Original Article

Total intravenous anaesthesia with tumescent infiltration anaesthesia without definitive airway for early excision and skin grafting in a major burn - A prospective observational study

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ABSTRACT

Background and Aims: Patients with major burns posted for early tangential excision and skin grafting pose peculiar challenges for anaesthesiologists. The purpose of the study was to assess safety and efficacy of total intravenous anaesthesia (TIVA) with tumescent infiltration anaesthesia (TIA) for these burn procedures. **Methods:** This observational single-arm study was conducted on 48 cases of a tertiary centre burn unit, requiring early tangential excision and skin grafting between third and fifth days of burn injury. TIVA was administered using a combination of intravenous (iv) infusion of injection dexmedetomidine and iv boluses of fentanyl, ketamine, propofol, midazolam and paracetamol. TIA was administered in burn wounds after aseptic preparation. Spontaneous breathing was maintained with oxygen supplementation. Haemodynamic and respiratory monitoring was done intraoperatively every 15 minutes and for 6 hours postoperatively. Modified Aldrete's score was calculated at 10 minutes after completion of surgery. Statistical analysis was done using statistical package for the social science software (version 16). Descriptive statistics were used for quantitative variables. **Results:** Baseline mean HR was 106.95 ± 11.17 bpm (beats per minute). HR settled at 73.17 ± 6.97 bpm during the intraoperative period. The baseline mean arterial pressure (MAP) of 82.42 ± 10.04 mmHg was maintained at 81 ± 7.32 mmHg during the intraoperative period. In all, 95.8% achieved early recovery with mean modified Aldrete's score of ≥9 at 10 minutes post-surgery. There was no episode of apnoea or desaturation. **Conclusion:** TIVA in combination with TIA minimally interferes with homeostasis and promotes early recovery in patients undergoing early excision and grafting in major burns.

Key words: Burn, total intravenous anaesthesia, tumescent infiltration anaesthesia

INTRODUCTION

A burn is a complex trauma and one of the leading causes of morbidity and mortality. A major burn is defined as a burn covering 25% or more of the total body surface area.[1] Loss of skin covers predisposes patients to infectious complications. The presence of denatured proteins and thermocoagulated tissue result in bacteraemia. The primary management goal is to stabilise the patient haemodynamically and offer biological cover on burn wounds.

Early tangential excision and grafting, within the first 3-5 days of injury is the recommended surgical approach.[2] This not only reduces the risk of wound infection and sepsis but the mortality rate and hospital stay are also decreased.[3] The risk of this approach is the physiological insult of surgery and anaesthesia to a patient who may be undergoing major fluid shifts

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rapidly from their initial injuries.[4] Other anaesthesia concerns for the procedure include difficulties in intravenous access and monitoring. Haemodynamic fluctuations and blood loss can affect organ functions. Sepsis and temperature homeostasis disruption can affect coagulation and metabolism adversely. Airway management can pose a serious challenge, especially if the patient suffers inhalation burns.

The present study aimed to assess the safety and efficacy of the technique of total intravenous anaesthesia (TIVA) in combination with tumescent infiltration anaesthesia (TIA) for early excision and skin grafting in a major burn. The primary objective of the study was to monitor haemodynamic changes in patients undergoing early excision. Secondary objectives were to assess recovery, calculate total doses of drugs required, and monitor complications if any.

METHODS

This prospective, observational, single-arm study was conducted over a period of 6 months. It included 48 cases of major burns admitted in the burn unit of a tertiary care centre. The patients were posted for early tangential excision and skin grafting in the first week of burn injury. Patients who refused to participate in the study, those with abnormal coagulation profiles, inhalation burns, and hypersensitivity to anaesthetic drugs were excluded from the study. Patients who required endotracheal intubation for resuscitation, pregnant or lactating women, and age <18 or >60 years were also excluded from the study.

After approval from the institutional ethics committee, written informed consent was obtained from the patients. They were posted for early tangential excision and skin grafting of 10%-12% of the total burn area, which was about 40%. It was a mix of partial to full-thickness burn. Burn unit personnel carried out adequate fluid resuscitation in the first 48-72 hours of burn injury using Parkland formula. Internal jugular vein cannulation was done for all the patients as per the standard of care. Laboratory tests like complete blood count, serum electrolytes, serum creatinine, arterial blood gas, and serum lactate were obtained on the morning of the surgery.

The procedure was carried out anytime between third and fifth days of the burn. Patients were wheeled inside the operation theatre and standard routine monitors were attached depending on the available sites. The emergency airway cart was kept ready before the induction of the anaesthesia for emergency airway resuscitation. Baseline readings of heart rate (HR), systolic, diastolic, mean arterial blood pressure (MAP), respiratory rate (RR), end-tidal carbon dioxide ($ETCO_2$) by nasal cannula and peripheral blood saturation (SpO_2) were noted. Oxygen was administered via nasal prongs @ 2-4 l/min or Hudson mask @ 5 l/min as deemed appropriate.

Injection (inj) ondansetron 0.1 mg/kg was administered intravenously (iv) for antiemetic prophylaxis. A background iv infusion of inj dexmedetomidine was started at the rate of 0.5 μg/kg/h for sedoanalgesia. Inj paracetamol 1 g iv, and inj fentanyl 2 μg/kg iv were administered for analgesia over 10 minutes. Inj midazolam 0.02 mg/kg was administered iv for anxiety and amnesia. Induction of anaesthesia was done with inj ketamine 1 mg/kg and inj propofol 1 mg/kg. An additional iv bolus of inj fentanyl 0.5 μg/kg was given before the removal of burn dressings and surgical cleaning of the wounds.

TIA was prepared as: 500 ml normal saline + 30 ml 2% lignocaine + 1 ml adrenaline (1:1000) + 1500 U hyaluronidase. A maximum of 100 ml of TIA was injected by the surgeon at the donor and recipient graft site with 24 gauge hypodermic needles. After 10 minutes of infiltration, debridement of the burn wound and harvesting of the graft was carried out. 5-10 mg boluses of ketamine and propofol were used alternately for the maintenance of anaesthesia at regular intervals of about 5 minutes. The maintenance dose was calculated as a one-tenth dose of an intravenous induction dose of ketamine and propofol. The aliquots were also injected in response to HR, MAP, RR, body movement to a painful stimulus, lacrimation or phonation. If blood pressure was on the lower side, the clinician had the choice of using more boluses of ketamine and if blood pressure was on the higher side, the clinician had the choice of using more boluses of propofol.

Patients were administered iv antibiotics, as the standard of care, 10 minutes before the debridement. Monitoring of haemodynamics was continued and readings were noted at every 15-minute interval during the intraoperative period for statistical purposes.

Warm ringer lactate solution was infused for the fluid replacement. All the patients were transfused one unit of packed cell volume after the excision. The

input-output chart was maintained. Recovery from anaesthesia was monitored at 10 minutes post-surgery using a modified Aldrete's score. Once the score was ≥9, patients were shifted to the ward from the recovery area. Postoperative emergence and nausea-vomiting were monitored. Total doses of drugs required during surgery were calculated. In the postoperative period, monitoring was continued for 6 hours.

Statistical analysis was done with the help of SPSS (Statistical Package for the Social Science; SPSS Inc. Chicago, IL, USA) version 16 software. All variables were quantitative in nature. Frequency, mean, standard deviation (SD) at 95% confidence interval were calculated. *P* value <0.05 was considered statistically significant. Sample size of 48 was calculated as per the formula $n = Z^2 (1\text{-}x/2)\ P\ (1\text{-}P)/d^2$, where P = expected Proportion, taking 0.18 as highest, d = absolute Precision, taking 5%, 1-x/2 = desired confidence level, taking 95% for validity.

RESULTS

The baseline mean HR was 106.95 ± 11.17 bpm. HR settled at 73.17 ± 6.97 bpm during the intraoperative period. Change in HR was statistically significant ($P < 0.05$). In the postoperative period, it was maintained at 77.33 ± 4.93 bpm [Figure 1]. Baseline MAP was 82.42 ± 10 mmHg. MAP was maintained at 81 ± 7.32 mmHg during intraoperative and 86 ± 5.66 mmHg in the postoperative period with insignificant statistical changes ($P > 0.05$) [Figure 2]. Baseline median RR was 20 breaths/minute with interquartile range 16-22. It was maintained at 17 breaths/minute with interquartile range 16-20 in the intraoperative period and 18-22 in the postoperative period [Figure 3]. There was no episode of apnoea. The baseline mean oxygen saturation was 99.58%. All the cases maintained oxygen saturation above 98% during the intraoperative and postoperative periods. $ETCO_2$ was maintained at 34.52 ± 4.2 mmHg during the intraoperative period.

At 10 minutes post-surgery, the mean modified Aldrete's score was 9 in 46 cases suggesting prompt recovery from anaesthesia, while two cases were observed for an additional 30 minutes before a score of 9 could be achieved [Table 1]. The total mean dose required was 50.39 µg for inj dexmedetomidine, 126.25 µg for inj fentanyl, 167.70 mg for inj propofol, and 166.87 mg for inj ketamine [Table 2]. These doses were required to maintain anaesthesia for the mean surgical duration of 101.25 ± 37.56 minutes [Table 3] in patients with a mean body weight of 55.43 kg. No patients experienced any emergence phenomenon or postoperative nausea-vomiting (PONV).

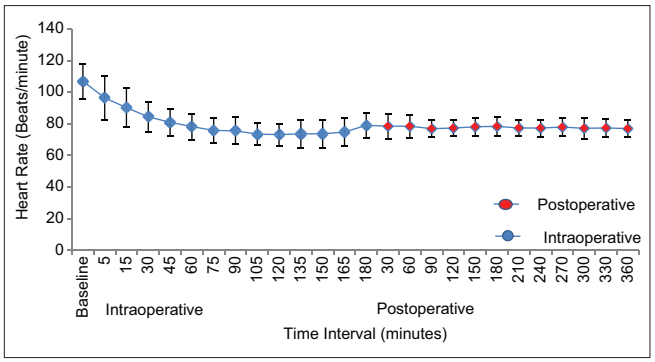

Figure 1: Monitoring of mean Heart Rate during intraoperative and postoperative period. Error bars represent standard deviation

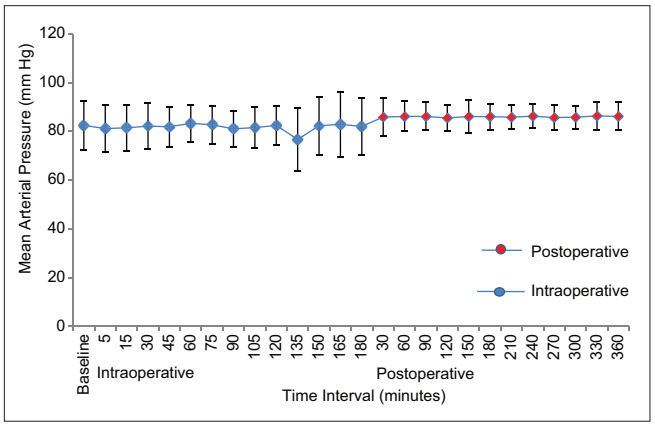

Figure 2: Monitoring of Mean Arterial Pressure during intraoperative and postoperative period with representation of standard errors

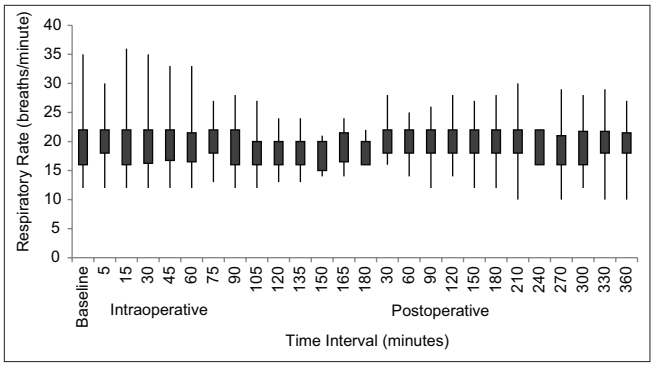

Figure 3: Monitoring of Respiratory Rate (showing interquartile range) during intraoperative and postoperative period

Table 1: Modified Aldrete's score at 10 min post-surgery

No. of cases (*n*)	Modified Aldrete score
23	10
23	9
2	8

Table 2: TIVA drugs

Descriptive statistics of drugs

Drugs	Number of cases (*n*)	Minimum	Maximum	Mean	Std. deviation
Dexmedetomidine (μg)	48	12	160	50.396	30.52571
Fentanyl (μg)	48	50	200	126.25	35.13685
Ketamine (mg)	48	70	210	166.87	34.24577
Propofol (mg)	48	70	280	167.7	52.5206

Table 3: Mean duration of surgery

No of cases (*n*)	Minimum duration of surgery (min)	Maximum duration of surgery (min)	Mean duration	Std. deviation
48	30	180	101.25	37.5609

DISCUSSION

Burn injury involves two distinct phases-the initial phase of hypovolaemia and burn shock followed by a prolonged phase of hypermetabolism after 48 hours.[5] It also initiates a systemic inflammatory response leading to massive fluid shifts. A major burn causes massive tissue destruction and loss of protective cover, exposing patients to a risk of infection and sepsis.[5] Early excision of the necrotic tissue and grafting of the total burn area under anaesthesia, is the recommended surgical approach to improve outcomes in a major burn.[2] However, early excision is offered only in centres with a speciality burn unit. Cover for the entire burn surface area is carried out if facilities for aggressive monitoring and post-surgical care can be offered. In resource and personnel strained settings, the surgical exercise of early excision of the entire burn area may expose patients to a severe, multisystem pathophysiological turmoil.

The present study was conducted in patients with major burns posted for early excision and grafting of only 10%-12% of the total burn area, under anaesthesia in the first-week post-injury. The subsequent two sittings to cover the entire burn area were carried out on alternate days using similar anaesthetic technique but those were not parts of the present study.

The use of the staged surgical approach limited the fluid loss, blood loss and subsequent haemodynamic fluctuations and coagulopathy in major burn patients. It also shortened the surgical duration, thereby avoided the need for airway intervention using endotracheal intubation or supraglottic airway. The methodology included administration of TIVA along with TIA without definitive airway. The conventional technique of general anaesthesia with endotracheal intubation and positive pressure ventilation may suppress the host immune responses by bypassing natural upper airway defences.[6] The choice of anaesthetic technique appears to affect the release of cytokines, which is of great significance in patients with a major burn. The release of pro-inflammatory cytokines is seen more with inhalational agents than iv agents and is related to an increase in postoperative complications and morbidity.[7] Positive pressure ventilation promotes the translocation of tracheal bacteria into the bloodstream.[6] This can lead to infectious complications in patients with major burn injury.

Burn injury results in pain, anxiety, hypermetabolic state, and severe systemic inflammatory response, which in turn causes tachycardia despite optimum fluid resuscitation. Administration of atropine or glycopyrrolate can worsen this, so it was avoided in these patients. Also, salivary secretion decreases drastically during deep sedation and no movement state.

Early excision and grafting are extremely painful procedures and need a multimodal analgesic approach. The combination of inj propofol, ketamine, midazolam, dexmedetomidine, fentanyl, and paracetamol was used in our study cases to provide TIVA. The purpose of using polypharmacy in our case was to obtain synergistic effects of the drugs and reduce the individual drug doses to reduce the side effects.

Propofol, a non-barbiturate anaesthetic, has the advantage of rapid elimination from the blood leading to prompt recovery of cognitive and psychomotor functions with a very low incidence of PONV.[8,9] However, propofol causes dose-dependent respiratory depression and fall in blood pressure.[10] Lack of analgesic properties of propofol necessitates the need for supplementary analgesic agents.[11] Ketamine, a phencyclidine derivative, produces dissociative

anaesthesia by N-methyl-D-aspartate (NMDA) receptor antagonism.[12] Ketamine has been used for many years for a change of burn dressings but not many studies have been cited for early excision. In our study, drug-related haemodynamic fluctuations were avoided because of a combination of propofol and ketamine as the cardiovascular effects are opposing in action. The addition of ketamine to propofol preserved MAP without prolonging recovery or increasing the incidence of adverse events. Also, ketamine-induced tachycardia and hypertension were not evident in patients treated with the propofol-ketamine combination. Badrinath *et al.* found similar results in their study on the use of a ketamine-propofol combination during monitored anaesthesia care.[13] In various studies, it has been found that when propofol is used as a monotherapy, it can cause increased drug requirements and more incidences of desaturation.[14-16] In our study, the adjunctive use of ketamine along with propofol provided significant analgesia and minimised the need for supplemental opioids. The use of intermittent boluses of propofol and ketamine in this study gave the clinician the flexibility of drug choice, depending on the surgical stimulus and haemodynamic parameters. The study published by Arora S. on combining ketamine and propofol ("ketofol") in procedural sedation and analgesia concluded that the fixed infusion rate may cause rising, declining in stable concentrations, leading to a risk of under or overdosage.[14]

In our study, fentanyl, a short-acting opioid with potent analgesic effects further reduced the requirement of propofol doses for maintenance of anaesthesia and obtundation of haemodynamic responses to noxious stimuli. Darlong V *et al.* showed that administration of fentanyl 5 minutes prior to propofol causes marked reduction in propofol dose requirement with significantly reduced incidence of hypotension during induction.[17] Midazolam provided amnesia along with anxiolysis, sedation and sympatholytic effects.

The alpha-2 agonist dexmedetomidine has sedative, anxiolytic, hypnotic, analgesic, and sympatholytic effects with minimal respiratory depression. These effects make dexmedetomidine a versatile adjuvant anaesthetic agent. It is also helpful in decreasing ketamine-induced salivation due to sympatholytic effect. It significantly reduces emergence agitation in the postoperative period and promotes smooth recovery.[18] Use of dexmedetomidine as premedication to decrease postoperative emergence agitation in paediatric age group have been studied by Dave NM.[19] Use of dexmedetomidine infusion @ 0.5 μg/kg/h provided propofol and opioid-sparing effect in the present study. Similar results were concluded in the studies done by Gupta N *et al*. and Kaur S *et al*.[20,21] Dexmedetomidine decreases the requirement of ketamine and propofol during burn debridement and dressing.[22] It also delays the postoperative analgesic use, without delay in recovery.[23,24] In our study, we found similar results as dexmedetomidine reduced the ketamine, propofol, and opioid dose requirements. It provided early and smooth recovery.

In our study, 1 g iv infusion of inj paracetamol provided pre-emptive analgesia for nociceptive surgical pain. The co-administration of opioids, benzodiazepines, ketamine, alpha-2 adrenoceptor agonists resulted in a marked reduction in the required brain propofol concentration. Nimmo AF *et al.* conducted a study on guidelines for the safe practice of TIVA and concluded that TIVA uses several drugs in tailoring doses to provide anaesthesia, preserve haemodynamic parameters, improve recovery and minimise the side effects.[25]

The required propofol concentration also depends on the degree of the surgical stimulus. If surgical stimulus can be reduced by TIA, TIVA drug requirements can be reduced significantly. TIA is a widely used type of regional anaesthesia for cutaneous surgery. This technique makes it possible to administer high doses of lidocaine and adrenaline within the safety limits, leading to a reduction in pain and bleeding as concluded in a study done by Gümüş N on tumescent infiltration for burn surgery.[26] A total of 80-100 ml TIA was used at donor and recipient sites to provide surgical site analgesia in all our study patients. TIA also helped in easy debridement and smooth graft removal.

Thus, in our study, a combination of TIVA and TIA allowed tachycardia to settle down to a statistically and clinically significant value while allowing MAP to maintain close to the baseline value. None of the cases had an episode of apnoea or upper airway obstruction as observed by clinical and $ETCO_2$ monitoring. This was most likely, due to the reduced requirement of propofol when used in combination with other iv drugs. The total dose required for propofol and ketamine was 3 mg/kg each for a surgical procedure of 101 minutes duration. This is much less than the standard induction and maintenance doses required

when used individually and without TIA. Close monitoring of respiration is very important for these patients under TIVA with spontaneous respiration as access to the airway may be difficult for patients with head, face, neck burns. SpO_2 was maintained >98% in all patients throughout the perioperative period. No patient required mask ventilation or ventilatory support in the intraoperative or the recovery phase. Forty-six out of forty-eight cases achieved modified Aldrete's score of 9 or above at 10 minutes, suggesting faster redistribution and elimination of TIVA drugs.

A patient undergoing surgical excision of 12% major burn wound is bound to have blood loss around 400-500 ml. One unit of packed cell volume was transfused intraoperatively in all our study patients to prevent sudden haemodynamic collapse. Further transfusion was based on the postoperative value of haemoglobin and haematocrit.

A study published by Leopoldo Cancio *et al*. from the US Army Institute concluded that TIVA is a viable approach to general anaesthesia in critically ill burn patients.[27] The choice of drugs with favourable pharmacokinetic profiles and synergistic effects results in stable haemodynamic parameters and prompt recovery from anaesthesia.

In our study, TIVA with TIA without endotracheal intubation was offered for early excision of only about 12% of the burn area. If early excision of the total burn area of 40% was planned in a single sitting, then the physiological insult created by massive fluid and haemodynamic fluctuations would have been difficult to manage without a definitive airway.

Our study has some limitations. It was a single-arm study, without having a comparison with the use of general anaesthesia and endotracheal intubation. Depth of anaesthesia monitoring using BIS would have been desirable but it was not available at our centre when this study was conducted.

The early excision was restricted to 10%-12% of the total burn surface area for the major burn patients in the study. The subsequent sittings were carried out on alternate days similarly under TIVA and TIA to cover the remaining burn area, were not parts of the present study. So a study that would include all the sittings of early excision would be ideal to generate good quality evidence regarding the benefits of TIVA and TIA in major burn patients.

CONCLUSION

TIVA with inj propofol, ketamine, fentanyl, midazolam, dexmedetomidine infusion, and paracetamol in titrated doses, offers haemodynamic stability, with the maintenance of spontaneous respiration and prompt postoperative recovery. TIA used in combination with TIVA provides surgical site analgesia and reduces anaesthetic drug requirement, thereby facilitating recovery and greatly decreasing the potential for side effects. Thus, TIVA with TIA is safe and effective for early excision and grafting of about 10%-12% of burn area in patients with a major burn.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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