Subcutaneous dissociative conscious sedation outside the operating theatre: prospective randomised double-blind study

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Abstract

Introduction
Colonoscopy is among the common diagnostic and therapeutic gastrointestinal interventions, which is routinely done outside the operating room. The painful nature of the procedure and patient anxiety resulting from gas insufflation propose using sedatives and analgesics during the colonoscopy procedure. The goal of this study is to compare the safety of different methods of conscious sedation in remote location anaesthesia.

Materials and methods
Our prospective randomised double-blind study was conducted among 90 adult patients who were scheduled for elective colonoscopy. Patients were randomly assigned to one of the three groups: subcutaneous ketamine in conjunction with opioid, propofol in conjunction with opioid and midazolam in combination with opioids. Extra doses of opioids were administered on demand during the procedure. Heart rate, blood pressure and blood oxygen saturation were measured throughout the procedure. Adverse effects and recovery events were recorded.

Results
All patients tolerated the colonoscopy well. Three study groups were comparable with regard to heart rate, BP, apnoea and blood oxygen saturation. Pain score and opioid consumption were significantly lower in ‘subcutaneous ketamine in conjunction with opioid’ group. Patient cooperation and endoscopist satisfaction were significantly higher in the ‘subcutaneous ketamine in conjunction with opioid’ group. Recovery time was comparable in three groups and all patients experienced an uneventful recovery.

Conclusion
Subcutaneous dissociative conscious sedation, a recently reported method of conscious sedation, provides more safety and patient satisfaction in comparison with conventional methods. Subcutaneous ketamine in conjunction with opioid could be considered as a safe and efficient method of conscious sedation in remote location anaesthesia.


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about the possible risks and benefits of the study and a written consent was received from the patients.

Anaesthetic method

Patients were randomly assigned to one of the three groups; s.c. ketamine in conjunction with opioid (sDCS), propofol in conjunction with opioid and benzodiazepines in conjunction with opioids. Extra doses of opioids were administered on demand during the procedure. Heart rate, blood pressure (BP) and blood oxygen saturation (SpO₂) were measured throughout the procedure. Adverse effects and recovery events were recorded.

Patient with American Society of Anesthesiologists class III and IV, cardiovascular disease, hypertension, history of drug abuse, history of hypersensitivity to medications, and any cognitive disorders were excluded from the study.

Patients were continuously monitored using standard techniques including electrocardiography, pulse oximetry and non-invasive sphygmomanometry. All procedures were performed out of the operating room and by the same endoscopist.

All patients were administered (i.v.) meperidine 0.5 mg/kg and i.v. fentanyl 1µg/kg. Then, they were randomly assigned to receive s.c. ketamine 0.6 mg/kg (sDCS group), infusion of propofol 50 µg/kg/min (propofol group) and midazolam 0.015 mg/kg (midazolam group) at least 5 min before starting the procedure when the desirable level of conscious sedation had been achieved. The site of s.c. injection in all patients was on the anterior side of the forearm. An extra dose of i.v. fentanyl 1 µg/kg to maximum dose of 3 µg/kg, and in the case of inefficient sedation an additional dose of pethedine 0.5 mg/kg was administered.

During the procedure, heart rate and BP were recorded at 5-min intervals. Continuous monitoring of SpO₂ and echocardiogram was established throughout the procedure. Adverse events, such as apnoea, desaturation, hypotension, bradycardia, needed immediate intervention, and patient movements resulting from pain or agitation were recorded.

Patients received supplemental oxygen by face mask. Desaturation (SpO₂ < 90) was recovered by jaw trust and head tilt manoeuvre. Mask ventilation devices were available to interfere with probable apnoea.

The period of recovery (the time needed for patients to become fully awake and obedient) was recorded. A duration of 20 min was considered as normal recovery time and more than this defined as prolonged recovery.

At the end of the recovery, patients were asked about experiencing pain or discomfort during the procedure and satisfaction with their sedation. Also any event of nausea, vomiting, vertigo, visual disturbance and hallucination during the procedure and recovery period was recorded.

At the end of procedure, the endoscopist was asked about his satisfaction with the quality of sedation concerning the feasibility of the procedure case by case.

Statistical analysis

Data were recorded through a questionnaire form. Statistical calculations were performed using SPSS software, version i8.0 and analysed by Student's t-test and two-tailed Fisher test. Differences were considered significant at \( P < 0.05 \).

Results

All patients tolerated the colonoscopy well. No patient was excluded from the study. Mean age in the study group was 33.00 ± 7.64 years, and 56% of the patients were men. No significant demographic differences were observed between the study groups.

Three groups were comparable with regard to heart rate and BP. Haemodynamic changes, more than 20%, was detected in one case in group sDCS (3.3%), no case in group propofol and three cases in group midazolam (10.0%) (\( P = 0.160 \)). No event of SpO₂ < 90% in sDCS group was recorded. Four patients in propofol group (13.3%) and one patient in midazolam group (3.3%) showed desaturation (\( P = 0.064 \)) that was statistically non-significant.

Pain score and opioid consumption were significantly lower in sDCS group. Two patients experienced pain in sDCS group (6.6%), eight patients in group propofol group (26.6%), and 12 patients in group midazolam group (40%) (\( P = 0.010 \)). One patient in group sDCS (3.3%), 10 patients in group propofol (33.3%) and 11 patients (36.6%) in group midazolam needed additional doses of fentanyl (\( P = 0.040 \)).

No patient in group sDCS needed additional dose of meperidine. Seven patients (23.3%) in group propofol and nine patients (30.0%) in group midazolam received additional dose of meperidine (\( P = 0.006 \)).

Patient cooperation and endoscopist satisfaction were significantly higher in sDCS group. Patients were completely satisfied with their anaesthesia in group sDCS and propofol and no recall was reported by the patients. In group midazolam, 17 patients (56.6%) were not satisfied with their sedation and recall was reported by all 17 patients (\( P = 0.001 \)). A 93.3% (28 cases) satisfaction was reported by the endoscopist in sDCS group, 70.0% (21 cases) in group propofol and 33.3% (10 patients) in group midazolam (\( P = 0.001 \)).

Recovery time was comparable in all three groups and all patients experienced uneventful recovery.

The duration of recovery more than 20 min was detected in two cases in sDCS group (10.0%), five cases in propofol group (16.6%), and eight cases in midazolam group (26.6%) (\( P = 0.115 \)), which was not statistically significant (Table 1).
Discussion

Colonoscopy is an important, common gastrointestinal therapeutic and diagnostic intervention, which is performed outside the operating theatre by endoscopists. Despite considerable improvement in gastrointestinal procedures, this is still a high-risk area for outpatient procedures.

Patient anxiety and pain related to gas insufflation propose using sedatives and analgesics during the colonoscopy procedure. Endoscopists usually prefer using intravenous (i.v.) sedation or even general anaesthesia to achieve patient comfort and optimal situation to prevent failure of the procedure. In addition, most patients undergoing gastrointestinal interventions are outpatients and a short PACU admission period is desirable. Conventional regimens including a combination of benzodiazepines and opioids have been used to provide analgesia and amnesia. Using hypnotics in combination with opioids improves the quality of sedation and reduces probable complications. Propofol has been recommended as a safe hypnotic drug in colonoscopy. It is a hypnotic agent with rapid onset and short duration of action, and it is preferred for sedation in procedures with short duration. One of the most important side effects of propofol is respiratory depression, and some studies demonstrated high end-tidal CO₂ levels in deep sedation with propofol. Therefore, it is recommended that this agent should be administered with appropriate monitoring by an anaesthesiologist.

Given the characteristics of remote location procedures (outside operating theatre), choosing an appropriate method of anaesthesia or analgesia with the least risk of haemodynamic changes and respiratory depression is a priority.

Ketamine is an old anaesthetic with known effects of analgesia and amnesia and has been widely used by different routes of administration for inducing anaesthesia and sedation. Ketamine is a non-competitive N-methyl-D-aspartate receptor antagonist and has been widely used as a hypnotic agent or in combination with opioids and benzodiazepines. Ketamine has unique characteristics of the drug. This agent has been administered widely as a solitary sedative agent or in combination with opioids. Ketamine is indicated for use as a hypnotic agent with rapid onset and short duration of action and it is preferred for sedation in procedures with short duration. One of the most important side effects of propofol is respiratory depression, and some studies demonstrated high end-tidal CO₂ levels in deep sedation with propofol. Therefore, it is recommended that this agent should be administered with appropriate monitoring by an anaesthesiologist.

Intact airway protective reflexes and lack of respiratory depression are unique characteristics of the drug. This agent has been administered widely as a solitary sedative agent or in combination with opioids and benzodiazepines.

sDCS using s.c. injection of sub-anaesthetic doses of ketamine in conjunction with narcotics has recently been reported by Javid et al. as a safe and efficient method of conscious anaesthesia and conscious sedation.

It was successfully used as an alternative to general anaesthesia in laparoscopic peritoneal dialysis catheter implantation.

By keeping the plasma concentration of ketamine at or below 150 ng/ml there was no risk of hallucination, adverse cardiovascular effects and airway hypersecretion.

Considering the feasibility to preserve spontaneous ventilation, patient co-operation and considerable amnesia as prominent characteristics of the sDCS method, we decided to evaluate and compare the efficiency of this method of conscious sedation with conventional methods in patients undergoing colonoscopy.

This study shows that dissociative conscious sedation (use of s.c. injection of low-dose ketamine in conjunction with narcotics to achieve an acceptable level of sedation, pain relief and amnesia) is an effective method for procedures outside the operating theatre. Patients remain considerably co-operative and obedient, but are sufficiently sedated and pain-free. Besides, the study shows that s.c. administration of ketamine provides efficient conscious sedation accompanied by a significantly lower pain score, opioid consumption and recall rate and higher rate of patient and endoscopist satisfaction. This might be because of the increased analgesic effect of opioids when they are used in combination with ketamine (sDCS method). No significant cardiovascular side effect of ketamine was observed. These findings were similar to the previous experiences of sDCS in other procedures.

The limitation of this study was lack of ETCO₂ monitoring because the side stream capnograph device was not available in the colonoscopy department.

Table 1. Incidence of recorded parameters.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group sDCS (%)</th>
<th>Group Propofol (%)</th>
<th>Group Midazolam (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desaturation</td>
<td>0.0</td>
<td>13.3</td>
<td>3.3</td>
<td>0.064</td>
</tr>
<tr>
<td>Pain</td>
<td>6.6</td>
<td>26.6</td>
<td>40.0</td>
<td>0.010</td>
</tr>
<tr>
<td>Additional fentanyl</td>
<td>3.3</td>
<td>33.3</td>
<td>36.6</td>
<td>0.040</td>
</tr>
<tr>
<td>Additional meperidine</td>
<td>0.0</td>
<td>23.3</td>
<td>30.0</td>
<td>0.006</td>
</tr>
<tr>
<td>Increased HR and BP &gt;20%</td>
<td>3.3</td>
<td>0.0</td>
<td>10.0</td>
<td>0.160</td>
</tr>
<tr>
<td>Cooperation in positioning</td>
<td>100.0</td>
<td>33.3</td>
<td>96.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Nausea</td>
<td>20.0</td>
<td>6.6</td>
<td>23.3</td>
<td>0.372</td>
</tr>
<tr>
<td>Vomiting</td>
<td>13.3</td>
<td>6.6</td>
<td>16.6</td>
<td>0.484</td>
</tr>
<tr>
<td>Recall</td>
<td>0.0</td>
<td>0.0</td>
<td>56.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Patient’s satisfaction</td>
<td>100.0</td>
<td>100.0</td>
<td>43.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Endoscopist’s satisfaction</td>
<td>93.3</td>
<td>70.0</td>
<td>23.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Prolonged recovery</td>
<td>10.0</td>
<td>16.6</td>
<td>26.6</td>
<td>0.115</td>
</tr>
</tbody>
</table>

BP: blood pressure
HR: heart rate.
Conclusion
sDCS, a recently reported method of conscious sedation, provides more safety and patient satisfaction for anaesthesia outside the operating theatre in comparison with conventional methods.

sDCS could be considered as a safe and efficient method of conscious sedation in remote location anaesthesia.

Acknowledgement
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Abbreviations list
BP, blood pressure; i.v., intravenous; PACU, post-anaesthesia care unit; s.c., subcutaneous; sDCS, subcutaneous dissociative conscious sedation; SpO2, blood oxygen saturation

References


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