PROCEDURAL SEDATION AND ANALGESIA DURING ENZYMATIC DEBRIDEMENT OF BURN PATIENTS

ANALGÉSIE ET SÉDATION PENDANT UNE PROCÉDURE DE DÉBRIDEMENT ENZYMATIQUE CHEZ LES BRÛLÉS

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SUMMARY. Procedural sedation and analgesia (PSA) is a widely used strategy in various fields to carry out numerous diagnostic and therapeutic procedures. However, there is limited information on its efficacy and safety during enzymatic debridement of burn patients with Nexobrid®. The aim of our study was to describe the U-type PSA procedure in a series of patients requiring enzymatic debridement. We carried out a retrospective, descriptive study involving 28 patients requiring enzymatic debridement of a limb, trunk or multiple locations, who had been admitted to the Burn Unit of the University Hospital Complex of A Coruña (Spain). Of these, 17 patients (not requiring invasive mechanical ventilation [IMV]) received intravenous PSA and two received local/regional anesthesia. Among those patients who received PSA, the most frequently used sedative during the application and removal of Nexobrid® was ketamine following premedication with midazolam (median Ramsay sedation score = 3; range = 2-4). The most common type of analgesics prescribed for the debridement procedure was opioids. Three patients required rescue analgesia because of the intensity of their pain (Visual Analogue Scale [VAS] ≥ 4). The patients did not experience any of the complications analyzed. In our case series, U-type PSA proved to be a satisfactory and safe support strategy for enzymatic debridement of burn patients not requiring IMV due to another cause.

Keywords: burns, procedural sedation, analgesia, enzymatic debridement

RÉSUMÉ. L’analgésie-sédation (AS) est largement utilisée au cours d’actes diagnostiques et thérapeutiques. Cependant, nous ne disposons que de peu de données concernant son efficacité et son innocuité et son efficacité durant le débridement enzymatique par Nexobrid® chez les brûlés. Nous décrivons ici une série rétrospective de 28 patients hospitalisés dans le CTB de La Corogne (Espagne) ayant bénéficié d’un débridement enzymatique du tronc, des membres ou de localisations multiples sous analgo-analgésie séquentielle avec rétrocontrôle. Parmi ces patients, 17 n’étaient pas ventilés et ont reçu une AS intraveineuse, 2 ont bénéficié d’anesthésie locale ou locorégionale. L’agent hypnotique le plus utilisé lors de la mise en place et du retrait de Nexobrid® était la kétamine (après prémédication par midazolam). Le score de sédation (Ramsay) médian était de 3 (interquartiles 2 et 4). Les opiacés étaient les analgésiques les plus fréquents. Trois patients ont eu besoin d’analgésie supplémentaire, indiquée par une EVA ≥ 4. Aucune complication n’a été retrouvée. Dans cette série, l’analgoo-analgésie séquentielle avec rétrocontrôle apparaît comme un moyen efficace et sûr d’assurer l’analgésie pendant un débridement enzymatique chez des brûlés en ventilation spontanée.

Mots-clés: brûlures, sédation, analgésie, procédurale, débridement enzymatique

Introduction

The recent advances made in multiple areas of medical interventionism (radiology, endoscopy, cardiology, etc.), including pain management, explain the substantial growth in the number of procedures performed under the effects of sedatives and/or analgesics outside the operating room. Procedural sedation and analgesia (PSA), formerly referred to as “conscious sedation”, is defined as a technique of administering sedative or dissociative agents, with or without analgesics, to induce a state that allows the patient to tolerate unpleasant procedures while maintaining their cardiorespiratory function.

At present, enzymatic debridement with Nexobrid® serves as an alternative strategy for the acute management of patients with deep partial or full thickness thermal burns. The use of this technique in several benchmark European centers is growing, and there is a global agreement on the need for supporting the procedure with analgesia and sedation. The 2017 European guidelines regarding this matter do not reach a global consensus on the best strategy for the management of pain and anesthesia in patients requiring enzymatic debridement of a limb, and there are no well-defined protocols on the depth of analgesedation needed by these patients to tolerate the procedure. We hereby report our experience in the use of a moderate sedation and analgesia procedure in burn patients requiring enzymatic debridement but not mechanical ventilation due to another cause.
Materials and methods

We performed a review of a series of patients treated with Nexobrid® at the Burn Unit of the University Hospital Complex of A Coruña (CHUAC), Galicia (Spain), from December 2015 to December 2017. All patients aged ≥ 18 years who had a thermal burn (scalds, flame or contact burns) on a limb, trunk or multiple locations treated with enzymatic debridement (Nexobrid®), excluding those whose lesion was limited to the face, were included in the review. A total of 28 patients underwent enzymatic debridement during this period; nine patients were assisted with invasive mechanical ventilation (IMV) upon admission to hospital due to the nature of their lesions, 17 did not receive sedation or breathing support and were managed with intravenous (i.v.) PSA, and two were treated with local/regional anesthesia.

Data collection was performed in compliance with the ethical principles in research with human participants.

Measurements

Variables related to the patients’ pre-PSA assessment were collected: demographic variables (age and sex); injury variables (extent of the burn and inhalation syndrome); comorbidities (arteficial hypertension, mental illness, toxic habits, chronic heart disease, chronic liver disease, chronic kidney disease, morbid obesity, age > 70 years); severity scale scores (injury severity score [ISS] and acute physiology and chronic health evaluation II [Apache II]; surface treated and result of the enzymatic debridement; monitoring, sedative and analgesic agents used during the i.v. PSA; and complications linked to the procedure (apnea or desaturation, hypotension, vomiting, oversedation with a Ramsay score > 4, conversion of the procedure to general anesthesia).

Definitions

Intravenous sedation and analgesia: the level of sedation sought with the PSA was a score of 3-4 in the Ramsay Sedation Scale (RSS) during the application and removal of Nexobrid®. Pain control throughout the debridement procedure was assessed by means of the Visual Analogue Scale (VAS), where scores < 4 were considered optimal and scores ≥ 4 were managed with rescue analgesia.

Inhalation injury: this type of lesion was defined either as the existence of damage to the upper or lower airways, or evidence of systemic intoxication.

As for the associated complications, apnea was defined as a respiratory rate < 8 rpm; desaturation as an oxygen saturation (SaO2) < 90%, measured by pulse oximetry; and hypotension as a need for management with vasopressors.

Enzymatic debridement procedure with Nexobrid®

The enzymatic debridement procedure was prescribed and performed by a plastic surgeon belonging to the Burn Unit, inside the patient cubicle. In all cases, an occlusive moist dressing consisting of gauze pads soaked in 0.9% physiological saline or Prontosan® Wound Irrigation Solution (B. Braun Mesulgen AG, Germany) was applied on the burns upon admission to the hospital. Prior to performing the enzymatic debridement, the keratin detritus present on the wound was gently removed, and the area to be treated was then delimited with sterile petroleum jelly (Vaseline®). The preparation was performed according to the instructions set forth in the summary of the product characteristics, by mixing the gel with the lyophilized substrate to obtain a homogenized mixture.

Gel application: a 1 - 2 mm thick film of the gel was spread over the area to be treated and subsequently covered by a sterile plastic sheet.

Debridement: following application of the gel, the product was left to act on the wound for up to four hours, or less in the case of more superficial wounds.

Gel removal: the gauze pads soaked in physiological saline were removed from the wound. The effectiveness of the procedure was then assessed, and an occlusive dressing containing Prontosan® Wound Gel and a hydrocolloid dressing (Varihesive®) were applied.

Support PSA for enzymatic debridement

The intravenous PSA was prescribed and administered by an intensivist, following the operating scheme below:

- Pre-PSA assessment: its aim was to assess the potential risks of the sedation and reduce associated adverse effects. The pre-PSA assessment included: a) collecting information on the patient’s age, weight, allergies, substance abuse, medical and surgical history, prior experiences with sedation and analgesia, usual medication, current clinical status (vital signs, cooperation problems and pain tolerance); b) a physical examination; c) laboratory studies (as applicable).

- Obtaining information on the plan defined by the plastic surgeon responsible with respect to the extent and location of the area to be treated, as well as the estimated duration of the enzymatic debridement procedure.

- Informing the patient (or their legal representative, if applicable) about the PSA, including its risks, benefits and the procedural strategy. Administering the informed consent form for signature.

- Selecting, calculating and preparing the dose of sedatives and analgesics needed for the procedure.

- Monitoring the patient: including clinical observation at the patient’s bedside; continuous monitoring of: EKG, pulse oximetry, capnography (only in selected patients), respiratory rate and non-invasive blood pressure monitoring. Administering supplemental oxygen to the patient during the procedure and gathering sufficient human and material equipment to administer respiratory and/or hemodynamic support, if necessary.

Considering that enzymatic debridement is a painful procedure, particularly during application and removal of the product, in our hospital we chose to use U-type PSA, administering the analgosedation during the application and removal of Nexobrid®, and basal analgesia during the debridement procedure (Fig. 1).

![Fig. 1 - U-type PSA strategy: analgosedation during the application and removal of Nexobrid®, and basal analgesia during the debridement procedure.](image-url)
Results

We performed a descriptive analysis of our case series. The variables examined were described in terms of their frequency (%) and mean (standard deviation [SD]).

The demographic and injury characteristics of the patients presenting with a burn lesion on a limb, the trunk or multiple locations are shown in Table I, classified according to the need for IMV upon admission to the hospital. The mean age of the group of sedated patients receiving IMV was 55.3 ± 15.8 years, with a mean of 0.8 ± 0.8 comorbidities. The mean body surface area (BSA) affected by the burn was 20.7% ± 26.5%, and three of these patients presented with smoke inhalation syndrome. Among the group of patients who did not receive IMV, 17 were treated with i.v. PSA, and two with local/regional anesthesia. The mean age of the patients who received i.v. PSA was 48.0 ± 18.7 years. In this group, the mean BSA affected by the burn was 7.7% ± 6.3%, and no patient experienced smoke inhalation syndrome. The comorbidity mean in this group was low (1.2 ± 1.3), and none of the patients had an acute organic dysfunction. On the other hand, the mean age of the patients who received local/regional anesthesia was 43.5 ± 2.1 years. None of these patients had comorbidities, and the mean BSA affected by the burn was lower than that of the other two groups (1.5% ± 0.7%).

Table I - Demographic and injury characteristics of patients requiring enzymatic debridement of a limb, the trunk or multiple locations, from December 2015 to December 2017

<table>
<thead>
<tr>
<th>Demographic variables</th>
<th>Patients receiving IMV(^1)</th>
<th>Patients not receiving IMV and treated with i.v. PSA(^2)</th>
<th>Patients not receiving IMV and treated with local/regional anesthesia n = 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (% of male patients)</td>
<td>7 (77.6%)</td>
<td>8 (47.1%)</td>
<td>2 (100%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>55.3 ± 15.8</td>
<td>48.0 ± 18.7</td>
<td>63.5 ± 2.1</td>
</tr>
<tr>
<td>No. of comorbidities(^1)</td>
<td>0.8 ± 0.8</td>
<td>1.2 ± 1.3</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>Infection(^1)</td>
<td>3 (33.3%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Total BSA (%)</td>
<td>20.7 ± 26.3</td>
<td>7.7 ± 6.1</td>
<td>1.5 ± 0.7</td>
</tr>
<tr>
<td>Injury Severity Score (ISS)</td>
<td>11.8 ± 4.6</td>
<td>8.1 ± 4.7</td>
<td>3.0 ± 4.2</td>
</tr>
<tr>
<td>Apache II score within the first 24 hours</td>
<td>12.6 ± 7.4</td>
<td>45.3 ± 3.8</td>
<td>4.0 ± 2.8</td>
</tr>
<tr>
<td>Treatment variables</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Need for grafting after enzymatic debridement</td>
<td>6 (66.7%)</td>
<td>11 (64.7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Time elapsed between the onset of the burn and the application of Nexobrid® (hours)</td>
<td>19 ± 3.5</td>
<td>18.5 ± 11.7</td>
<td>28.3 ± 11.0</td>
</tr>
<tr>
<td>Surface treated with Nexobrid® (%) BSA</td>
<td>15.0 ± 15.0</td>
<td>7.1 ± 5.7</td>
<td>1.5 ± 0.7</td>
</tr>
</tbody>
</table>

1 Arterial hypertension, mental illness, toxic habits, heart disease, chronic liver disease, chronic kidney disease, chronic lung disease, morbid obesity, age > 70 years
2 Total body surface area affected by the burn
3 Defined either as the existence of damage to the upper or lower airways, or evidence of systemic intoxication
4 Acute physiology and chronic health disease classification system II score
5 Invasive mechanical ventilation
6 Intravenous procedural sedation and analgesia

The drugs used during the U-type PSA strategy are outlined in Table II. The most frequently used drug during the procedure had to be replaced by general anesthesia.

Table II - Description of drugs used for i.v. U-type PSA

<table>
<thead>
<tr>
<th>Application (i.v. sedation and analgesia)</th>
<th>Sedatives</th>
<th>Analgesics</th>
<th>Rescue analgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>i.v. midazolam (2 mg) + i.v. ketamine (50-150 mg)</td>
<td>8 (47.1%)</td>
<td>4 (23.5%)</td>
<td>6 (35.3%)</td>
</tr>
<tr>
<td>i.v. propofol (3-15 ml)</td>
<td>1 (5.9)</td>
<td>2 (11.8)</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>i.v. paracetamol (1 g)</td>
<td>7 (39.4%)</td>
<td>2 (11.8)</td>
<td>3 (17.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Removal (i.v. sedation and analgesia)</th>
<th>Sedatives</th>
<th>Analgesics</th>
<th>Rescue analgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>i.v. midazolam (2 mg) + i.v. ketamine (50-150 mg)</td>
<td>9 (52.9%)</td>
<td>7 (41.2%)</td>
<td>6 (35.3%)</td>
</tr>
<tr>
<td>i.v. propofol (3-15 ml)</td>
<td>2 (11.8)</td>
<td>2 (11.8)</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>i.v. paracetamol (1 g)</td>
<td>7 (39.4%)</td>
<td>2 (11.8)</td>
<td>3 (17.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Debridement (i.v. analgesia)</th>
<th>Programmed analgesics</th>
<th>Rescue analgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>i.v. perfusion of morphine hydrochloride (0.5-2 mg/h)</td>
<td>3 (17.6)</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>i.v. dexketoprofen (50 mg)</td>
<td>4 (23.5)</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>i.v. paracetamol (1 g)</td>
<td>4 (23.5)</td>
<td>2 (11.8)</td>
</tr>
</tbody>
</table>

1 VAS - Visual analogue scale

The use of PSA has become more widespread due to the need to alleviate patient anxiety, discomfort and pain during invasive diagnostic and therapeutic procedures. Through further technological and clinical refinement, many of the recent advances made in Burn Units have focused on minimizing the invasive nature of all aspects of the debridement procedure, including anesthesia.

Our hospital developed and implemented a moderate U-type analgesedation strategy to ensure effective pain management during the application, treatment and removal of Nexobrid®. Our proposal considers, in the first place: the need for greater analgesedative support during the application and removal of Nexobrid®, maintaining an analgesic regimen during the debridement procedure; secondly: that the enzymatic debridement procedure does not generally entail a need for deep sedation requiring cardio-respiratory support in patients...
who do not need it for any other reason (type of lesion, old age or comorbidities), and it can be an alternative to regional anesthesia in some cases; and, thirdly: that the procedure’s safety environment does not involve the need for an operating room and it can be carried out with the necessary resources in the patient’s cubicle.

We hereby describe a case series of 17 burn patients seen at our hospital who underwent enzymatic debridement of a limb, the trunk or multiple locations in their cubicle and under U-type PSA (Figs. 2a,b,c).

Choice of drugs used for the PSA was based on the results of the clinical assessment performed prior to the procedure. The sedatives were administered at the dosage needed to achieve a Ramsay sedation score of 3-4 and were primarily combined with opiates. This strategy allowed for an adequate tolerance of the procedure, and we observed no complications related to the PSA in this case series.

Achieving an adequate level of analgosedation represents a clinical challenge, as sedation and analgesia comprise a “continuum” that covers anxiolysis to general anesthesia. As patients undergo these processes, they become more exposed to hemodynamic and respiratory complications. Due to the wide variability of patient responses, the appropriate drug dose to be used to achieve a specific degree of sedation is not always predictable. Several series have shown that special considerations must be taken when deciding the best pharmacological option to treat patients with a severe cardiovascular disease, obstructive sleep apnea syndrome, morbid obesity, chronic kidney disease and chronic liver disease, as well as patients over the age of 70 years. Further studies are needed to better characterize the risk and predictive factors of the need to convert moderate sedation to general anesthesia in burn patients. Management of the transition of level 3 to 4 sedation may require specific knowledge and technical skills (advanced airway/cardiovascular resuscitation) that, in general, are only fully mastered by intensivists or anesthesiologists; therefore, appropriate monitoring and management resources are essential.

Given that most of the drugs available for PSA do not cover both hypnotic and analgesic objectives, combinations of these drugs are almost always necessary. Thus, it is important to be aware of the principles of drug interactions in order to balance their clinical and side effects. Sedatives and opioids must be administered before the painful stimulus, and the drug boluses must be adequately spaced so as to avoid overdosing, considering the time elapsed until the peak effect. Likewise, it is important to avoid deeper levels of sedation to compensate for inadequate analgesia.

The patient’s level of pain must be evaluated often during the procedure with validated pain assessment scales. The current guidelines recommend that intravenous opioids be considered as the first-line drugs of choice to treat non-neuropathic pain in critically ill patients. When titrated to similar pain intensity endpoints, all i.v. opioids available are deemed equally effective. Remifentanil provides satisfactory PSA conditions for common procedures, but its performance and risks during the deep sedation required for enzymatic debridement have yet to be assessed. Intravenous opioids (fentanyl and morphine) are the most popular drugs used routinely in burn patients to alleviate their pain, however, both opioids and non-opioids can be used effectively in a multimodal strategy. In our case series, the most frequently used analgesic was morphine hydrochloride, and three patients required rescue analgesia during the debridement procedure, achieving adequate subsequent pain control. The use of “patient-controlled analgesia” during painful procedures allows patients to actively participate in the pain management regimen and has proven to be beneficial in multiple clinical settings; therefore, it could be a good strategy to implement during the debridement procedure.
The duration and level of sedation should be as short and superficial as possible. Short-acting and easily reversible sedative drugs should be preferred.\(^8\) Propofol continues to be the most widely used sedative drug in procedures involving PSA. Benzodiazepines are also used often, midazolam being the most frequently used agent. Ketamine also has analgesic properties; therefore, its application in monotherapy can be useful during painful procedures. Dexmedetomidine is also a sedative agent with a beneficial respiratory stability profile; however, there is limited experience regarding its use in PSA.

**Conclusions**

The sedative-analgesic intervention strategy in patients requiring enzymatic debridement is not yet well defined. Our experience suggests that U-type PSA is a satisfactory and safe support strategy for this intervention in patients presenting with burns on their limbs, the trunk or multiple locations, who do not require invasive mechanical ventilation due to another cause, and that it may be an alternative to local/regional anesthesia.

**BIBLIOGRAPHY**


**Conflict of interest.** None  
**Disclosure.** Nothing to disclose