A Prospective Evaluation of "Ketofol" (Ketamine/Propofol Combination) for Deep Sedation and Analgesia in Minor Painful Operations.

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ABSTRACT

Background: This prospective study was conducted at Soba and Khartoum hospitals for assessment and evaluation of the effectiveness and safety of the combination of ketamine and propofol in a small doses “ketofol” in the same syringe for deep sedation/analgesia in minor elective and emergency operations. Methods: Ninety ASA class I & II patients with age ranging from 1 month up to 75 years who underwent minor operations, elective or planned emergency (non-life threatening conditions) were selected. They received ketofol in a dose ranging from 0.5 mg to 0.8 mg per kg per dose given intravenously. Incremental doses were given according to the duration of operation, using Ramsay Scale of Sedation (RSS). Success and side effects were assessed throughout the procedures. Results: Ketofol is a very effective as a sole agent for painful procedures with low incidence of side effects as emergence phenomena, hypoxia and transient apnea. Haemodynamic stability was reported. There was no nausea or vomiting was reported. Supplemental analgesia for increased pain was not required. The procedures included evacuation and curettage (D & C), abscess drainage, debridement, excisional biopsy of breast fibroadenoma, vaginal polypectomy, dressing, reduction & immobilization of fractures. Duration of operation ranged from 15 to 60 minutes. Conclusion: Ketofol is a good and safe option for deep sedation/analgesia for painful minor operations with minimal side effects.

Keywords: sedation, analgesia, ketofol, propofol, ketamine.

INTRODUCTION

Sedation/analgesia practice has made a genuine revolution during the last years (sedation during regional anesthesia, sedation and analgesia as supplementation for general anesthesia, many minor procedures and sedation in ITU).

In many developing countries, ketamine is used as a sole anaesthetic agent for many minor painful operations because of its safety, availability and potent analgesic effect. However, due to its unpleasant side effects (dissociative phenomenon) emergence delirium, it has been restricted to limited use as in conditions as veterinaries, district, special pediatric cases, shocked patients, and war areas.

Propofol, which is an intravenous anesthetic agent is at the top of the group (benzodiazepines, barbiturates, ketamine and opioids) in sedation because of its rapid induction and recovery properties. However, it has no analgesic effect.

Deep sedation/analgesia with ketofol decreases the side effect of both ketamine and propofol as they potentiate each other and thus smaller doses are used. Ketamine in small dose gives a good analgesia with minimum sedation, which is increased by adding a small dose of propofol, thus deep sedation level is obtained. Deep sedation potentiates the analgesic effect of ketamine leading to a better satisfaction of patients and treating doctors.

MATERIALS AND METHODS

Definitions:--

Minimal Sedation (Anxiolysis):
A drug-induced state during which patients respond normally to verbal commands. Although cognitive function and coordination may be impaired, ventilator and cardiovascular function are unaffected.¹

Moderate Sedation/Analgesia (conscious Sedation):
A drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patient airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.¹

Deep sedation/analgesia:
A drug-induced depression of consciousness during which patients cannot be easily aroused but
respond purposefully following repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained. [1]

**General anaesthesia:**
A drug-induced depression of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilator function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug induced depression of neuromuscular function. Cardiovascular function may be impaired.

**Analgesia:**
Analgesia is the relief of pain. Pain is normally defined as an unpleasant sensory and emotional experience associated with potential or actual tissue damage. Analgesia is normally provided using one of several types of pharmaceutical preparations. [2]

**Ketamine:**
Ketamine is frequently described as a ‘unique drug’ because it has hypnotic (sleep producing), analgesic (pain relieving) and amnesic (short term memory loss) effects - no other drug used in clinical practice combines these three important features. It was first used clinically in 1970, and because of these combined effects it was thought that it might be the perfect anaesthetic agent. This is not quite the case, but its continued use in all parts of the world demonstrates that in certain situations, when used appropriately, it is a very valuable drug. [3]

Ketamine must be considered as a drug that is vulnerable to abuse, emphasizing the need to take appropriate precautions against its unauthorized use. [4]

Intense analgesia can be achieved with sub-anesthetic doses of Ketamine, 0.2 to 0.5 mg kg⁻¹ IV. Analgesia is alleged to be greater for somatic than for visceral pain. Analgesia can be produced during labor without associated depression of the neonate. [5,6]

Neonatal neurobehavioral scores of infants born by vaginal delivery with ketamine analgesia are lower than those of infants born with epidural anesthesia, but higher than the scores in infants delivered with thiopental-nitrous oxide (7).

**Emergence Delirium:**
Emergence from ketamine anesthesia in the postoperative period may be associated with visual, auditory, proprioceptive and confusional illusions, which may progress to delirium. Cortical blindness may be transiently present. Dreams and hallucinations can occur up to 24 hours after administration of ketamine. The dreams frequently have a morbid content and are often experienced in vivid technicolor. Dreams and hallucinations usually disappear within a few hours. [5]

Benzodiazepines had been used to decrease it, but thiopenital, or inhaled anesthetics may decrease the incidence of emergence delirium attributed to ketamine. Prospective discussion with the patient of the common side effects of ketamine (dreams, floating sensations, blurred vision) is likely to reduce the incidence of emergence delirium as much as any other approaches. [5]

**Propofol:**
Propofol is a phenol derivative (isopropylphenol) that is administered intravenously. It was identified in 1980 and used in 1986. Administration of propofol, 2 to 2.5 mg kg⁻¹ IV (equivalent to thiopenital, 4 to 5 mg kg⁻¹ IV, or methohexital, 1.5 mg kg⁻¹ IV) over 15 seconds or less produces unconsciousness within about 30 seconds. Awakening is more rapid and complete than that following induction of anesthesia with thiopenital or methohexital. This more rapid return to consciousness with minimal residual central nervous system effects seems to be the most important advantage of propofol over other drugs used to produce induction of anesthesia. [8]

Propofol is extremely lipid-soluble, but almost insoluble in water. It was formulated initially in Cremophor EL. However, that is associated with histamine release and so the high incidence of anaphylactic reaction. Consequently, it reformulated in a white, aqueous emulsion containing Soya bean oil and purified egg phosphatide. Ampoules of the drug contain 200 mg of propofol in 20 ml, and 50 ml containing 1% (10 mg/ml) or 20% (20 mg/ml) solution, and 100 ml bottles containing 1% solution, for infusion. 50 ml pre-filled syringe of 1 and 2% are designed principally for use in target-controlled infusion. [8]

Anaesthesia is induced within 20-40 sec after intravenous administration in a healthy young adult. Transfer from the blood to the site of action in the brain is slower than with thiopenital, and there is a delay in the disappearance of the eyelash reflex, used as a sign of unconsciousness after administration of barbiturate anaesthetic agents. Over dosage of propofol, with exaggerated side effects, may result if this clinical sign is used; loss of verbal contact is a better end-point. Electroencephalogram (EEG) frequency decreases, and amplitude increases.

Propofol reduces the duration of seizures induced by electro conversion therapy in humans. However, there have been reports of convulsions following the use of propofol and it is recommended to be used with caution in epileptic patients. Cerebral
blood flow & intracranial pressure are reduced. Recovery of consciousness is rapid and there is a minimal *hang-over* effect even in the immediate post-anesthetic period.[8]

In healthy patients, arterial pressure decreases to a greater degree after induction with propofol than thiopental, which results predominantly from vasodilatation although there is a slight negative inotropic effect. In some patients decrease more than 40% occur. The degree of hypotension is substantially reduced by decreasing the rate of administration of the drug. The pressure response to tracheal intubation is attenuated to a greater degree by propofol than thiopental. Heart rate may increase slightly after induction with propofol even there has been occasional reports of severe bradycardia and asystole during or just after administration of propofol and it is recommended that a vagolytic agent should be given in patients with a pre-existing bradycardia or when propofol is used in conjunction with other drugs which are likely to cause bradycardia.[9]

Apnea occurs more commonly, and for a longer duration compared with thiopental. Tidal volume is lowered and respiratory rate higher than in a conscious state during propofol infusion. There is decreased ventilatory response to carbon dioxide respiratory drive.

Ventilatory depression is more marked if opioids are administered.

Propofol has no effect on bronchial muscle tone and laryngospasm is uncommon. There is low incidence of cough or laryngospasm when a laryngeal mask airway is used due to the suppression of laryngeal reflexes and so regarded as the drug of choice in Laryngeal Mask Airway (LMA) introduction.[8]

Propofol does not appear to have any significant effect on uterine tone. It crosses the placenta. Its safety to the neonate has not established so its use in pregnancy (except for termination), in obstetric practice and in lactating mothers is not recommended.[8]

Prolonged propofol use in a critically ill, pregnant patient described by Badeva B, concluded that despite propofol’s pregnancy category B rating, data are lacking in humans regarding its safe use during pregnancy and long-term developmental outcomes in children after exposure to propofol in utero. The safety of propofol as a sedative agent for critically ill, pregnant patients remains unknown.[9]

**Impairment of fertility**

Female Wistar rats were administered either 0, 10, or 15 mg/kg/day Propofol intravenously for 2 weeks before pregnancy to day 7 of gestation did not show impaired fertility. Male fertility in rats was not affected in a dominant lethal study at intravenous doses up to 15 mg/kg/day for 5 days.[9]

**Pregnancy**

**Teratogenic effects**

**Pregnancy Category B**

Reproduction studies have been performed in rats and rabbits at intravenous doses of 15 mg/kg/day (approximately equivalent to the recommended human induction dose on a mg/m² basis) and have revealed no evidence of impaired fertility or harm to the fetus due to Propofol. Propofol, however, has been shown to cause maternal deaths in rats and rabbits and decreased pup survival during the lactating period in dams treated with 15 mg/kg/day (approximately equivalent to the recommended human induction dose on a mg/m² basis). The pharmacological activity (anesthesia) of the drug on the mother is probably responsible for the adverse effects seen in the offspring. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human responses, this drug should be used during pregnancy only if clearly needed.[9]

**Labor and Delivery**

Propofol Injectable Emulsion is not recommended for obstetrics, including cesarean section deliveries. Propofol Injectable Emulsion crosses the placenta, and as with other general anesthetic agents, the administration of Propofol Injectable Emulsion may be associated with neonatal depression.

**Nursing Mothers**

Propofol Injectable Emulsion is not recommended for use in nursing mothers because Propofol Injectable Emulsion has been reported to be excreted in human milk and the effects of oral absorption of small amounts of Propofol are not known.[9]

**Patients and methods**

This prospective hospital base study was performed in Soba University Hospital and Khartoum Teaching Hospital in Sudan at the period from 12th of October 2006 to 9th of April 2007. The study was approved by Ethical Committee of Anaesthesia and intensive care of Sudan Medical Specialization Board, hospitals, and surgical departments. Verbal information’s about the study was explained for patients and consent was obtained.

Ninety males and females of ASA class I & II, including paediatric cases, undergoing painful operations; orthopedic (reduction and immobilization of simple bones fractures), gynecological (D & C, evacuation and vulvar abscess) and general surgical (i.e. excisional biopsy of breast lumps, debridement, and abscess drainage). Exclusion criteria included; age of less than one month, ASA class III or more, prolonged
operations, lactating women, pregnant, and patients with contraindication to ketamine or propofol. For drug preparation 2 ml of ketamine (50 mg/ml) is taken into 20 ml syringe to which 8 ml of water for injection is added then mixed with 10 ml of propofol (10mg/ml). Concentration of 5 mg/ml for ketamine & propofol is reached. An additional person or persons (anaesthetic assistant or registrar of anaesthesia) other than the practitioner performing the procedure are responsible for the direct monitoring and documentation of the patient during deep sedation/analgesia which included; heart rate, noninvasive blood pressure, oxygen saturation, and respiratory rate. This monitoring started before procedure and continue throughout it and in recovery area till discharge of patient. Resuscitation equipment’s including bag/mask ventilation (e.g., Ambu bag), oxygen and suctioning machine were available with emergency drugs.

<table>
<thead>
<tr>
<th>Date:</th>
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<th>PrNo:</th>
<th>Consent:</th>
<th>Hospital</th>
<th>Fasting</th>
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**Patient Data Form**

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<td>Mean Arterial Pressure</td>
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<td>Oxygen Saturation</td>
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<td>Dose: Ketamine Propofol</td>
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- **Recovery evaluation**:  Response to Painful stimul .......... Sleeping but response to minor stimul .......... Awake with confusion .......... Fully awake with minor confusion .......... Fully awake .......... Time from last dose to recovery .......... min


- **1-12 Satisfaction Scale**

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<thead>
<tr>
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<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
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<td>Doctor</td>
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<td>Nurse</td>
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Score < 5 = Bad Satisfaction; Score > 5 = Good Satisfaction

- Need for rescue treatments:
  - Analgesia ........................................ Oxygent ...
  - Ventilatory support: .................. .................. Oxygent ...
  - Airway manipulation: .................. .................. Oxygent ...
  - Oral or nasal airway: .................. .................. Oxygent ...
  - Intubation or Laryngeal mask: .................. Spontaneous ........... Controlled ...........
  - Postoperative analgesia: .................. .................. Oxygent ...
  - Discharge: .................. Signature .......... 12 used to evaluate doctor's, nurse's and patient's satisfaction. Score from 1 to 4 reflected poor satisfaction, from 5 to 8 moderate satisfaction while those ranging from 9 to 12 regarded as good satisfaction.

Needs for airway manipulation, rescue analgesia, sedatives, anesthetics, oxygen or postoperative anxiolytics were recorded. Complications such as pain, hypertension, hypotension, nausea or vomiting, hypoventilation, apnea and hypoxia all were recorded with their management. Dysphoric experience such as bad

Adult patients were given 0.5 mg of atropine and paediatric cases according to their weight, intravenously. Then ketofol was given slowly with dose ranging from 0.5 – 0.8 mg/kg until optimum level of sedation was reached, using Ramsay scale of sedation. Start of operation must be at 5 or 6 level Top up of the patient also depend on clinical signs & Ramsay sedation scale, when the level decrease to 4. Ramsay sedation scale used for both start and top up of ketofol. Satisfaction scale ranging from 1 to 12 used to evaluate doctor's, nurse's and patient's satisfaction. Score from 1 to 4 reflected poor satisfaction, from 5 to 8 moderate satisfaction while those ranging from 9 to 12 regarded as good satisfaction.
feeling, hallucinations, nightmares and euphoria were recorded in addition to their management. The patient vital signs including; BP, RR, PR and SPO2 were monitored every 5 minutes. Monitoring end and patient discharged form procedure are when returned to baseline level of consciousness, had protective reflexes (i.e., ability to maintain a patent airway and ventilate), and oxygen saturation is greater than 92% on air or is back to the normal baseline by discharge order by the practitioner. Patient provided with post-procedure instruction sheet. Patients were advised to avoid alcohol, sedatives, or analgesics for the remainder of the day as their effects can be unpredictably potentiated by this medications.

Data were analyzed using computer. Results were obtained and subjected to statistical analysis using pearson chi-square test, where variable consider to be significant when P value is less than 0.05

RESULTS

Figure 1: The age distribution

Figure 2: Sex distribution

Figure 3: Location distribution

Figure 4: The operation urgency distribution

Figure 5: The types of operation distribution

Duration of the operation ranged from 10 - 60 minutes (mean = 22.72, std = 11.98) [Table 1].
The dose ranged from 0.5 – 0.8 mg/kg per dose.
The time from the last dose to full recovery ranged from 10 – 20 min [Table 2].
The incidence of bad emergence phenomena was low. Four Patients (4.4% ; P value = 0.000 ) had emergence phenomena, of these 2 ( 2.2% ; P value = 0.000) had hallucinations & both received midazolam, 2 ( 2.2% ; P value = 0.000 ) had euphoria; of these 1(1.1%; P value = 0.011 ) received midazolam [ Table 3]).
Respiratory complications which recorded were low, including transient hypoxia and apnea. Three ( 3.3% ; P value = 0.000 ) had transient hypoxia; of these 2 ( 2.2% ; P value = 0.000 ) required repositioning of airway malalignment, 1 ( 1.1% ; P value = 0.011 ) had transient apnea and required bag-valve-mask ventilation for one minute. No hypoventilation, hyperventilation or cyanosis was recorded. No patient needed airway, LMA or intubation [Table 4].
No patient developed hypertension, hypotension, tachycardia, bradycardia, pain or vomiting. One
(1.1%; P value = 0.011) had a mild nausea which didn’t need medication [Table 5]. Satisfaction score recorded by patients, doctors & nurses all among good limits. Patients recorded 95.6% as 12 score, 3.3% as 11 score and only 1.1% of 10 score. No less than 10 score recorded. Doctors recorded only 12 & 11 scores; 94.4% as 12 score and 5.6% as 11 score. Nurses recorded 92.2% as 12 score, 6.75 as 11 score and only 1.1% as 10 score. The total score of satisfaction recorded by all were as follow; of 12 were 94.1%, of 11 were 5.2% and of 10 is only 0.7% (P value = .000) [Table 6].

Table 2: The time from the last dose to full recovery.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
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<tbody>
<tr>
<td>10</td>
<td>27</td>
<td>30%</td>
</tr>
<tr>
<td>15</td>
<td>48</td>
<td>55.3%</td>
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<tr>
<td>20</td>
<td>15</td>
<td>16.7%</td>
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<tr>
<td>Total</td>
<td>90</td>
<td>100%</td>
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P value < 0.05 is significant (Chi-Square Test)

Table 3: The incidence of unpleasant emergence phenomena

<table>
<thead>
<tr>
<th>Type</th>
<th>No</th>
<th>%</th>
<th>DF</th>
<th>P value (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hallucinations</td>
<td>2</td>
<td>2.2</td>
<td>1</td>
<td>0.60</td>
</tr>
<tr>
<td>Epilepsia</td>
<td>2</td>
<td>2.2</td>
<td>1</td>
<td>0.60</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>4.4</td>
<td>2</td>
<td>0.00</td>
</tr>
</tbody>
</table>

P value < 0.05 is significant (Chi-Square Test)

Table 4: The incidence of respiratory complications

<table>
<thead>
<tr>
<th>Type</th>
<th>No</th>
<th>%</th>
<th>DF</th>
<th>P value (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchitis</td>
<td>3</td>
<td>3.3</td>
<td>1</td>
<td>0.09</td>
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<tr>
<td>Atenes</td>
<td>1</td>
<td>1.1</td>
<td>1</td>
<td>0.01</td>
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<tr>
<td>Total</td>
<td>4</td>
<td>4.4</td>
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<td>0.00</td>
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P value < 0.05 is significant (Chi-Square Test)

Table 5: The incidence of other complications

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<thead>
<tr>
<th>Type</th>
<th>No</th>
<th>%</th>
<th>DF</th>
<th>P value (95% confidence interval)</th>
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<tbody>
<tr>
<td>Nausea</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
<td>0.11</td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
<td>0.01</td>
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P value < 0.05 is significant (Chi-Square Test)

Table 6: 1–12 satisfaction scale

<table>
<thead>
<tr>
<th>Satisfaction</th>
<th>1–12 Satisfaction</th>
<th>P value</th>
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<tbody>
<tr>
<td>Patient’s satisfaction</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Doctor’s satisfaction</td>
<td>11</td>
<td>12</td>
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<tr>
<td>Nurse’s satisfaction</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Total Satisfaction</td>
<td>11</td>
<td>12</td>
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</tbody>
</table>

P value < 0.05 is significant
Ketofol, or ketamine and propofol mixed in the same syringe, has demonstrated efficacy in the operating department and in ambulatory settings, but has not previously been studied in the emergency department for procedural sedation and analgesia.[12]

The dose ranged from 0.5 – 0.8 mg/kg per dose with a mean of 0.65. This doesn’t match Willman EV, and Andolfatto G[13]; the median dose of medication administered was ketamine at 0.75 mg/kg and propofol at 0.75 mg/kg (range 0.2 to 2.05 mg/kg each of propofol and ketamine). Regarding that they give a single dose as their study involved short procedure.

The results revealed that the incidence of dissociated anaesthesia (bad emergence phenomena) were low. It matches the results reached by Badrinath S, et al.[14] subhypnotic dosages of ketamine, 9 ± 2 to 18 ± 7 μg · kg⁻¹ · min⁻¹, administered in combination with propofol infusion for sedation contributed significant analgesia without hemodynamic and respiratory depression or psychotomimetic side effects. Four patients developed dissociated phenomena (4.4%). Two of them had hallucination, which responded to small doses of midazolam. While 2 patients had euphoria and 1 of them needed midazolam for social stigma.

No patient developed pain or vomiting. However one (1.1%; P value = 0.011) had a mild nausea which did not need medication.

All patients had cardiovascular stability; no one developed hypotension, hypertension, tachycardia, bradycardia or other arrhythmias. This finding matches Badrinath S et al;[14] ketamine-induced tachycardia and hypertension was not evident in the hemodynamic response of patients treated with the propofol/ketamine combination. However, this in contradistinction to Ravindra V, et al;[12] the use of ketamine in combination with propofol did not alter the incidence of adverse effects compared to propofol alone. Which suggested that prospective study is needed to confirm the efficacy and safety of ketamine with propofol in ambulatory surgery.

The incidence of respiratory complications were low. Three patients had transient hypoxia of whom one patient had transient apnea who needed positive pressure ventilation with face mask for one min. Other 2 patients just needed airway mal alignment (repositioning of the head). This matches Willman EV, and Andolfatto G[13] (2.6%; 95% confidence interval [Cl] 0.6% to 7.5%) had transient hypoxia; of these, 1 (0.9%; 95% CI 0.02% to 4.8%) required bag-valve-mask ventilation. Four patients (3.5%; 95% CI 1.0% to 8.7%) required repositioning for airway mal alignment.

The time from the last dose to full recovery ranged from 10 – 20 min, mean is 15 minutes. This matches Willman EV, and Andolfatto G.[13]
Median recovery time was 15 minutes (range 5 to 45 minutes; IQR 12 to 19 minutes).

Satisfaction of patients, nurse and doctors were determined and found to be high. Patients recorded 95.6% as 10 score, 3.3% as 9 score and only 1.1% of 8 score. No less than 8 score recorded. Doctors recorded only 10 & 9 scores; 94.4% as 10 score and 5.6% as 9 score. Nurses recorded 92.2% as 10 score, 6.75 as 9 score and only 1.1% as 8 score. The total score of satisfaction recorded by all were; of 10 were 94.1%, of 9 were 5.2% and of 8 is only 0.7% (P value = .000). This differ slightly from Willman EV, Andolfatto G;[13] in which median physician, nurse, and patient satisfaction scores were 10 on a 1-to-10 scale. However, in our study satisfaction scores reached are highly clinically and statistically significant.

CONCLUSION

The study involved ninety patients who undergone minor painful operations and the result revealed low incidence of cardio respiratory complications, dissociative phenomena and gastrointestinal upset. Moreover, the results showed that the assessment of operating doctors, patients and nurses satisfaction were excellent. Ketofol produces an effective deep sedation/analgesia for minor painful operations, which could be elective or emergency, with rapid induction and recovery. Ketofol appears to be safe, with fewer adverse side effects that where either self-limited or responded to minimal interventions. Ketamine and propofol counteract each other at the level of their adverse effects giving this magic mixture. Staff and patients were highly satisfied. It seems that it will get back ketamine to the circle of anaesthetic practice after it became used within special conditions.

Recommendation:

1- Ketofol is found to be:
   • Effective.
   • Safe.
   • Simple in use.
   • Satisfied patients and treating doctors.
2- Thus ketofol should be used for deep
3- Sedation/analgesia among those patients who fulfill inclusion criteria.
4- Other studies with large number of patients should be carried to support its use.

REFERENCES

1. American Society of Anesthesiologists, Practice Guidelines for Sedation and Analgesia by Non-Anesthesiologists; Inc.