EVALUATION OF KETOFOL
(KETAMINE PROPOFOL COMBINATION)
AS TOTAL INTRAVENOUS ANAESTHESIA FOR
BURN DRESSING IN ADULT PATIENT

Sanad MA*, Islam MS†, Ahmed M‡, Maruf AA§

Abstract
Introduction: Pain management during burn dressing changes is a critical part of treatment in acute burn injuries. Objective: This study was carried out with the objective of finding out an ideal analgesic, sedative and/or amnestic combination that could serve the purposes as well as minimize the unwanted effects of traditionally used ketamine.
Methods: A total of 28 patients with burns of 15-50% of total body surface area were included in this study. Each patient received Propofol and Ketamine 1mg/kg body weight as induction dose and Ketamine 1mg/kg/hour and Propofol 3mg/kg/hour as maintenance dose till procedure ends. All perioperative vital parameters, events and complications were recorded and subsequently analyzed.
Results: Mean age of the patients was 31.46 years while mean duration of the surgery was 341.42 minutes. Mean induction time was 24.65.13 seconds. Heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were increased during the procedure, but were within acceptable limits. Five patients had raised HR and two had raised SBP 20% above their baseline level for transient period which came to normal level without any active management. All patients maintained adequate oxygenation throughout the procedure. There was no incidence of apnoea or hyperventilation or vomiting. One patient had mild form of emergence delirium. Mean recovery time from induction to 52.14 minutes while time gap for further analgesic requirement after surgery was 126.114 minutes. Conclusions: Ketamine and Propofol combination (Ketofol) for procedural sedation and analgesia is effective and appears to be safe and is more psychologically acceptable to nurses and patients in painful burn dressing. Few subtle adverse events occurred and were self limited or responded to immediate interventions.

Keywords: Ketofol, sedation, analgesia, burn dressing

Introduction
Burn pain induces one of the most severe form of acute pain. Burn dressing changes require profound analgesia for a short duration and opioid administration is the mainstay of procedure related pain management in patients with burn. General anaesthesia for repeated dressing changes is not suitable due to the high risk of uncomplicated postoperative complications. The combination of potent analgesic ketamine and profound sedative propofol (Ketofol) for minor but extremely painful procedure like burn dressing theoretically may be beneficial with the rationale of being that using lower doses of each agent may result in reduction of the undesirable adverse effects of both agents while maintaining optimal conditions for performing procedure. This study was carried out to find out the efficacy and safety of combination of ketamine and propofol as analgesic in patients undergoing burn dressing.

Materials and Methods
This prospective study was carried out in Bangladesh Naval Ship Patenga Hospital and Combined Military Hospital (CMS), Dhaka during the period of Nov 2007 to Jul 2011 on 28 burn patients who required elective dressing change in operation theatre. No patient was considered twice in the study.

Inclusion criteria
• Age within the range of 18 to 60 years
• ASA physical status of patient was grade I and II
• Percentage of burn within the range of 15 to 50%

Exclusion criteria
• Patients with hemodynamic instability, electrolytic imbalance, impaired hepatic & renal function and psychologically unstable
• Patients having signs of raised intracranial pressure, history of epilepsy, ischemic heart disease
• History of allergy to any of the drugs used
• Unwilling to undergo study

Following local ethics committee approval, informed written consent was obtained from each patient. Premedication checkup carried out thoroughly 24 hours before procedure and all were premedicated with Tablet Bromazepam 0.5 mg at bed time on day before operation. Study subjects were in routine preoperative fasting of 6 hours and during the procedure all were infused with Hartman’s solution at the rate of 25 ml/hour. On operation date vital parameters (heart rate, systolic and diastolic blood pressure, respiratory rate, oxygen saturation and electrocardiogram) were monitored and recorded in the following sequence:
• 0 - baseline (just before induction)
• 1 - 0 minutes after induction
• 2 - 15 minutes after induction
• 3 - 30 minutes after induction
• 4 - 45 minutes after induction
• 5 - 60 minutes after induction

All patients were induced by Injection Ketamine 1mg/kg and Injection Propofol 3mg/kg and anesthesia was maintained by drip of Ketamine 1mg/hour and Propofol 4mg/kg/hour mixed with normal saline, using infusion pump. Intermittent stressors were manifested by hand-accleration of infusion, lift swimming, limb movement were noted. The induction time (interval between induction dose and abolishment of cycloph reflex) was also recorded in each patient. Recovery (Score >7) from anesthesia was assessed by Post Anaesthesia Alertness-Recovery score in the recovery room or postoperative ward. Vital Analog Scale (VAS) score (0-10) were assessed after complete recovery. Analgesics (Injection pethidine 0.5 mg/kg) were administered when VAS score was >5 and the time gap from induction to analgesic requirement was noted for each patient. Throughout this period each patient was observed for any other complications like apnoea or hyperventilation (respiratory rate < 20/min) desaturation (SpO2 < 90%), shivering, vomiting, emergence delirium (manifested by excitement, confusion, fear, euphoria etc.). Complications were managed accordingly. Postoperative questionnaire were carried out on the next day of procedure. All data were collected in a predefined data sheet and subsequently analyzed using statistical package of social science (SPSS). Results were expressed as mean±SD and categorical data were expressed in percentage (%) and frequency (f).

Results
Mean age of the patient was 31.46 years. Mean percentage of surface area burnt was 24.41±73% (Table-I). Hemodynamic parameters (heart rate, SBP, DBP) all increased during the procedure but were not out of normal range. Electrocardiogram showed sinus rhythm in all patients. Respiratory parameters (respiration rate & oxygen saturation) were very stable during the procedure (Table-II). One patient showed signs of inadquate anaesthesia in the form of lacrimation and sweating (Table III). Five patients had clinically insignificant tachycardia and two had raised systolic BP (>20% of baseline level) which came to normal level within five minutes in the absence of any active management. No patient had vomiting or developed hyperventilation (respiration rate > 28/min) or apnoea during or after the procedure. One patient had minor delirium without agitation which continued for about 10 min after the procedure (Table IV). Mean time of dressing required with bolus Ketofol was 24.5±13 sec and recovery time was 52.18±17 min. Mean time required for further analgesic demand by each patient was 126±11.46 min (Table V).
EVALUATION OF KETOFOL (KETAMINE PROPOFOL COMBINATION) AS TOTAL INTRAVENOUS ANAESTHETIC FOR BURN DRESSING IN ADULT PATIENT

Sanad MA', Islam MS', Ahmed M', Maruf AA*

Abstract
Introduction: Pain management during burn dressing changes is a critical part of treatment in acute burn injuries. Objectives: This study was carried out with the objective of finding out an ideal analgesic, sedative and/or hypnotic combination that would serve the purpose as well as minimize the unwanted effects of traditionally used ketamine.

Aim: A total of 28 patients with burns of 15-50% of total body surface area were included in this study. Each patient received Propofol and Ketamine 1mg/kg body weight as induction dose and Ketamine 1mg/kg/hour and Propofol 4mg/kg/hour as maintenance dose till procedure ends. All perioperative vital parameters, events and complications were recorded and subsequently analyzed.

Results: Mean age of the patients was 21±4.49 years while mean duration of the surgery was 341.92 minutes. Mean induction time was 246.13 seconds. Heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were increased during the procedure, but were within acceptable limits. Five patients had raised HR and two had raised SBP 20% above their baseline level for transthoracic pacemaker came to normal level without any active management. All patients maintained adequate oxygenation throughout the procedure. There was no incidence of apnea or hypventilation or vomiting. One patient had mild form of emegence delirium. Mean recovery time from sedation was 52.44 minutes while time gap for further analgesic requirement after surgery was 126±14.6 minutes.

Conclusions: Ketamine and Propofol combination (Ketofol) for procedural sedation and analgesia is effective and appears to be safe for clinically painful procedures like burn dressing. Few subtle adverse events occurred and were self limited or responded to rapid intravenous fluid challenge.

Keywords: Ketofol, sedation, analgesia, burn dressing

Introduction
Burn pain induces one of the most severe forms of acute pain. Burn dressing changes require profound analgesia for a short duration and opioid administration is the mainstay of procedure related pain management in patients with burn. General anesthesia for repeated dressing changes can have unpalatable and obvious background analgesic demand. The combination of potent analgesic ketamine and profound sedative propofol (Ketofol) for minor but extremely painful procedure like burn dressing theoretically may be beneficial with the rationale of being that lowering doses of each agent may result in reduction of the undesirable adverse effects of both agents while maintaining optimal conditions for performing procedure. This study was carried out to find out the efficacy and safety of combination of ketamine and propofol as anaesthetic in patients undergoing burn dressing.

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Unwilling to undergo study

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On operation data vital parameters (heart rate, systolic and diastolic blood pressure, respiratory rate, oxygen saturation and electrocardiogram) were monitored and recorded in the following sequence:
• HR - baseline (just before induction)
• HR - 0-5 minutes after induction
• HR - 5-10 minutes after induction
• HR - 15-30 minutes after induction
• HR - 30-45 minutes after induction
• HR - 45-60 minutes after induction

All patients were induced by Injection Ketamine 1mg/kg and Injection Propofol 1mg/kg and anaesthesia was maintained by drip of Ketamine 1mg/hr and Propofol 4mg/hr/hour mixed with normal saline, using infusion pump. Intermittent stressors manifested by acapnia, hypoxia, warming, Emb movement were noted. The induction time (interval between induction dose and abolishment of cyclical reflex) was also recorded in each patient. Recovery (Score >7) from anaesthesia was assessed by Post Anaesthesia Alertness-Respiration score [5] in the recovery room or postoperative ward. Visual Analog Scale (VAS) score (0-10) were assessed after complete recovery. Analgesics (Injection pethidime 0.5 mg/kg) were administered when VAS score was >5 and the time gap from induction to analgesic requirement was noted for each patient. Throughout this period each patient was observed for any other complications like apnoea or hypventilation (Respiration <10/min) desaturation (SpO2 < 90%), shivering, vomiting, emergence delirium (manifested by excitement, confusion, fear, euphoria etc). Complications were managed accordingly. Postoperative questionnaire were carried out on the next day of procedure. All data were collected in a preformed data sheet and subsequently analyzed using statistical package of social science (SPSS). Results were expressed as mean±SD and categorical data were expressed in percentage (%) and frequency (f).

Results
Mean age of the patient was 31±4.69 years. Mean percentage of surface area burned was 24.41±7.37% (Table-I). Haemodynamic parameters (heart rate, SBP, DBP) all increased during the procedure but within normal range. Electrocardiogram showed sinus rhythm in all patients. Respiratory parameters (respiration rate & oxygen saturation) were very stable during the procedure (Table-II). One patient showed signs of inadequate anaesthesia in the form of lacrimation and sweating (Table III). Five patient had clinically insignificant tachycardia and two had raised systol BP (>20% of baseline level) which came to normal level within few minutes under active management. One patient had vomiting and developed hypotension (respiration rate >28/min) or apnoea during or after the procedure. One patient had minor delirium without agitation which continued for about 10 min after the procedure (Table IV). Mean time required for further analgesic demand by VAS score was 58±13.3 sec and recovery time was 52±17.8 min. Mean time required for further analgesic demand by score was 126±11.46 min (Table V).

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Table I: Patient data (n=28)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Unit</th>
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<td>Min age</td>
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<tr>
<td>Mean height (kg)</td>
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<td>66 ± 2.44</td>
</tr>
<tr>
<td>Age (years)</td>
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<tr>
<td>Mean height (kg)</td>
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Table II: Progressive Vital parameters (n=28)

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<tr>
<td>Mean height (kg)</td>
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Table III: Diabetic Signs/symptoms of inadequate anaesthesia (n=28)

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<td>Fentanyl</td>
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<tr>
<td>Oral intake</td>
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<td>Hypoglycaemic</td>
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<tr>
<td>Ketamine</td>
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Table IV: Anaphylactic Complications (n=28)

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<td>Hypoglycaemia</td>
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<td>01</td>
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<tr>
<td>Intravenous</td>
<td>01</td>
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<td>Anaphylactic</td>
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Table V: Other important findings (n=28)

<table>
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<td>375 ± 57</td>
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<tr>
<td>Mean infection time</td>
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<td>55 ± 32</td>
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<td>Max urine output</td>
<td>Ml</td>
<td>375 ± 57</td>
</tr>
<tr>
<td>Mean urine output</td>
<td>Ml</td>
<td>210 ± 46</td>
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</tbody>
</table>

Discussion

In conclusion, burn patients suffer from daily background pain as well as procedural pain. General anaesthesia for burn procedures brings down background pain and analgesic requirement. The combination of Ketamine and Propofol in total intravenous anaesthesia for these dressings provides excellent intraoperative conditions, stable haemodynamics and respiratory parameters and prolonged postoperative analgesia with a low incidence of emergence delirium.

References

6. Kissin I, Bright CA, Bradley Jr EL. The effect of ketamine on opioid-induced acute tolerance: can it explain reduction of opioid consumption with ketamine-iodine analogues combinations?
combines, like Ketamine-Midazolam, Ketamine-Fentanyl, Ketamine-Dextromethorphan have been used with more or less success. Ketamine reduces propofol injection pain by attenuating the efficient pain pathway. The advantages of Ketamine in terms of better haemodynamics intraoperatively when compared with other drugs as observed in our study is supported by other studies too. Hemandez et al compared these techniques for intravenous anaesthesia (Midazolam+Ketamine, Propofol + Ketamine, Propofol + Fentanyl). They found that Propofol+Ketamine had more stable haemodynamics. Midazolam+Ketamine had higher number of hypertensive peaks. In our study we continued both Propofol and Ketamine drips and the changes of haemodynamics were clinically insignificant. The major advantage of Ketamine is that it usually preserves airway patency and respiratory function as also observed in our study there was no single case of apnoea, hyperventilation or even desaturation which is not uncommon when propofol used alone or in combination with fentanyl. The most frequently mentioned adverse effect of Ketamine is emergence reaction or hallucination and the incidence varies from 9% to 50% patients. Rosando, Mortero, et al found a significant reduction in the incidence of emergence delirium when propofol and Ketamine were used in combination to Ketamine alone, but it can totally abolish it as also found in our study (1 to 28 cases). In our study there was no single case of per or postoperative vomiting. Green et al found that emesis occurring after Ketamine administration modestly associated with increasing age and higher incidence in those patient older than five years of age (12.1%) compared with younger patients (5.3%) which can be reduced by coadministration of Ketamine. Mean Recovery time from Ketofol in our study was 52 + 8.17 mins and it significantly reduced requirements of postoperative analgesic and detected by VAS score. Mean time required for further analgesic requirement was 126-114 mins. It would be delirious if we could assess the depth of anaesthesia by Bispectral Index (BIS), the facility for which we don't have. Instead we used clinical parameters which detected one in 28 patients with inadequate anaesthesi who subsequently expressed his dissatisfaction with the anaesthetic technique. The primary limitations of our study was small sample size, the lack of double blind configuration and the large number of end points in relation to sample size. Further research with larger samples comparing Ketofol to other common procedures in operating room or for procedural sedation and analgesia outside operating room.

Conclusion
In conclusion burn patients suffer from daily background pain as well as procedural pain. General anaesthesia for burn procedures brings down background pain and analgesic requirement. The combination of Ketamine and propofol in total intravascular anaesthesia for these dressings provides excellent intravenous conditions, stable haemodynamics and respiratory parameters and prolonged postoperative analgesia with a low incidence of emergence delirium.

References
6. Kissi I, Bright CA, Bradly Jr EL. The effect of ketamine on opioid-induced acute tolerance: can it explain reduction of opioid consumption with ketamine-opioid analgesic combinations?
MALIGNANT TUMOUR
ARISING IN MATURE OVARIAN TERATOMA

Iqbaque WS', Alam M', Islam SMJ', Karim MI', Yeasmin S', Ahmad M'

Abstract
Introduction: Mature teratoma is a common ovarian tumour. They are predominantly cystic (rarely solid) composed exclusively by mature adult type tissues. Malignant transformation of the mature elements of mature teratomas is very rare, but malignant transformation may occur in any of the mature components of teratoma. Keeping in mind about this rare malignant transformation which often present as an incidental pathologic finding may allow early detection.

Objective: The objective is to observe prevalence of this rare form of tumour in Bangladesh and also to observe the pattern of malignant component of these malignant tumours.

Methods: This was a retrospective study carried out in Armed Forces Institute of Pathology (AFIP), Dhaka between the period February 2005 and January 2012. This study was based on retrieval of data of all cases with ovarian mature teratoma from a surgical pathology register of Histopathology Department of the Institute. The Histopathology report and microscopic sections were reviewed with available clinical information for the purpose of the study.

Results: A total of 205 cases of mature teratomas of ovary were diagnosed at AFIP during the study period. Among these 205 cases only two cases were identified as malignant tumour arising on the top of mature ovarian teratoma.

Conclusion: Though rare, malignant transformations of mature teratomas should be kept in mind for early detection which in turn is important for patient survival.

Keywords: Mature teratoma, malignant transformation, ovary, squamous cell carcinoma

Introduction
Mature cystic teratoma is the most common ovarian tumour. Predominantly cystic mature teratomas (MCT) are composed exclusively of mature adult type tissues. Mature teratomas consist of well differentiated derivatives of three germ layers with any type of combination of mature, adult type tissues. Ectodermal tissue is the most abundant and typically manifests in the form of squamous epithelium, brain tissue, glia, retina, choroid plexus and/or ganglia. Adipose tissue, smooth and skeletal muscle, teeth, bone and cartilage are common mesodermal components. Ectodermal tissue may form bronchial and gastrointestinal epithelium, thyroid glands and/or salivary glands. Monodermal teratomas consist of exclusively endodermal or ectodermal tissue type; teratoma ovary is the most common monodermal teratomas of the endoderm. Malignant transformation of the mature elements of mature teratomas is very rare but that rare transformation may occur from any of the mature components of the teratoma. In this study we reviewed the reported cases of ovarian mature teratoma over last 7 years in Armed Forces Institute of Pathology, Dhaka with a search for components of malignant transformation.

Methods
This was a retrospective study carried out in Armed

References

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