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CLINICAL SAFETY OF NEXOBRID® IN THE MANAGEMENT OF BURN WOUNDS: A REVIEW OF CLINICAL STUDIES

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ABSTRACT

Background: NexoBrid® is an enzymatic debridement agent approved as an alternative to surgical excision in the treatment of burns. While highly effective in the selective removal of necrotic tissue, its clinical safety remains a paramount consideration.
Objective: The aim of this review was a systematic evaluation of the safety profile of NexoBrid in the adult population suffering from burn injuries.
Materials and Methods: The literature search was performed in PubMed and Embase and included studies published from 2012 to 2026. The articles were investigated in terms of adverse events, such as pain, bleeding, infection, hypersensitivity and systemic response.
Results: The analysis identified procedural pain as the most prominent complication, which was effectively managed through standardized anesthetic protocols. The risk of bleeding or infection emerged as being similar or lower compared to traditional surgical treatment. No allergic reactions or anaphylactic events were reported, likely due to implemented exclusion criteria. Minor systemic response was recorded; however it was usually mild and transient.
Conclusions: NexoBrid appears to present a robust safety profile and remains a reliable alternative to tangential excision in adults.

KEYWORDS

NexoBrid; Bromelain, Burn Care, Enzymatic Debridement, Patient Safety, Adverse Events

CITATION

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Introduction

Burn injuries remain a significant challenge in clinical practice due to the therapeutic complexity. To a large extent, the risk of complications is associated with inadequate or delayed treatment. Inappropriate management may result in disfigurement, functional impairment of the affected area and in severe cases, increased mortality.

In deep partial-thickness and full-thickness burns, tissue damage leads to the formation of an eschar. The presence of this necrotic tissue delays the accurate diagnosis and contributes to the occurrence of infection, scarring and other systemic complications. (Rosenberg et al., 2014; Rosenberg et al., 2012) Therefore, effective wound debridement is essential to promote healing and prevent these adverse outcomes.

Early surgical debridement followed by autografting has long been regarded as the standard of care (SOC) for burn patients. Despite its effectiveness and improvement in long term outcomes, escharotomy has several limitations. The procedure is invasive, often requires general anaesthesia and may result in substantial blood loss. Furthermore, inaccurate removal of tissue may lead to unnecessary damage to viable structures which can contribute to scarring or unfavorable cosmetic outcomes. (Bordeanu-Diaconescu et al., 2024)

Enzymatic debridement offers an alternative to surgical approach. It provides a tissue-sparring technique that enables selective removal of an eschar that aims to preserve viable tissue to the greatest extent possible.(Mattern et al., 2022) Multiple plant-derived compounds have been evaluated as potential agents for burn wound treatment throughout the history, however bromelain remains the only one commonly used in clinical practice. Extracted from pineapple, this proteolytic enzyme possesses antiedematous, anti-inflammatory, anti-thrombotic and fibrinolytic properties. (Maurer, 2001) NexoBrid® (MediWound Ltd., Yavne, Israel) is a bromelain-based debridement that consists of proteolytic enzymes (anacaulase-bcdb, thiol-endopeptidases, peroxidases, phosphatases, glucosidases, and cellulases). It has been approved for deep-partial and full-thickness burn wound treatment by the European Medicines Agency (EMA) in 2012 and by U.S. Food

and Drug Administration (FDA) in 2022. (Bordeanu-Diaconescu et al., 2024) The clinical development that led to these approvals began with the early, prospective studies, most notably the work by Krieger et al. (2012), which evaluated the efficacy of enzymatic debridement in deeply burned hands. This prospective study provided significant evidence that a single application of bromelain-based enzymes could selectively remove eschar often without damaging viable dermis.

Since NexoBrid's introduction to the market, numerous studies have evaluated its efficacy, particularly in comparison with the SOC. However, the available evidence regarding its safety remains limited and heterogeneous. Study design and reporting of the adverse events differ across studies, which makes direct comparison challenging. Furthermore, data regarding long-term outcomes and the safety of NexoBrid in specific patient populations remain insufficiently investigated, highlighting the need for further research. The aim of this review was to extract data on adverse events and evaluate the clinical safety profile of NexoBrid in burn wound management.

Methods

A literature search was conducted in PubMed and Embase to identify relevant studies published from 2012 to 2026. The search used combinations of following keywords: „NexoBrid", „bromelain", „bromelain-based enzymatic debridement", „burns", „burn wound", „clinical outcomes" and „safety". Studies were eligible for inclusion if they were retrospective case-series, retrospective cohort or clinical studies evaluating the safety of NexoBrid in human subjects, included exclusively adult populations and were published in English. They were excluded if the full text was unavailable, if they did not explicitly define the age of participants or included mixed populations without subgroup analysis, if they did not report data on adverse events or safety outcomes or if they were systematic reviews or meta-analyses. Case reports and case series with fewer than five patients were excluded due to limited generalizability. Additionally, the reference lists of selected studies were screened to identify further relevant studies. A total of 15 articles meeting the inclusion criteria were analyzed. Data extracted from the literature consisted of: (1) baseline characteristics of the eligible studies and (2) safety measurements, which included: pain levels, analgesia requirement, bleeding events, need for transfusion, allergic reactions and other adverse events.

Table 1. Baseline Characteristics of the Included Studies

Author (Year)	Country	Study design	Sample size (*N*)	Control group	Age (mean/range)	TBSA - mean (%)/range	Burn depth
Lugilde Guerbek et al. (2025)	Spain	RCS	43	None	>= 65 years (mean age 74.5)	11%	Deep partial to full thickness
Kaita et al. (2025)	Japan	SC- RCoS	17 (treated with NXB n=7; treated without NXB n=10)	Treated without NXB – SD alone	50–71 years (mean age 59)	46 % / 34–55	The median FTBA – 22%
Bulla et al. (2025)	Spain	RCS	300	None	>18 years (mean age 41)	8 %	Deep dermal and full thickness
Breidung et al. (2025)	Germany	RCS	75	None	>18 years (mean age 48.6 ± 18.9)	4.6 ± 2.9% (all patients <10%)	Deep second-degree or third-degree
Deplazes et al. (2024)	Switzerland	SC- RCoS	269 (bromelain treatment n=83; no bromelain treatment n = 186)	No bromelain treatment group	>18 years (mean age 50)	19%	Severe burn injuries ABSI Score, median (IQR) = 6 (5-8)
Capitelli-McMahon et al. (2024)	United Kingdom	SC- RCoS	52 (NXB group n=26; SD group (SOC) n=26)	SD group	>18 years (mean age 44.5 - NXB group; 44 – control group)	35.5% - NXB group; 35.8% - control group	Deep partial thickness burns or full thickness
Tapking et al. (2023)	Germany	SC- RCoS	169 (geriatric group >65 years n=34; younger group 18-65 years n=135)	Younger group	>18 years (mean age 77.4 ± 7.3 - geriatric group; 39.6 ± 13.7 - younger group)	26.8 ± 17.1% - geriatric group; 24.2 ± 20.4 % - younger group	Mixed, partial, or full thickness

Author (Year)	Country	Study design	Sample size (*N*)	Control group	Age (mean/range)	TBSA - mean (%)/range	Burn depth
Alekseev et al. (2023)	Russia	OPCS	15	None	25–67 years (mean age 37.3 ± 11.6)	3-15 (mean 9.5 ± 4.1%)	Mixed-depth partial thickness
Claes et al. (2022)	Belgium	SC- RCoS	67 (data for adult subgroup extracted)	None / Pediatric group	19 – 86 years (mean age 49.1) (adult subgroup only)	10.8%	Deep dermal and full thickness
Bowers et al. (2022)	United Kingdom	RCS	29	None	23-74 years	30.1%	Partial, full thickness
Waldner et al. (2021)	Switzerland	RCoS	32 (early treatment (<72h) group n=16; delayed treatment (>72h) group n=16)	Early treatment (<72h) group	>18 and <80 years (mean age 54)	24.2 ±17.4%	Partial thickness
Hofmaenner et al. (2021)	Switzerland	SC- RCoS	59 (regular use group n=49; off-label use group n=10)	Regular use group	31-59 years (mean age 42)	11.5% (5-16) - regular use group 42.75% (24-65) - off-label use group	Superficial dermal, deep dermal
Arkoulis et al. (2021)	United Kingdom	RCS	20	None	Mean age 42.5	20%	Deep dermal or full thickness
Schulz et al. (2017)	Germany	SC-CT	26 (NXB group n=13; SD group n=13)	SD group	18–78 years	16% - enzymatic debridement with NXB group, 34% - SD group	Deep dermal or deeper (facial burn)
Cordts et al. (2016)	Germany	POS	16	None	Mean age 47.8 ± 14.9	20.1% (2–66); On the upper extremities - 7.3% (2–15)	Deep partial to full thickness

Abbreviations: RCS – Retrospective Case Series; RCoS – Retrospective Cohort Study; SC- RCoS – Single-Centre Retrospective Cohort Study; SC-CT – Single-Centre Clinical Trial; OPCS – Observational Post-Registration Clinical Study; POS – Prospective Observational Study; NXB – NexoBrid; SD – surgical debridement; TBSA – Total Burn Surface Area; FTBA – Full-Thickness Burn Area; ABSI – Abbreviated Burn Severity Index; IQR – interquartile range

Table 2. Safety measurements

Author (Year)	Pain (VAS / % severe / NRS)	Analgesia required	Bleeding events (%)	Need for transfusion (%)	Infection rate (%)	Allergic reactions	Other adverse events
Lugilde Guerbek et al. (2025)	NR	Multimodal analgesic regimen (Paracetamol and NSAIDs for background pain, supplemental opioids for breakthrough pain)	NR	25.6	25.6 (affecting the NXB-treated area)	NR	Mortality – 25,6% Hypertrophic scarring – 8 patients
Kaita et al. (2025)	NR	Ketamine during the application and removal of NXB	NR	NR explicitly (Median RBC transfusion in NXB group - 3080 mL, in non-NXB group - 3360 mL)	71 – NXB group (bacteriemia) 90 – non-NXB group (bacteriemia)	NR	Mortality – 29% NXB group; 30% non-NXB group

Author (Year)	Pain (VAS / % severe / NRS)	Analgesia required	Bleeding events (%)	Need for transfusion (%)	Infection rate (%)	Allergic reactions	Other adverse events
Bulla et al. (2025)	NR	Regional nerve blocks or general anaesthesia during the procedure	NR	7	14	NR	Early post-ED fever – 14% Coagulation alteration – 40% (out of available data) Scar hypertrophy – 58 patients Passed away during the time study – 15 Burn contractures – 2 patients
Breidung et al. (2025)	(NRS) Before NXB - 2.3 ± 1.9 After NXB - 2.7 ± 2.2	Smaller burn areas - local infiltration anaesthesia; larger or more sensitive areas - regional anaesthesia (plexus block) or sedation/general anaesthesia	NR	NR	NR	NR	Increase in body temperature (37.0 ± 0.7°C) Decreased Hb levels (13.3 ± 1.6 vs 12.6 ± 1.7 g/dL) Decreased PT ratio (82.0 ± 13.3% before vs. 76.8 ± 14.9% after (% of normal) CRP levels increased (4.8 ± 5.8 mg/dL before vs. 10.8 ± 7.2 mg/dL after Mortality – 4%
Deplazes et al. (2024)	NR	NR	NR	NR	Bromelain treatment – 27 No bromelain treatment – 21 (bacteriemia)	NR	Mortality - 40 (15%)
Capitelli-McMahon et al. (2024)	NR	NR	NR	None observed	NR	NR	Changes in platelet count - not statistically significant Small increase of aPTT - not clinically significant
Tapking et al. (2023)	None observed	NR	NR	NR	NR	None observed	Damage to healthy skin – none observed Mortality - 47.1% geriatric group; 8.9% younger group
Alekseev et al. (2023)	(VAS) 2.7 ± 0.3 points before the application; 7.5 ± 0.3 during the application; 5.8 ± 1.2 after the removal of the bandage	Non-narcotic analgesics - all patients Intravenous anaesthesia - most patients during removal of the gel and wound debris	NR	NR	NR	NR	NR
Claes et al. (2022)	(NRS) 89% patients - mean <3 11% patients - 3-5 * Data from 28/30 patients treated with NXB under regional (27/28) or no anaesthesia (1/28)	a standard pain treatment protocol before, during and after debridement; regional/general anaesthesia	NR	NR	NR	NR	None reported

Author (Year)	Pain (VAS / % severe / NRS)	Analgesia required	Bleeding events (%)	Need for transfusion (%)	Infection rate (%)	Allergic reactions	Other adverse events
Bowers et al. (2022)	Pre-procedure mean pain score of 2.7 Intra-operative pain - 1.7 After procedure - 2.2	The Pinderfields Pain Protocol	NR	None observed	3.45 (wound infection)	NR	Mortality – 6.9%
Waldner et al. (2021)	NR	NR	NR	NR	18.8 - delayed treatment group; 6.3 - early treatment group (wound infection)	NR	Initial decrease in Hb levels – both groups Increased CRP levels during the initial post-ED phase, flattening after POD 3 – both groups
Hofmaenner et al. (2021)	NR	Analgosedation (1/49;0/10), axillary plexus block (5/49;0/10), femoral block (2/49; 0/10), general anaesthesia (41/49;10/10)	None observed	NR explicitly (no difference in blood transfusions between two groups)	12.2 - regular use group; 40 - off-label use group (wound infection)	None observed	None observed
Arkoulis et al. (2021)	NR	BICU patients - sedated Ward-level patients - regional blocks/opioid infusion	NR	NR	NR	NR	Mortality – 5%
Schulz et al. (2017)	No severe pain	One patient in the EDNX group - local anaesthesia, 12 patients - sedation	NR	NR	None observed	NR	NR
Cordts et al. (2016)	(NRS) 1.1–5.2 in general analgesia group 1.8–4.1 in plexus block group	pain medication; brachial plexus nerve block; general anaesthesia	NR	None observed	None observed	NR	Mortality 18.8%

Abbreviations: NR – Not reported; NXB – NexoBrid; PT – prothrombin time; CRP – C-reactive protein; Hb – hemoglobin; EDNX – Enzymatic Debridement with NexoBrid

Results

The literature search and screening process identified 15 studies that met pre-defined inclusion criteria. The results of this review are based on analysis of retrospective cohort studies, retrospective case-series and clinical trials which represent a diverse range of clinical settings across Europe, Asia and North America. Data were synthesized from a total population of 954 patients treated with NexoBrid. These patients primarily presented partial-thickness and full-thickness burns, with Total Body Surface Area (TBSA) ranging from 0.5% to 66%. The follow-up period varied significantly, spanning from hospital discharge to long term evaluations lasting several years. The baseline characteristics of selected studies, incorporating study design, sample size and patient demographics, are summarized in Table 1.

This review focused on extracting safety parameters and adverse outcomes associated with NexoBrid treatment for burn wounds from the available literature. The key measurements are outlined in Table 2.

Pain outcomes

In the analyzed studies, pain intensity was monitored using standardized scales, primarily the Numerical Rating Scale (NRS) and the Visual Analogue Scale (VAS). The majority of the publications state that patients either did not complain of severe pain at any point during enzymatic debridement or rated their distress at a low to moderate level (Alekseev et al., 2023; Bowers et al., 2022; Breidung et al., 2025; Claes et al., 2022; Cordts et al., 2016; Tapking et al., 2023). The highest score was reported by Alekseev et al. (2023), with a

mean of 7.5 ± 0.3. However, it is worth emphasizing that this peak was observed during the application of NexoBrid and prior to the addition of intravenous anaesthesia.

The approaches for pain assessment varied significantly among the authors. While some performed serial measurements (before, during and after the procedure) others reported a single mean score for the entire follow-up period. Cordts et al. (2016) for instance, evaluated pain intensity in correlation to specific analgesic regimen applied.

Notably, in several included studies, pain outcomes were not addressed at all (Arkoulis et al., 2021; Bulla et al., 2025; Capitelli-McMahon et al., 2024; Deplazes et al., 2024; Hofmaenner et al., 2021; Kaita et al., 2025; Lugilde Guerbek et al., 2025; Waldner et al., 2021), or were omitted as the authors focused solely on the description of anesthetic protocols and the clinical management of analgesia. Multimodal protocols were predominantly employed, ranging from regional anaesthesia, such as plexus blocks (Breidung et al., 2025; Cordts et al., 2016; Hofmaenner et al., 2021) to intravenous sedation or general anaesthesia (Alekseev et al., 2023; Breidung et al., 2025; Bulla et al., 2025; Claes et al., 2022; Cordts et al., 2016; Hofmaenner et al., 2021; Schulz et al., 2017).

Bleeding risk

Another important safety factor is the occurrence of bleeding and the potential requirement for blood transfusion related to enzymatic debridement. Most of the analyzed papers did not mention any bleeding events and Hofmaenner et al. (2021) explicitly noted the absence of such complications in their cohort. Transfusion rates were addressed only in a few studies. Cordts et al. (2016) and Hofmaenner et al. (2021) stated that no blood transfusions were necessary, while Lugilde Guerbek et al. (2025) and Bulla et al. (2025) reported that 25.6% and 7% of their investigated population required hematic support.

Infection rates

The findings regarding infectious complications varied significantly amongst the analyzed studies, reflecting differences in patient populations and clinical settings. Reported rates fluctuated from 3.45% up to 90%. However, it is important to underline that these results encompassed both topical and systemic infections. Some earlier articles either denied the occurrence of wound or systemic infections in their cohorts or did not mention them in their analysis (Alekseev et al., 2023; Arkoulis et al., 2021; Breidung et al., 2025; Capitelli-McMahon et al., 2024; Claes et al., 2022; Cordts et al., 2016; Schulz et al., 2017; Tapking et al., 2023). More recent investigations, such as Deplazes et al. (2024) and Kaita et al. (2025) specifically addressed episodes of transient bacteriemia during the debridement process. Notably, both studies compared the incidence of this adverse event between patients treated with bromelain and a control group. Although the infection rates varied, ranging from 27% in Deplazes' cohort to 71% in Kaita's small study group, this difference did not reach statistical significance. Similarly, Waldner et al. (2021) and Hofmaenner et al. (2021) adopted a comparative methodology, evaluating their findings across two distinct populations. Waldner et al. (2021) assessed delayed enzymatic treatment and identified a higher number of wound infections in the study group. Hofmaenner et al. (2021) evaluated off-label use and their results in this parameter exhibited a lack of statistical significance, largely due to the limited sample size.

Hypersensitivity reaction

Only Tapking et al. (2023) and Hofmaenner et al. (2021) reported a lack of allergic reactions following NexoBrid debridement. The majority of the remaining articles did not address this complication in their research. No cases of anaphylaxis or severe hypersensitivity were identified in the reviewed literature. Noticeably, these outcomes are consistent with the exclusion criteria often applied in clinical protocols of patients treated with bromelain.

Other adverse events

In the evaluation of clinical safety of NexoBrid, it is important to take other, less common adverse events into consideration. These include mortality rates, laboratory fluctuations and dermatological outcomes. Among these, patient mortality was most frequently addressed in the included studies. Reported rates varied significantly, reaching from 4% (Breidung et al., 2025) to 47.1% in the geriatric group (Tapking et al., 2023). However, Arkoulis et al. (2021) stated that no deaths could be directly attributed to the use of NexoBrid. It is noteworthy that Kaita et al. (2025) compared mortality rates between bromelain-based debridement and control, finding them to be nearly identical.

Laboratory findings covered decreased hemoglobin levels (Breidung et al., 2025; Waldner et al., 2021), alterations of coagulation mostly presenting as increased prothrombin time (Breidung et al., 2025; Bulla et al., 2025; Capitelli-McMahon et al., 2024) and changes in platelet count (Capitelli-McMahon et al., 2024). Additionally, Breidung et al. (2025) and Waldner et al. (2021) reported increased levels of C-reactive protein (CRP). These fluctuations were generally mild and transient. Regarding long-term outcomes, Lugilde Guerbek et al. (2025) and Bulla et al. (2025) documented hypertrophic scarring in their studies. Despite these occurrences, Tapking et al. (2023) highlighted that there was no damage to healthy skin in their population.

Discussion

The present review synthesized clinical data from various study designs to evaluate the safety and adverse event profile of NexoBrid burn wound management. The main findings suggest that enzymatic debridement represents a safe alternative to traditional surgical methods, with a systemic impact that is mostly transient and manageable. The high rates of some complications reported by some authors were largely associated with the severity of the initial injury or the complexity of the patient population rather than the enzymatic agent itself.

These observations align with the landmark phase 3 randomized controlled trial (RCT) conducted by Rosenberg et al. (2014) and the detailed analysis of hand burns by Krieger et al. (2017). Although these seminal studies were excluded from the primary data tables of this review due to the inclusion of mixed pediatric and adult population, their results remain of paramount importance. Rosenberg et al. (2014) established the efficacy and safety of NexoBrid, showing that it could effectively remove eschar while significantly reducing the need for surgical intervention and lowering blood loss compared to standard of care. Furthermore, Krieger et al. (2017) demonstrated that early enzymatic debridement in burned hands reduces the surgical burden and the risk of compartment syndrome without increasing infectious or hemorrhagic complications.

Pain Management and Anaesthetic Protocols

Procedural pain is a recognized and the most clinically apparent side effect of NexoBrid usage. The mechanism of this bromelain-based agent involves the proteolytic digestion of necrotic tissue inevitably triggering a nociceptive response. The available literature indicates that, although nearly universal, pain can be managed with adequate anaesthetic strategies. Studies in which proactive, multimodal protocols were applied - incorporating oral or parenteral analgesics, regional nerve blocks and intravenous or general anaesthesia - reported significantly lower pain levels (Bowers et al., 2022; Breidung et al., 2025; Claes et al., 2022; Cordts et al., 2016; Schulz et al., 2017). The high mean score reported by Alekseev et al. (2023) reflects a peak observed before the implementation of fully optimized systemic anaesthesia. Therefore, it appears that distress level is highly dependent on the analgesic regimen and anaesthetic protocol employed.

Bleeding risk

The current standard of care for deep burns, which is tangential excision, is inherently associated with substantial blood loss, due to its non-selective nature, which requires cutting through vascularized tissue layers (Rosenberg et al., 2014; Shoham et al., 2023). This review aimed to analyze whether enzymatic debridement's high selectivity impacts the risk of bleeding. It revealed that while most included articles did not address this complication, the available evidence supports a favorable hemostatic profile. Hofmaenner et al. (2021) explicitly stated an absence of bleeding in their cohort, reinforcing the theory that bromelain-based enzymes are only active in necrotic tissue, presenting no risk to viable vascularized structures. Another proxy for evaluating blood loss was transfusion rate, also sporadically mentioned by authors. While Lugilde Guerbek et al. (2025) and Bulla et al. (2025) reported that 25.6% and 7% of their investigated population required hematic support, these rates are most likely multifactorial. In the context of severe burns, such interventions often reflect the overall severity of the injury and the patients' clinical condition, rather than being directly related to the NexoBrid treatment itself. The overall scarcity of reported hemorrhagic events, combined with Hofmaenner et al. (2021) findings, suggest that enzymatic debridement does not pose a significant hematological risk. Consequently, enzymatic debridement appears to offer a superior safety profile to non-selective surgical methods.

Infectious Complications and Bacteremia

Burn injury causes loss of the skin's barrier functions with associated lower resistance to infection; as a result, the eschar is rapidly colonized by endogenous bacteria. Potentially leading to the systemic response, infectious complications represent a considerable concern in burn care (Sheridan, 2001). A critical safety question in NexoBrid debridement was whether the proteolytic dissolution of the necrotic tissue could inadvertently facilitate the systemic translocation of these colonizing bacteria. Recent evidence from Deplazes et al. (2024) and Kaita et al. (2025) has provided some clarity on this issue by specifically monitoring events of bacteremia. While the high incidence rates reported in these studies might initially seem concerning, a more precise evaluation reveals that they speak in favor of enzymatic debridement - demonstrating lower infection rates - or do not reach statistical significance. Altogether these findings suggest that NexoBrid usage does not pose a higher infectious risk than traditional surgical methods and that bacterial translocation is a procedural phenomenon rather than a specific risk of this bromelain-based agent.

Hypersensitivity reactions

NexoBrid is a mixture of proteolytic enzymes enriched in pineapple-derived bromelain (Maurer, 2001). Due to its proteinaceous structure, the agent possesses the theoretical potential to provoke allergic reaction or anaphylaxis. However, the analyzed studies did not report any such events during enzymatic debridement, or they explicitly confirmed its absence in their cohorts. These favorable outcomes are most likely correlative with exclusion criteria which routinely disqualified patients with a known allergy to pineapple, papaya (due to cross activity with papain) or any other components of the NexoBrid concentrate. Consequently, while the risk of hypersensitivity remains a valid clinical consideration, it appears to be effectively reduced by thorough pre-procedural screening.

Systemic Response and Other Adverse Events

Beyond the primary complications, the reviewed literature analyzed other effects of NexoBrid treatment. The reported mortality rates varied significantly across studies, however these figures most likely reflected the severity of the burn injury rather than the intervention itself. The observed laboratory fluctuations were generally mild and transient, and most authors concluded that they did not reach clinical significance and were consistent with the expected systemic response to burn trauma. However, some investigators emphasize the need for further analysis of coagulation abnormalities associated with the use of bromelain. Taken together, these findings suggest that while enzymatic debridement triggers a measurable systemic response, it does not compromise the overall stability of the patient, further supporting its safety profile.

Limitations of the Study

Despite its clinical significance, several limitations must be acknowledged. Firstly, the analyzed literature presented a high level of heterogeneity regarding burn severity, anatomical locations of the injury, studied populations and standardized reporting of adverse events. Furthermore, this review focused solely on the adult cohort due to limited safety data for pediatric patients and it extracted complications occurring in the acute phase of the treatment to ensure a targeted analysis of procedural safety. Consequently, long-term outcomes and the clinical safety of NexoBrid in children's burn wound treatment necessitate a separate and more targeted analysis. Lastly, a significant portion of the included literature consists of retrospective studies with relatively small sample sizes. Future research should prioritize standardized, prospective multicenter trials to further consolidate the safety evidence for enzymatic debridement.

Conclusions

The findings of this review demonstrate that enzymatic debridement performed with NexoBrid appears to be a safe and highly selective alternative to traditional surgical methods in adults. The primary complication is procedural pain, which can be effectively managed with proper analgesic and anesthetic protocols. Furthermore, the risk of clinically significant bleeding and infection seems to be comparable or even superior to tangential excision. Regarding other safety parameters, systemic responses and minor laboratory fluctuations may appear, however they are usually transient and do not compromise overall physiological stability. Finally, pre-procedural screening for allergies effectively minimizes the risk of hypersensitivity. In conclusion, NexoBrid offers a robust safety profile that supports its integration into standard burn care for adults, although further comparative research is encouraged to strengthen these observations.

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