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Analgesia And Post-Burn Care In Animal Models: Gaps, Guidelines And Future Directions

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ABSTRACT

Burn injuries continue to rank among the most devastating types of traumas, with significant rates of morbidity, death, and long-term aftereffects. Animal models are essential for understanding the intricate pathophysiology of burns and for assessing new treatment approaches. The ethical precepts, methodological techniques, and post-burn management techniques used in experimental burn research are covered in this review. Current guidelines for the use of analgesics and welfare monitoring are summarised, together with standardised methods for inducing burns in various species.

The review also highlights critical components of post-burn care, including fluid resuscitation, pain management, nutritional support, wound care, antimicrobial therapy, and experimental approaches such as stem cell and growth factor-based treatments. Despite the fact that research on animals has greatly expanded our knowledge of the mechanisms underlying burn injuries, translational gaps still exist because of interspecies heterogeneity and uneven methods. To improve the reproducibility and human relevance of burn research, future studies should concentrate on creating sophisticated ex vivo, in vitro, and in silico models, improving ethical frameworks, and encouraging standardised procedures.

Keywords- Burn injuries, Wound care, Animal Model, Analgesics, Pain management

INTRODUCTION

Burn injuries varies in their cause kinds and intensity; consequently, their treatment might be tough to be controlled. The first and second degrees of burn injuries normally are treated with the moisturizer, the topical drugs, and/or an antibacterial cream prescribed by the doctor. This ailment will normally heal within 2 weeks. (1) On the other hand, because third degree of burn injuries destroys all the skin layers, the majority of wound will tend to severely long-term consequences and cannot be managed by the primary healing process, so the additional surgical procedures, including skin grafting, skin substitutes, and the application of advanced wound dressing, are required.(2) They act as filler to increase the dermal

component of wound, improve the re-epithelization, and reduce the inhibitory factors and the inflammatory responses of wound healing, and therefore subsequent scarring. Numerous options for skin substitutes, dermal analogy, and advanced dressings existed, which can be broadly divided and utilized depending on the severity of burn injuries. However, removing and covering the wound as early as possible are crucial since the main challenge in treating third degree of burn injuries is avoiding infection from any contaminations. In addition, appropriate deep burn care providing protection from physical damage and supporting the circulation of gas and moisture as well as a comfort enhancing the functional recovery should also be the priorities in severe burn wound care.(3)

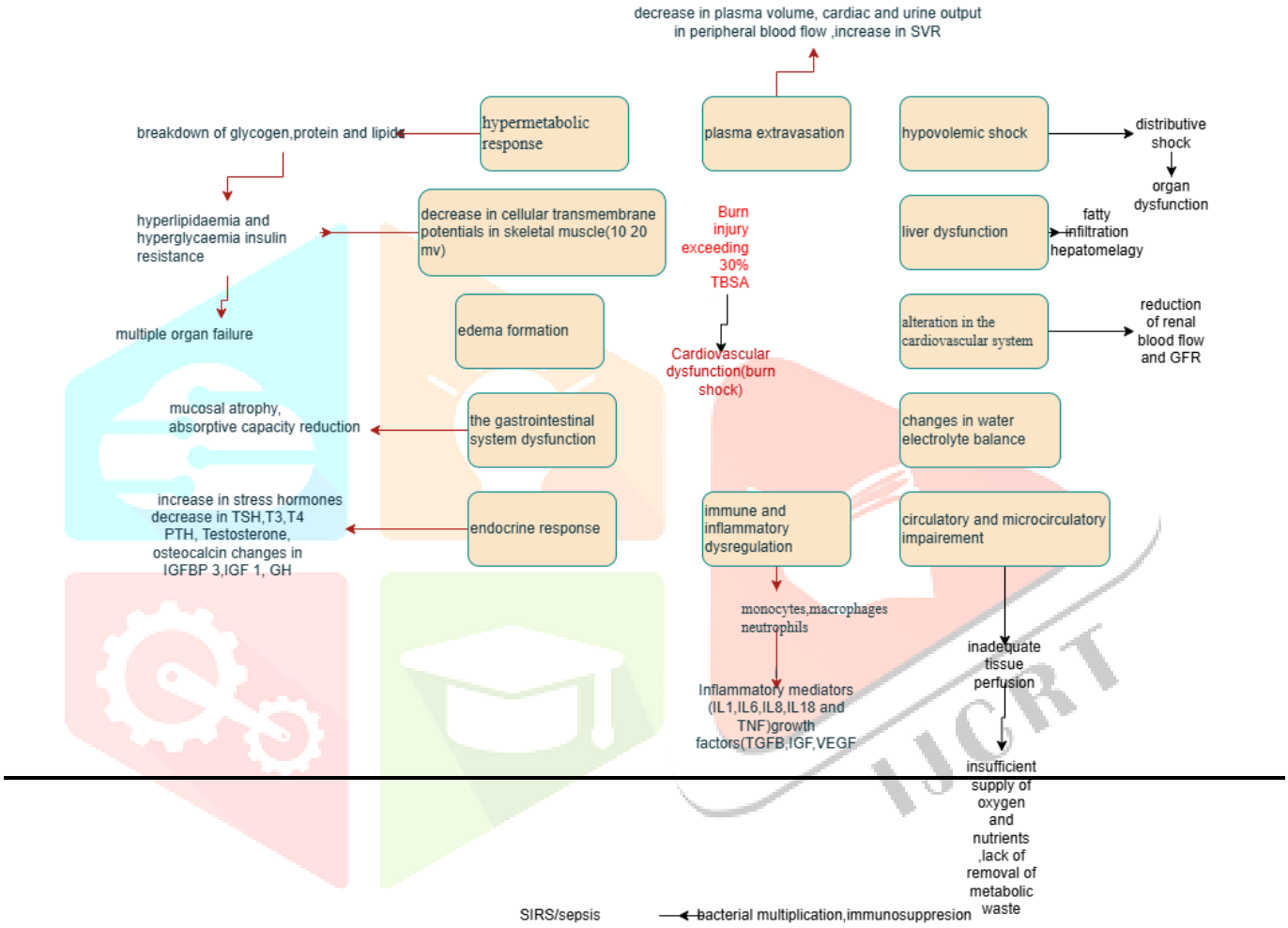

Figure 1- Pathophysiological changes after major burn injury (>30%TBSA) (4)

NEED OF ANIMAL MODEL

Bernard was the first to incite the use of animals as experimental models in a variety of biological studies for transfer into human physiology in 1865.(5) Over time, numerous researchers have been motivated to examine a wide range of causes and treatments in animal models before applying their findings to humans due to the striking anatomical and physiological parallels between humans and animals. Hot water, hot metal tools, electricity, and heated paraffin are some popular methods used in burn research to cause wound burns in the animal model. These techniques involve shaving the animal's back and applying a hot substance to the skin to create the appropriate burn surface area.(6) Each of the several burn models requires certain criteria, such as elevated temperatures and exposure time. Additionally, it is essential to estimate

the integral planning for the burn animal model experiment. The density of hair is the primary distinction between animal and human skin histology. The hair cycle has a significant impact on the architecture of hair follicles and the speed of reepithelialization; this has an impact on the planimetry area of the wound and the microscope data of observable skin biopsies. (7)

For example, rodents have a short hair cycle (around 23–28 days). Rodents with similar birth dates should be utilized for the evaluation of the wound in order to avoid their hair cycle impacts. The particular temporal consideration of each animal model must be emphasized because various animals have varied hair cycles. Animal hair must be completely depilated because it may also hinder heat transfer and conceal a source of dangerous diseases. The hair can be completely removed by shaving with a hair clipper and then using hair removal cream. However, the hair removal cream's administration time should be carefully regulated because it may cause contact dermatitis. Finally, to increase the animal's chances of survival, proper post-operative care must be considered. The appropriate administration of analgesics can increase the animal's appetite and reduce self-harm, while the prudent use of antibiotics can avoid wound infections. Large burns can also result in a significant loss of bodily fluids; for this reason, animals must be closely watched and handled to prevent dehydration.(8)

ETHICS, PRINCIPLES IN ANIMAL EXPERIMENTATION

The concept of the proposed experiments' moral acceptability under particular circumstances serves as the foundation for legislation pertaining to animal experimentation. the importance of research ethics in ensuring that experimental animals are treated humanely. It is crucial to adhere to ethical guidelines when doing animal research in order to prevent animals from suffering unnecessarily.(9) From an ethical and scientific perspective, it is crucial to give these animals the finest care possible. Experimental results may result from inadequate animal care. Therefore, the scientific knowledge and conclusions derived from tests may be compromised and may be difficult to duplicate, which is a characteristic of scientific research, if experimental animals are mistreated. Currently, the majority of ethical guidelines operate under the premise that animal testing is acceptable due to the substantial potential advantages to humans.(10)

PRINCIPLE OF THE 4 Rs

The use of animals in research is governed by national and international legislation, which is mostly based on the universal theory known as the concept of the three Rs, which was introduced by Russell and Burch in 1959. Protocols pertaining to the use of animals in research are governed by the three Rs: reduction, refinement, and replacement. Another "R" of accountability for the experimental animal as well as the social and scientific standing of animal experiments has been put out by some researchers.

• The initial "R," Reduction is the process of examining the experimental design to make sure that the number of experimental animals used in a study has been lowered to the bare minimum needed for accurate results. Improved experimental design, a thorough literature search to prevent experiment duplication, the use of cutting-edge imaging techniques, resource and data sharing, and appropriate statistical data analysis

that minimizes the number of animals required for statistically significant results are some of the methods employed for this purpose.

• The second "R," refinement, entails process enhancements that lessen the detrimental impacts of the planned tests on the animals involved, such as lowering pain, suffering, and distress in a way that improves animal welfare overall. Improved living conditions for research animals, appropriate training for those who handle animals, the use of anesthesia and analgesia when necessary, and the necessity of euthanizing the animals at the conclusion of the experiment to lessen their suffering are a few examples of this.

• The third "R," Replacement, describes methods that either completely eliminate or substitute the use of experimental animals. These strategies include the use of in vitro techniques like cell and tissue culture testing, in silico methods, computerized techniques, and software, as well as relative replacement techniques that substitute invertebrates like fruit flies, nematode worms, and microorganisms for vertebrates and higher animals. The use of alternative blood sources, the exploitation of commercially used animals for scientific study, appropriate training without the use of animals, and the utilization of specimens from earlier trials for additional research are examples of how these initial "3R2 principles" should be applied.

• The fourth "R," responsibility refers to concerns about advancing animal welfare through enhancing the social lives of experimental animals, developing cutting-edge scientific techniques for objectively assessing sentience, consciousness, pain perception, and intelligence in the animal kingdom, and effectively participating in the professionalization of the public discourse on animal ethics.(11)

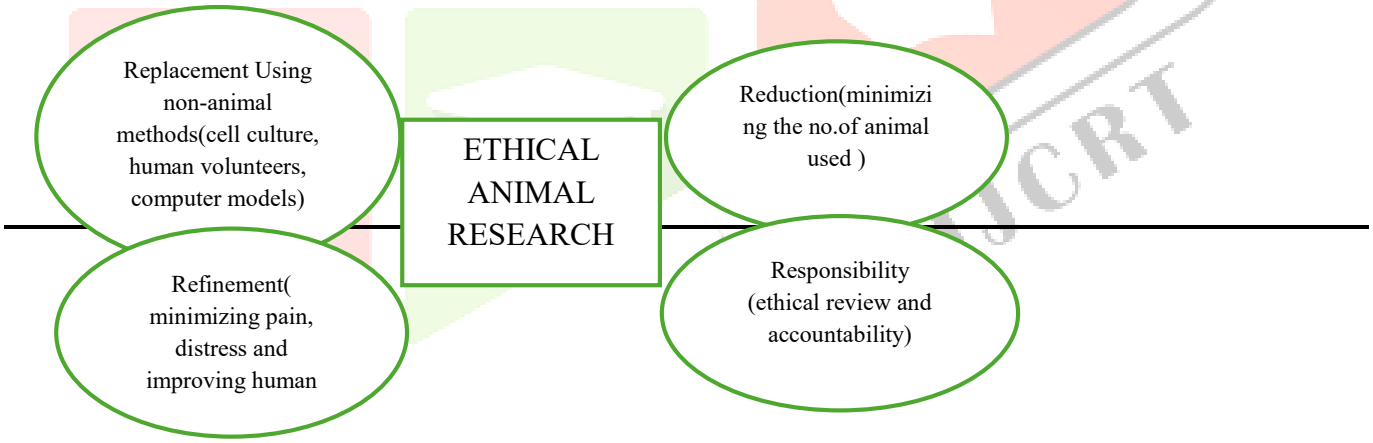

Figure 2 – Principle of 4Rs - Improving animal welfare in research(12)

ANIMAL MODEL OF BURNS

The technique employed to cause burns in test animals may be the most important component of clinical relevance. In experimental animal models, burn surfaces have been produced via direct contact with heated metal, electricity, and heated water.(13)

Standardized scalding burn model in mouse

The model typically uses tiny, healthy mice that are 6–8 weeks old. First, intraperitoneal injections of ketamine, xylazine, or other anesthetics are used to put the mouse to sleep. In certain cases, the mouse is also given 1 milliliter of saline subcutaneously along its spine to protect its spinal cord from damage. To guarantee even burn wounds, the dorsum's hair is then shaved off. The dorsum is the best option since it is

hard for the animal to get to, which keeps the wound area from getting worse. After that, the mouse is positioned on its back in a template made of a flame-resistant plastic mould, with the window revealing a predefined skin surface area. (14)

After that, the mouse's exposed portion from the template is submerged in a water bath at 100 °C for 8 seconds to cause a full-thickness burn. After that, the animals are regularly checked for signs of discomfort or pain, and if necessary, they are given buprenorphine or other analgesics. Each study has a different temperature (60–100 °C) and exposure duration (8–12 s). Our team has demonstrated through experimentation that the method described may cause a full-thickness burn. Because mice can only withstand a 30% TBSA burn, one is constrained by their size. However, in burn injuries with less than 40% TBSA, the hypermetabolism phase is not fully engaged clinically.

Table 1: Size of mouse scald burn model

TBSA	SPECIES	TEMPERATURE	LENGTH OF EXPOSURE	Reference
2.5	Mouse	54	25	(15)
7	Mouse	65	45	(16)
10	Mouse	65	20	(17)
18	Mouse	90	9	(18)
15	Mouse	85	9	(19)
		95	7-8	(20,21)
		100	-8	(22,23)
20	Mouse	90	7	(24,25)
25	Mouse	90	9	(26,27)
30	Mouse	90	9	(28)
		95	6	(29)
35	Mouse	80	15	(30)
		97	7-10	(31,32)

Standardized scalding burn model in rat

Similar to the mouse model, the rat scalding burn model is simple and is accomplished in precisely the same way, with a few little variations like the temperature and duration of exposure to the heated water. Additionally, because rats are larger, they can withstand burns up to 60% TBSA by utilizing the model on their dorsum and adding another wound to their abdomen. According to our observations, rats with burn wounds larger than 60% TBSA have worse survival and are not suitable for experimentation. The requirement for a burn injury model large enough to induce the hypermetabolism seen in clinical burns with high TBSA is another factor to consider.(33)

Humans experience hyperglycemia in the early post-burn phase due to an accelerated rate of glucose appearance and poor tissue extraction of glucose, which results in an overall increase of lactate and glucose. As a result, even though the rat burn model is better than the mouse at simulating hypermetabolism, it

becomes difficult to mimic the post-burn sepsis observed in patients with more than 60% TBSA when an infection element is added.

Table 2: Size of rat scald burn model

TBSA	SPECIES	REGION	TEMPERATURE	EXPOSURE TIME	REFERENCE
10	Rat	Dorsum	80	10	(34)
15	Rat	Dorsum	95	8	(35)
20	Rat	Dorsum	60	25	(36)
			80	6	(37)
			90	10	(38)
			100	10	(39)
30	Rat	Dorsum	60	40,27	(40,41)
			90	10	(42)
			92	20	(43,44)
			97	10	(45)
			98	12,15	(46–48)
			100	30	(49)
			106	9	(50)
35	Rat	Dorsum	100	15	(51)
40	Rat	Dorsum	100	10	(52,53)
		Ventral		2	(52,53)
45	Rat	Dorsum	87	10	(54)
		Ventral		3	(54)
55	Rat	Dorsum	80	15	(55)
		Ventral		8	(55)
60	Rat	Dorsum	96	10	(56)
		Ventral		2	(56)
		Dorsum	98	10	(57,58)
		Ventral		2	(57,58)

Modelling inhalation injury in animals

The use of sheep to simulate inhalation harm after burns is an intriguing new topic in burn research, despite the fact that rodents and other small animals have grown in popularity due to genetic and financial factors.(59) The majority of deaths in burn centers worldwide are caused by inhalation injuries, which have a complicated etiology, a variety of onset patterns, and clinical presentations. The discovery of successful clinical treatments that can lower the high death rates connected to this particular kind of thermal injury will be aided by an animal burn model that accurately reflects the complexity of this burn injury. Sheep

have been acknowledged as the gold standard for researching this kind of injury, despite studies on smaller animals such as rodents.(60) When it comes to simulating the clinical, physiological, and histological changes associated with smoke-induced inhalation injuries in humans, sheep are superior to all other animal models. For instance, sheep also exhibit histological alterations of the respiratory tract, such as disruption and loss of cilia and loss of respiratory epithelium following inhalation damage, as observed clinically in humans. Because physiological factors like mean arterial pressure and arterial oxygen tension are monitored in this kind of injury, animal size is another crucial factor to consider when choosing suitable animal models to study inhalation injuries. To understand the pathological changes of inhalation injury on blood gases, plasma cytokines, and leukocyte counts over time, it is simpler to get sufficient blood or plasma from larger animals.(61)

Not only does the sheep's body size make it suitable for such studies, but the model is also easily replicable. Additionally, nitric oxide (NO) has been linked to the pathophysiology of inhalation damage in clinical investigations. It is crucial to consider the significant species-dependent variations in NO pathways in light of this discovery. In particular, different species produce different amounts of NO during the innate immune-mediated response to Mycobacterium TB. For example, rat macrophages create a lot of NO, but human macrophages produce very little. Sheep are a prominent model for inhalation injury research because to their low cost, natural hardiness, and resistance to chemical and surgical treatment. The sheep model has been extremely successful in replicating some of the clinical signs of this injury, but no single animal model can replicate every aspect of human inhalation injury.(62)

ANALGESIA IN BURN MODEL

Pain reduction without unconsciousness is known as analgesia. Since it is challenging to measure pain in animals, indirect indicators like as irregular posturing, vocalisation, decreased hunger, and self-mutilation are frequently utilised to detect discomfort. Animal welfare standards mandate that analgesia be administered whenever a surgery is being performed or a condition that is likely to cause pain is present because it is impossible to tell when an animal is in pain. It is believed that anything that causes pain in humans will similarly cause pain in animals until there is proof to the contrary. Analgesia should ideally be administered proactively, or before the uncomfortable process, as opposed to after clinical indicators of pain are noticed.(63)

Analgesics, either local or systemic, may also lessen the need for anaesthesia. There are numerous effective ways to alleviate pain in lab animals for a variety of uses. To offer the best analgesia feasible, a multi-model strategy (providing numerous medicines with distinct mechanisms of action) can and should be used. This covers the use of NSAIDs, opioids, and local analgesics (where appropriate). When performing procedures on animals that could result in more than transient or mild pain or discomfort, the proper sedation, analgesia, or anaesthesia should be used.

Opioids (Buprenorphine)

The central nervous system's opiate receptors are where opioids work. Acute, deep, or visceral pain can all be effectively treated with opioids. Buprenorphine, which treats mild to moderate pain, is the most used

opioid in laboratory animal medicine. Respiratory depression, nausea, vomiting, and pica (in rats) are possible adverse effects. and in rats and mice, sustained-release buprenorphine has been linked to dermatitis and ulcers at the administration site. Since all opiates are classified as prohibited substances, their usage necessitates certain documentation.(63)

Non-Steroidal Anti-inflammatory Drugs (NSAIDs) (Carprofen, Meloxicam, Ketoprofen)

Drugs that block one or more steps in the metabolism of arachidonic acid (AA) are often classified as NSAIDs. NSAIDs mainly work by blocking cyclooxygenase (COX), which lowers prostaglandin generation. NSAIDs work well for inflammatory pain. NSAIDs work well on their own to treat mild to moderate pain. Changes in renal function, disruption of platelet function, and gastric or intestinal ulcers are possible adverse effects.(64)

Local Analgesia (Lidocaine, Bupivacaine)

There are various ways to deliver local analgesics. Depending on the medication used, anaesthetic effects might appear 15 minutes after delivery and persist anywhere from 45 minutes to several hours.

1. Before or after an operation, infiltration, also known as infusion, is injected into the skin and other tissue layers along the site of an incision.
2. Injection into soft tissues far from the actual incision in a pattern that crosses the nerve feeding the surgical site is known as a field block or ring block.
3. Nerve conduction block, which involves injecting a tiny quantity of medication or placing it right next to the sheath of a nerve that supplies the surgical site.
4. For certain surgical wounds, topical local anaesthetics like lidocaine jelly may be helpful.

GUIDELINES FOR ANALGESIC USE IN ANIMAL

If the following are included in the Animal Care and Use Protocol, analgesics may be given by drinking water for operations that result in more than mild, transient pain or discomfort:

The IACUC procedure needs to contain:

- A concise scientific explanation explaining why the study cannot employ direct administration.
- An account of how clinical pain evaluations will be carried out and a description of the procedures required to make sure animals are drinking the proper amount of analgesic water.
- Determining the most effective ways to complete these duties is the investigator's job, after consulting with the attending veterinarian.

Examples of tracking fluid intake include, but are not limited to, weighing or measuring the water bottle to make sure that a suitable amount of fluid displacement has taken place over the daily period. To guarantee proper food and drink intake, each animal should be weighed every day.

Identifying symptoms like hunched posture, decreased or hyperactivity, dehydration indicated by a prolonged skin tent when scuffed, ruffled hair coat or lack of grooming, self-mutilation, altered mobility,

decreased hind limb rearing behaviour, decreased faecal output, or poor nest incorporation are examples of clinical assessment of pain.

- A description of criteria for the provision of rescue analgesics (additional doses or routes of analgesia given) or euthanasia for any animals identified as having unexpected or unrelieved pain.
- an outline of procedures for replacing analgesic water when an empty water bottle is identified on weekends, nights, and holidays.

Lab personnel must:

- Provide water bottles containing analgesics at least 12-24 hours before the painful procedure. Rodents are neophobic, and they may initially decline to consume water that contains new substances.
- Include documentation in post-operative records that a daily assessment for the presence or absence of signs of pain was performed
- Maintain correct identification of the cages getting medicated water by labelling bottles appropriately and placing signs on the cage that specifies the analgesic used, the date the bottle was manufactured, and the drug's dosage.

Table 3: Recommended Analgesics for Rats

	DRUG	DOSE	ROUTE	FREQUENCY	REFERENCE
OPIOIDS	Buprenorphine-HCL	0.01-0.05 mg/kg	SQ, IP	Q 4-6 hrs for first 12 hrs, Q 8-12 hours afterward	(65)
	Buprenorphine (Sustained Release)	1.0-1.5 mg/kg	SQ	Q 48-72 hrs	
NSAIDS	Carprofen	5 mg/kg	SQ, IP	Q 24 hrs	
	Meloxicam	1-2 mg/kg	SQ, PO	Q 24 hrs	
	Ibuprofen*	60-150 mg/kg Children Motrin in 475 ml water	PO	Continuously in water (change water every 3 days).	
	Ketoprofen**	2.5-5 mg/kg	SQ	Q 24 hrs, for 3 days maximum.	

LOCAL ANALGESIA	Lidocaine	4 mg/kg (0.4 mL/kg of a 1% solution)	Local infiltration	Do not exceed 7 mg/kg total dose	
	Bupivacaine	1-2 mg/kg (0.4-0.8mL/kg of a 0.25% solution)	Local infiltration	Do not exceed 6 mg/kg total dose	

POST BURN CARE IN ANIMAL MODEL - SUPPORTIVE THERAPIES

1. Fluid Resuscitation

In animal models, fluid resuscitation is an essential component of post-burn therapy. If left untreated, severe burns can cause severe fluid loss and circulatory instability, which can culminate in burn shock (66). To maintain organ perfusion, restore circulation volume, and avoid hypovolemic shock, isotonic crystalloids like Ringer's lactate or regular saline are frequently used. To ensure proper resuscitation, the amount of fluid given should be calculated depending on the animal's size and the severity of the burn, and vital signs should be continuously monitored.(67)

2. Analgesia and Pain Management

In animal burn models, pain management is essential to reducing stress and enhancing recovery. Burn injuries are extremely painful, and untreated pain can affect wound healing, change physiological reactions, and jeopardise experimental results. Local anaesthetics, non-steroidal anti-inflammatory medications (NSAIDs), and opioids like morphine are common analgesics. To guarantee adequate analgesia without causing toxicity or sedation-related problems, dosages should be carefully adjusted and tracked using behavioural and physiological pain markers.(68)

3. Nutritional Support

Burn injuries significantly raise metabolic needs, leading to nutritional depletion, protein catabolism, and hypermetabolism. Thus, nutritional supplementation is a crucial part of animal post-burn therapy.(69) Parenteral nutrition can be utilised when enteral intake is not practical, however enteral feeding is recommended to preserve gastrointestinal function. Sufficient nourishment promotes wound healing, tissue repair, and the maintenance of body weight and general physiological stability.(70)

4. Wound Care

To avoid infection and encourage healing, proper wound care is essential. Antiseptic solutions like povidone-iodine or chlorhexidine should be used to carefully clean burn wounds. (71) Sterile and non-adherent dressings are necessary to shield the wound from contamination and mechanical damage. To evaluate the healing process and identify early indicators of infection, frequent dressing changes and wound examinations are required.(72)

5. Topical and Antimicrobial Therapy

When it comes to preventing infection and hastening the healing of burn wounds, topical therapies are crucial. A popular topical antibiotic that aids in lowering bacterial colonisation is silver sulfadiazine. (73) To improve epithelialisation, lower inflammation, and encourage tissue regeneration, experimental topical formulations—such as growth hormones, herbal remedies, or sophisticated polymers—are frequently tested in animal models.(74)

6. Experimental Therapeutic Interventions

Animal burn models provide a platform to evaluate novel therapeutic approaches. Stem cell therapies, such as mesenchymal stem cells, have been shown to accelerate wound healing by promoting collagen deposition, angiogenesis, and epithelial regeneration.(75) Growth factor therapies and advanced biomaterial dressings are also tested for their ability to improve tissue repair, modulate inflammation, and optimize the healing environment.(76)

7. Monitoring and Assessment

Vital signs, wound development, and behavioural markers must be continuously monitored to guarantee animal welfare and the reliability of study findings. Heart rate, respiration rate, body temperature, weight fluctuations, and wound measurements are examples of parameters that offer vital information on the physiological reaction to burns and the effectiveness of treatments.

8. Ethical and Regulatory Compliance

Institutional and national ethical rules for the use of animals in research must be followed by all post-burn therapies in animal models. Maintaining repeatability, ensuring humane treatment, and upholding scientific integrity all depend on thorough documentation of procedures, treatments, and results. Reliability and ethical responsibility are guaranteed by ethical compliance (77)

Standard Burn Care Considerations: The following metrics are carefully monitored as part of standard care for severe burns:

Haemodynamic resuscitation; co-morbidity management; prompt burn debridement and excision; wound closure; wound infection management; pain management; nutritional assistance; and strategies to prevent excessive scar formation (78)

• Rehabilitation, which includes passive range of motion in cases when joints are affected by burns. Stratification by centre may be necessary for randomisation in multicentre burn trials since big burn centres typically have established, unique standard treatment regimens. Every attempt should be made to obtain consensus among site investigators and record real care provided in the CRFs because standard care practices have significant impacts on clinical outcome.

• The frequency of full wound closures the most objective and therapeutically significant wound healing endpoint is full closure of a chronic, nonhealing wound. Complete wound closure is characterised by skin reepithelialization that is verified at two consecutive study visits spaced two weeks apart and does not require drainage or dressing.

The incidence of complete wound closure in the treatment group and the control groups within a predetermined time is typically measured in trials to provide an indication of complete wound closure (landmark analysis). In the most basic scenario, a treatment effect would be proven if a statistically and clinically significant higher percentage of participants in the treatment group compared to the control arm had full wound closure. The predicted response to conventional care in the control arm, the estimated time course for the treatment effect, and the natural history of the disease process should all be taken into consideration when scheduling the endpoint measures. Trial participants should stay in the study for a follow-up assessment at least three months after their wounds have completely healed. This follow-up time is intended to help differentiate between true wound healing and temporary wound coverage, ascertain whether the product influences the strength of wound closure in comparison to conventional treatment, and keep an eye out for any negative effects on surrounding tissue (such as skin, bones, and supporting structures).

If prospectively defined, measurement of partial wound healing in early phase clinical trials may reveal pertinent biological activity and aid in the design of subsequent trials. However, since the therapeutic effect of incremental wound size changes has not been proven, partial healing would not be enough as a primary goal in phase 3 research. A. Nonetheless, a quantifiable study objective of clinical benefit may be partial healing that makes surgical wound closure easier.

• Accelerated wound closure: Using a time-to-event analysis, an indicator of accelerated wound closure should show a clinically significant decrease in the time to healing (the event being complete closure). To identify a significant difference in time to closure across treatment groups, assessments should be conducted often enough. The study should be planned to identify both effects if claims are made for both quicker healing and a higher incidence of wound closure. (79)

The expected clinical benefit should be considered when evaluating clinical endpoints for a product that speeds up donor site closure because partial thickness donor sites typically heal in two to three weeks with standard care regimens. For instance, if a product could be used safely in patients with severe burns who needed to repeatedly harvest donor sites, it may have a clinical advantage if it could speed up donor site healing by just one or two days. Graft take should not be exacerbated by a treatment that speeds up donor site healing; hence it is crucial to evaluate the engraftment of tissue obtained by re-harvesting as a safety measure in studies were Facilitating the closure of surgical wounds

Studies should be devised to determine the incidence of complete wound closure after the necessary surgical procedure if the claim is that partial healing facilitates surgical wound closure. To make sure the surgical wound closure has no negative effects, its quality and longevity should be evaluated throughout time.

- Better Handling of Wounds

We acknowledge that, in comparison to standard care, items designed for wound management may offer significant patient benefits without increasing the frequency or timing of wound closure. But it's crucial to show that these products don't seriously hinder healing. donor site wounds are selected as the major target for efficacy determinations.(80)

- Wound infection treatment

Healing is hampered by infection at the location of the wound. Therefore, healing, infection prevention, or infection cure can be the main effectiveness outcomes for topical antimicrobial wound-treatment treatments. These antimicrobial products ought to have a recognised and suitable range of antibacterial action.(81)

- Debridement

For most burns, debridement of necrotic tissue is typically regarded as part of conventional therapy. Examples of clinically relevant endpoints include better wound healing (increased incidence or acceleration of complete closure), less pain during the debridement process, or less blood loss during or immediately after debridement, though there is disagreement over the best trial design to evaluate the effectiveness of debriding products.

The study should assess if the debriding product hinders healing in comparison to standard of care when wound closure is not the selected primary efficacy goal.(82)

- Pain management for wounds

Assessment tools that are prospectively defined and suitable for measuring the kind of pain for which an indication will be sought should be included with wound pain amelioration endpoints. An evaluation of the product's impact on the healing process itself needs to be a safety endpoint in these investigations.(83)

- Short-Term Dressings

To offer supportive care until definitive closure can be achieved, temporary dressings—including interactive temporary dressings—are used. Like human skin, temporary bandages are supposed to act as a barrier. Retardation of fluid loss or decreased infection rates are examples of clinically significant barrier functions that should be reflected in trial goals other than healing. Healing should be considered a safety endpoint if it is not the main effectiveness target.(84)

FUTURE PROSPECTS

Although the maximal lifespan of tissues in these models is two weeks,(85) ex vivo and in vitro models are often helpful substitutes to overcome this shortcoming. Studies of burn wound dynamics in vitro are

likely to advance with future developments and better procedures for the long-term maintenance of tissue cultures.(86,87)

More advanced models will be needed in the future to replicate the composition and capabilities of human organs. Additionally, studies involving human volunteers and sophisticated computer modelling methods—often referred to as in silico models—may come next. However, the conclusions pertaining to the evaluation and management of burn injuries in humans may be obscured by the variety of animal models and the inadequate translation of findings into the human system. Second, several isolated reports with observations that cannot be compared have been produced because to variations in the technical equipment and (88,89)experimental burn protocols used.(90)

CONCLUSION

Our knowledge of burn injuries, analgesia, and post-burn treatment has greatly improved thanks to animal models. However, maintaining experimental reliability, translational application to human treatment, and ethical consistency continue to present difficulties. To promote recovery and guarantee humane treatment, optimal post-burn management in animal research necessitates a comprehensive strategy that incorporates efficient analgesia, suitable fluid therapy, nutritional support, and careful wound care. Upholding the 4Rs—Reduction, Refinement, Replacement, and Responsibility—is essential to preserving both scientific validity and ethical integrity. In the future, developments in computational modelling, Long-term in vitro systems and tissue engineering show potential for decreasing animal use while increasing clinical relevance. To develop standardised, morally sound, and translationally significant burn models for upcoming biomedical innovation, veterinary scientists, doctors, and regulatory bodies must work together more closely.

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