research Center, Guilan University of Medical Sciences, Rasht, Iran

⁵ Department of Burns, Third Faculty of Medicine, Charles University, Prague, Czech Republic, and University Hospital Královské Vinohrady, Prague, Czech Republic

Burn injuries require intricate pain management. Ineffective pain management can result in reduced patient adherence and the possibility of delayed healing, which can have significant impacts on quality of life. Currently, opioids form the foundation of analgesia for patients with thermal trauma.

However, the administration of these drugs is commonly linked to a range of side effects. Therefore, it is recommended to combine their administration with other drug groups such as ketamine, NSAIDs, paracetamol, pregabalin, anxiolytics, and others. Presently, an increasing number of studies explore the potential therapeutic effect of cannabinoids on pain. Non-pharmacological techniques like hypnosis, meditation, and virtual reality are also incorporated into the systematic approach to address burn pain. The management of opioid administration in patients with thermal trauma is a complicated process that necessitates the consideration of multiple factors, including the length of hospital stay, duration of opioid administration, and recurrent surgical procedures performed under general anaesthesia. It is crucial to note that the repeated or continuous administration of opioids results in a significant reduction of their effectiveness.

The management of burn pain presents a challenge to healthcare providers and is of utmost importance for burn patients. While opioids are frequently used, it is imperative to identify fresh therapeutic targets and develop enhanced analgesics based on the molecular mechanisms underpinning burn pain. Cytokines and chemokines act as vital regulators of the wound healing process. Potential therapeutic targets for burn wounds may encompass various pro-inflammatory chemokines (such as CCL2, CCL21, CXCL12), pro-inflammatory cytokines (including IL-1ß, IL-2, IL-3, IL-5, IL-6, IL-12p70, IL-17, GM--CSF, KC, MIP-1α, RANTES, and TNF-α), and anti-inflammatory cytokines (such as IL-10, G-CSF, and IFN-y). By inhibiting the release of inflammatory cells that produce growth factors and cytokines, certain cytokines and chemokines can promote the healing of burn wounds.

While a highly specific pain receptors' antagonist might need years to proceed from the bench to the clinic, repurposing existing medicines may provide a temporary yet promising solution [1,2]. Identifying and integrating traditional practices backed by evidence to contemporary standards of care as a complement or a way to reduce exposure to opioids would also be in line with the outputs of the first Traditional Medicine Global Summit of the World Health Organisation [3]. Research elucidating novel therapeutic regimens for burn pain has greater chances to fulfil its mission, if it is embedded in a broader biopsychosocial and globally oriented understanding of the problem. Burns are a global public health challenge, associated with an estimated 180,000 deaths annually, approximately 2 million disability adjusted life years and subsequent financial losses ranging between 6-11 billion USD in different regions of the globe. Low- and middle-income countries are disproportionately affected and burns sustained by bread earners have multiple and complex implications on the ability of both the patients and their dependants to provide for themselves [4].

Basic research that generates novel insights into the regulation of immune mediators and their potential impact is essential for advancing the development of innovative clinical strategies for treating burn injuries.

Authors' contribution

Júlia Bartková – conception and design, analysis and interpretation, data collection, writing the article; Anna Príbojová – data collection, analysis and interpretation, critical revision of the article; Christos Tsagkaris – consulting authors, critical revision of the article; Bohumil Bakalář – consulting authors, critical revision of the article; Kubíčkova Lucie – consulting authors, critical revision of the article; Zahra Haghani-Dogahe – consulting authors, critical revision of the article; Anna Rábová – consulting authors, critical revision of the article; Marek Joukal – consulting authors, critical revision of the article; Břetislav Lipový – consulting authors, critical revision of the article.

Each author certifies that he/she has made a direct and substantial contribution to the work reported in the manuscript by participating in each of the following three areas: 1) conceiving and designing the study or collecting the data or analyzing and interpreting the data; 2) writing the manuscript or providing critical revisions that are important for the intellectual content; 3) approving the final version of the manuscript.

Disclosure

The authors have no conflicts of interest to disclose. The authors declare that this study has received no financial support. All procedures performed in this study involving human participants were in accordance with ethical standards of the institutional and/or national research committee and with the Helsinki Declaration and its later amendments or comparable ethical standards.

References

 McGovern Medical School. Acute Burn Pain Management. [online]. Available from: https://med. uth.edu/surgery/acute-burn-pain-management/.
Uptodate. Management of burn wound pain and itching. [online]. Available from: https:// www.uptodate.com/contents/management-ofburn-wound-pain-and-itching. 3. World Health Organization. Burns [online]. Available from: https://www.who.int/publications/m/item/who-traditional-medicine-summit-2023-meeting-report--gujarat-declaration.

4. Gerstl J., Kilgallon J., Nawabi N., et al. The global macroeconomic burden of burn injuries. *Plast Reconstruct Surg Global Open.* 2021, 9 (10 Suppl): 159–160.

Júlia Bartková, MD, MBA , MPH Department of Burns and Plastic Surgery University Hospital Brno Jihlavská 20 625 00 Brno Czech Republic bartkovaj@yahoo.com