Analgesic and sedative effects of intranasal dexmedetomidine in third molar surgery under local anaesthesia

C. W. Cheung1*, K. F. J. Ng1,2, J. Liu1, M. Y. V. Yuen3, M. H. A. Ho4 and M. G. Irwin1

1 Department of Anaesthesiology and 2 Department of Pharmacology & Pharmacy, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong
3 Department of Anaesthesiology, Queen Mary Hospital, Hong Kong
4 Department of Anaesthesia and Intensive Care, the Chinese University of Hong Kong, Hong Kong
* Corresponding author. E-mail: cheucw@hku.hk

Background. Dexmedetomidine (DEX) is an alpha 2-adrenoreceptor agonist, which induces sedation and analgesia. This study aimed to determine whether intranasal DEX offered perioperative sedation and better postoperative analgesia.

Methods. Patients having unilateral third molar surgery under local anaesthesia were recruited and allocated to receive either intranasal DEX 1 μg kg⁻¹ (Group D) or same volume of saline (Group P) 45 min before surgery. Patient-controlled sedation with propofol was offered as a rescue sedative. Perioperative sedation, postoperative pain relief and analgesic consumption, vital signs, adverse events, postoperative recovery, and satisfaction in sedation and analgesia were assessed.

Results. Thirty patients from each group were studied. Areas under curve (AUC) of postoperative numerical rating scale (NRS) pain scores 1–12 h at rest and during mouth opening were significantly lower in Group D (P=0.003 and 0.009, respectively). AUC BIS values and OAA/S sedation scores were significantly lower before surgery and at the recovery area (all P<0.01) with significantly less intra-operative propofol used in group D (P<0.01). In group D, heart rate was significantly lower at recovery period (P=0.005) while systolic blood pressure in different periods of the study (all P<0.01), but the decreases did not require treatment. More patients from placebo group experienced dizziness (P=0.026) but no serious adverse event was found. No difference was found in postoperative psychomotor recovery and satisfaction in pain relief and sedation.

Conclusions. Patients receiving intranasal DEX for unilateral third molar surgery with local anaesthesia were more sedated perioperatively with better postoperative pain relief. No delay in psychomotor recovery was seen.

Keywords: analgesia; dental; dexmedetomidine; intranasal; pain

Accepted for publication: 30 April 2011

Dexmedetomidine (DEX) is an alpha 2-adrenoreceptor agonist, which provides sedation, analgesia, and anxiolysis in clinical practice.1 Activation of central alpha 2-adrenoreceptors in the locus ceruleus2 is responsible for both analgesic and sedative effects. DEX has a very high alpha-2 to alpha-1 selectivity, 1620 to 1, or approximately eight times that of clonidine. It is also four to five times more potent than clonidine by weight.3

DEX has been studied for pain relief and sedation. I.V. DEX was shown to produce a comparable sedative effect to midazolam, but no better analgesia was demonstrated after third molar surgery under local anaesthesia.4 The analgesic effect of i.v. DEX is controversial. In an ischaemic pain model in healthy volunteers, a single bolus of DEX produced a 50% reduction in pain scores when compared with placebo.5 In another volunteer study using the cold pressor test, DEX 1 μg kg⁻¹ over 10 min followed by an infusion of 0.2 to 0.6 μg kg⁻¹ h⁻¹ reduced pain by ~30%.6 However, when administered as a target controlled infusion at concentrations ranging from 0.09 to 1.23 ng ml⁻¹, DEX had no analgesic effect in human volunteers subjected to heat and electrical pain, although sedation was produced.7 Clinically, i.v. DEX was shown to have a postoperative opioid sparing effect but not clear pain relief.7 In view of inconclusive clinical evidence,
future studies with different routes of administration and in multimodal analgesia have been suggested.

Intranasal DEX has been studied in healthy volunteers for sedation and pain relief. It was effective and well tolerated with reliable sedation, but no effect on pain pressure threshold. There have been few clinical studies evaluating intranasal DEX as premedication for paediatric patients. When intranasal DEX was compared with oral midazolam for premedication in paediatric anaesthesia, DEX was found to produce more sedation than oral midazolam. It also produces satisfactory premedication sedation in children when used alone. Talon and colleagues also demonstrated that intranasal DEX was more effective than midazolam in inducing sleep before operation in children with burns.

To date, no clinical study has been done to explore the analgesic and sedative effects of intranasal DEX for surgical procedures. Since dental surgery is a common model for the study of analgesia and sedation, we conducted this double-blinded randomized controlled study to assess the analgesic and sedative efficacy of intranasal DEX for unilateral third molar surgery under local anaesthesia.

Methods

The study protocol was approved by our local Institutional Review Board and registered at ClinicalTrials.gov with registration number NCT01132794. Written consent was obtained from all the participants. Eligibility for recruitment included ASA physical status I and II and age between 18 and 50 yr with unilateral impacted third molar teeth undergoing extraction under local anaesthesia and sedation. Exclusion criteria included clinical history or electrocardiographic evidence of heart block, ischaemic heart disease, asthma, sleep apnoea syndrome, impaired liver or renal function, alcohol consumption in excess of 28 units per week, pregnancy, patient refusal, known psychiatric illness, chronic sedative or analgesic use, and regular use of or known allergy to DEX, propofol, paracetamol, NSAIDs, or opioids. Patients with preoperative inflammation at the site of surgery were also excluded.

After obtaining written, informed consent, patients were randomly allocated to receive either DEX (Group D) or 0.9% saline (Group P) intranasally 45 min before surgery. A computer-generated random sequence was used for drug allocation, and this was prepared by a statistician who was unaware of the clinical nature of the study. The patients were assessed by the list anaesthetist the day before surgery, were fasted for at least 6 h, and did not receive any premedication before arrival at the operating theatre. They were educated on the use of the numerical rating scale (NRS) for pain and sedation assessment, where zero corresponds to no pain or no sedation whereas 10 represents the worst pain imaginable or extremely relaxed. It was also explained that rescue patient-controlled sedation (PCS) with propofol would be provided and the technique of use taught.

One hour before surgery, patients were sent to the induction room. A research assistant who was blinded to the study and not involved in patient care was responsible for data collection. Digit symbol substitution test (DSST), a timed test of psychomotor function, was performed and the scores obtained. Vital signs including heart rate, blood pressure, \( \text{SpO}_2 \), and ventilatory frequency (S/5 Anesthesia Monitor, Datex-Ohmeda, WI, USA), and sedation scores including Observer Assessment of Alertness/Sedation (OAA/S) and NRS sedation score were also recorded as baseline and every 5 min thereafter. Bispectral index (BIS) scores were recorded from administration of intranasal study drug to the time of discharge to the general ward from the recovery room. Intranasal study drug was administered by the list anaesthetist who did not participate in patient management or data collection. Study drug, either undiluted DEX 1 \( \mu \text{g kg}^{-1} \) (Group D) or the same volume of 0.9% saline (Group P) was administered to each naris as drops. Both preparations were clear solutions; therefore, patients, medical and nursing staff, and data collectors were all blinded to the allocated drug.

Forty-five minutes after study drug administration, a 20-gauge i.v. cannula was inserted in the dorsum of each patient’s left hand. Patients were then transferred to the operating theatre for the surgical procedure. Before the operation started, patients were given the handset of a PCA pump (Graseby 3300 Syringe Pump, Smiths Medical, London) and asked to press the button in order to get a dose of the rescue sedative medication if they did not feel relaxed enough. On pressing the button, they would receive a 15 mg (1.5 ml of 1%) increment of propofol. There was a lockout interval of 1 min between demands. The endpoint of sedation used in this study was the subjective relaxation of the patient. All the operations were done by the same surgical team of two maxillofacial surgeons. Local anaesthetic was given (2% lidocaine with 1 in 80 000 epi) and the volume used was recorded. Inadequate analgesia was managed by infiltrating local anaesthetic into the surgical site. Pain or discomfort during intranasal administration of DEX, i.v. cannulation, use of PCS with propofol, and local anaesthetic infiltration for regional block were graded by patients as NRS scores.

DSST was repeated hourly from the first postoperative hour for 2 h. Fitness for discharge was assessed using the post-anæsthetic discharge scoring system that is commonly used in ambulatory surgery. The patient is fit for discharge if the score is equal to or more than 9. The post-anæsthetic discharge score (PDS) was obtained from each patient from postoperative hour 1 until it reached 9. In the recovery area, blood pressure, heart rate, ventilatory frequency, oxygen saturation, and sedation scores were assessed every 5 min for half an hour. Vital signs were monitored hourly for 4 h after being discharged to the general ward. NRS pain scores were also charted hourly for 6 h then 4-hourly thereafter. Patients were prescribed two analgesic tablets, each containing paracetamol 320 mg and dextropropoxyphene 32.5 mg (Dolpocetmol®, Synco Limited, Hong Kong SAR, China), on an as required basis to a maximum of four times daily. The patients were told that the pain medications prescribed could be taken if the postoperative NRS pain score was more than 3.

Final hospital discharge was at the discretion of the attending dental surgeon. The senior surgeon of the surgical
team also determined the operating conditions according to a simple scale (Appendix 1) and the degree of difficulty of the surgery in terms of amount of bone removed as an NRS scale. Satisfaction with sedation by patients was assessed by asking them whether they thought they received an adequate amount of sedation, too little or too much, whether they were relaxed and whether they would undergo the same sedation regimen again. The oral analgesic medication described above was prescribed for 3 days after operation and patients were given a diary to record NRS pain scores at rest and upon mouth opening, analgesic consumption and side-effects at the 24th, 48th, and 72nd hour after operation. Global pain satisfaction using NRS (zero being least satisfied and 10 being most satisfied) was recorded at the 72nd postoperative hour.

Our primary outcome measurement was postoperative pain relief. We considered a clinically significant difference in areas under the pain score curve (AUC) for the first 12 h to be a mean of 24 (i.e. an average difference of NRS score of 2 per hour). From our previous work, we have estimated the mean NRS (AUC 1–12 h) to be 49 and standard deviation 31.\(^{13}\) With these estimates, a sample size of 28 per group would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of significance. To compensate for the possibility of dropout, we would give an 80% power of the test at the 5% level of signifi...
time for first analgesic request, total analgesic consumption, and the overall global pain satisfaction.

The trend of BIS values recorded is shown in Figure 2. AUC of BIS values were significantly lower for Group D than Group P both in the induction room and in the recovery area (P=0.007 and P<0.001, respectively). AUC of OAA/S was also significantly lower in the induction room and during the recovery period for Group D when compared with Group P (P=0.002 and P=0.001, respectively, Table 3). Consumption of rescue propofol for sedation is shown in Figure 3. Patients receiving intranasal DEX used significantly less propofol (P<0.01). All Group D patients achieved a PDS ≥9 at postoperative hour 2. The proportion of patients who attained DSST scores equal to or higher than their preoperative performance at postoperative hours 1 and 2 was similar between both study groups (Table 3).

Concerning the perioperative haemodynamic parameters, heart rate was significantly lower in Group D than in Group P in the recovery area (P=0.005, Fig. 4). Systolic blood pressure was significantly lower in the induction room, during surgery, and in the recovery area for patients from Group D compared with Group P (P=0.007, P=0.008 and P=0.001, respectively). None of these patients, however, developed clinically significant decreases that required vasoressor or anticholinergic support. Ventilatory frequency and oxygen saturation were similar in the whole study period for both groups. There was no respiratory depression (defined as a ventilatory frequency <10 min⁻¹), or any oxygen saturation <92%.

More patients from Group P experienced dizziness after operation (P=0.026). The incidences of other common side-effects such as headache, nausea, and tiredness were similar between groups. No serious adverse events occurred in this study. All patients could be discharged as scheduled without any complication.

More patients from Group D (29 [96.7%]) than Group P (22 [73.3%]) had surgical conditions graded as good by the surgeons (P=0.026). When patients were asked about satisfaction with sedation, a similar proportion from both groups felt they were relaxed during the procedure, got adequate sedation, and would use the same drug again.

Discussion

This is the first study evaluating the use of intranasal DEX in a surgical procedure. We demonstrated that patients given intranasal DEX experienced significantly less postoperative pain in the early postoperative period. They were more sedated peroperatively but without delay in psychomotor recovery.

Intranasal administration of medications is convenient and non-invasive. The drug may penetrate the blood–brain barrier and reach the central nervous system directly. Also, because of the high vascularity of the subepithelial surface of the nasal cavity, drugs may access the venous blood of the systemic circulation, which can avoid first-pass metabolism in the liver. Therefore, intranasal administration of DEX may potentially have useful analgesic and sedative effects in surgical procedures.
When intranasal DEX of 1 μg kg⁻¹ was used for premedication in children, the median onset time of sedation was 25 min with a median duration of 85 min. In a study conducted in healthy volunteers, intranasal administration of DEX 1 μg kg⁻¹ produced significant sedation within 45 min, with a clinical sedative effect lasting 180 min. Bioavailability of intranasal DEX has recently been evaluated in a small number of healthy volunteers. After intranasal administration of 84 μg of DEX, it was found that the median time to reach peak plasma concentration and the elimination half-life were 38 and 114 min, respectively, with the median absolute bioavailability of 65%. Pharmacological effects were demonstrated to be similar between intranasal and i.v. routes of administration except that onset was more rapid for i.v. administration. Because the onset of clinical sedation was at 30–45 min after intranasal administration, it was suggested to be given 45–60 min before a surgical procedure. Consequently, we gave DEX 45 min before third molar surgery. There was a wide time span from the intranasal medication to the start of surgery in this study, which probably reflects the real clinical situation. Clinically, having a fixed time for intranasal DEX administration before surgery may not be easily achieved. The duration for sedation for adults was shown to be >180 min in a previous study. Our study results show that intranasal DEX can be administered over a relatively wide time span and still provide good clinical analgesia and sedation.

Postoperative dental pain usually peaks within 12 h, but the duration of pain and other sequelae such as reduced mouth opening and facial swelling may last for 3 days. Alpha-2 agonists produce analgesia by acting on various sites including the brain, brainstem, spinal cord, and peripheral tissue. The clinical analgesic effect of DEX has recently been reviewed. DEX, when administered intravenously, mainly results in a reduction of analgesic consumption but not improvement in postoperative pain scores. The reduction in analgesic consumption without improvement in pain relief for acute pain control is considered undesirable. The use of i.v. DEX for multi-modal analgesia remains in question and other routes of administration and its use in different major operations need to be explored.

Apart from resting pain, we also assessed the magnitude of pain upon mouth opening as this is a simple and clinically

### Table 3

<table>
<thead>
<tr>
<th></th>
<th>Group D (n = 30)</th>
<th>Group P (n = 30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OAA/S</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Induction room AUC₆₀</td>
<td>4.2 [3.9–4.5 (3.3–4.9)]</td>
<td>4.7 [4.2–5 (3.3–5)]</td>
<td>0.002*</td>
</tr>
<tr>
<td>Intraoperative AUC₆₀</td>
<td>5 [4.1–5 (3–5)]</td>
<td>4.6 [4–5 (3.1–5)]</td>
<td>0.348</td>
</tr>
<tr>
<td>Recovery area AUC₆₀</td>
<td>4.6 [4.1–5.5 (3.5–5)]</td>
<td>5 [4.8–5 (4.1–5)]</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>NRS sedation scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Induction room AUC₆₀</td>
<td>8.2 [7–9 (3.8–10)]</td>
<td>7.5 [5–8 (0–10)]</td>
<td>0.047</td>
</tr>
<tr>
<td>Recovery area AUC₆₀</td>
<td>8.5 [6.4–9.7 (1.1–10)]</td>
<td>7.5 [5.2–9.6 (1.1–10)]</td>
<td>0.183</td>
</tr>
<tr>
<td>Postoperative DSST</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative 1 h</td>
<td>90% (27)</td>
<td>96.7% (28)</td>
<td>1.000</td>
</tr>
<tr>
<td>Postoperative 2 h</td>
<td>93.3% (29)</td>
<td>100% (30)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

*statistically significant.
relevant test of mechanical hyperalgesia.22 AUC NRS for 1–12 h showed that pain at rest and during mouth opening was significantly lower in patients who had intranasal DEX. These results suggested that a reduction in mechanical hyperalgesia was also achieved. Significant pain relief could not be found from AUC NRS 12–72 h, although the pain scores of Group D patients appeared to be lower. Probably, the reduction in pain during this period in Group D was not significant enough to demonstrate the difference. In our study, we noticed that intranasal DEX was not useful in improving the discomfort or pain for procedures such as i.v. cannulation or regional block, which could indicate that intranasal DEX by itself is not a strong analgesic. Nevertheless, better postoperative pain relief was demonstrated in our study after third molar surgery. DEX was found to augment the analgesic effect of lidocaine for i.v. regional anaesthesia.23 Whether intranasal DEX would enhance postoperative pain relief after regional block with lidocaine in third molar surgery warrants further investigation. Alpha-2 agonists have been found to have anti-inflammatory effects by decreasing the production of inflammatory cytokines via a central sympatholytic action.24 25 Reducing pain, therefore, might also be attributable to the anti-inflammatory effects of DEX because third molar surgery is an inflammatory pain model. The sustained sympatholytic effect as indicated by an extended reduction in blood pressure may produce a relatively prolonged anti-inflammatory effect, which results in less postoperative dental pain. Although patients having intranasal DEX experience less postoperative pain, no difference in satisfaction was found between the two study groups. Our study may not be sufficiently powered to detect small differences in patient satisfaction. Nonetheless, high satisfaction ratings may not directly reflect better pain control26 27 and patients are often reluctant to criticize their caretakers after surgery.26

Fig 4 Heart rate and systolic blood pressure of patients receiving intranasal DEX (Group D) and 0.9% saline (Group P) at induction room, at intraoperative period, at recovery period and in the ward. Data shown are mean (SD). Data points were slightly shifted horizontally to avoid overlapping. (a) Compared with Group P, heart rate in Group D was lower at recovery period ($P=0.005$). (b) Systolic blood pressure of patients from Group D was lower than Group P in the induction room, in the intraoperative period and in the recovery period ($P=0.007$, $P=0.008$ and $P<0.001$, respectively). IntraOp, intraoperative period.
Objective sedation was assessed using BIS values and OAA/S while subjective sedation by NRS sedation scores. NRS sedation score of 10 was graded if the patient was not arousable. Intranasal demedetomidine produced more sedation with much less rescue propofol consumed. Although patients having intranasal DEX were found to be more sedated in the induction room and the recovery area with BIS and OAA/S assessments after operation, they did not feel more sedated subjectively compared with the placebo group. In our study, a discrepancy between the results of subjective and objective assessments of sedation was demonstrated. Perhaps, the subjective scoring of the patient was inadequate if objective measures showed a difference. However, it is possible that patients sedated with intranasal DEX might have had inadequate subjective sedation even though objective sedation criteria were reached. Therefore, it is suggested that subjective and objective sedation could be assessed together in order to prevent possible under-sedation when intranasal DEX is used for sedation.

Intranasal DEX 1 μg kg⁻¹ produced the significant prolonged sedation of >3 h when compared with placebo in healthy volunteers. It is possible that there is a synergistic interaction between propofol and DEX. However, based on the results of DSST and PDS, the recovery in psychomotor function was not delayed when compared with patients having placebo with rescue PCS propofol alone. Such use of intranasal DEX, therefore, may be applicable to day surgery in view of the lack of delay in psychomotor recovery. No difference in the questions for satisfaction of sedation by patients between the two study groups was noticed, but this could only be truly evaluated with a crossover comparison as again our study may not be sufficiently powered to detect small differences in patient satisfaction with sedation. Nevertheless, surgeons commented that surgical conditions of patients in the intranasal DEX group were significantly better. It might be explained by the fact that these patients were more easily aroused and co-operative during dental surgery. Co-operation of patients is one of the main criteria for the grading of surgical conditions in this study (Appendix 1). I.V. DEX exhibits a modest decrease in blood pressure, heart rate, and cardiac output. This was also observed in our study. Our patients were all healthy and tolerated this well with no cardiovascular instability requiring intervention. Desaturation has been reported when i.v. DEX was used for sedation in third molar surgery. No patients developed respiratory depression or desaturation after intranasal DEX in our study. Interestingly, patients having placebo experienced more dizziness after surgery. This was probably because patients from this group used significantly more rescue propofol for sedation. Although there were no serious adverse events, this study was not powered to determine DEX safety.

There are some limitations to our study. First, patients were recruited for third molar surgery under local anaesthesia with conscious sedation. Therefore, rescue PCS with propofol was provided in case sedation was inadequate. The sedation technique we studied, in fact, was intranasal DEX with rescue PCS propofol as the supplement. However, we could demonstrate that intranasal DEX does have a role in sedation in view of the significantly deeper perioperative sedation with lower propofol consumption in Group D. Further dose-finding studies using intranasal DEX alone should be carried out. Secondly, patients in the placebo group used significantly more propofol, which could be a confounding factor for pain assessment. A previous study showed that patients anaesthetized with propofol had less postoperative pain. Therefore, propofol consumption does not affect our conclusion concerning pain relief in our study. Thirdly, although postoperative analgesia and perioperative sedation were shown using intranasal DEX for sedation in this study, we cannot conclude that it is superior to i.v. DEX for sedation. Clinical studies directly comparing intranasal and i.v. DEX for sedation would need to be conducted to evaluate this.

In conclusion, intranasal DEX appears to confer perioperative clinical sedation with improved postoperative analgesia for unilateral third molar surgery under local anaesthesia. No increase in complications or delay in psychomotor recovery was found. Further dose-finding studies using intranasal DEX alone in surgical procedures should be explored.

Acknowledgement
This study was supported in part by a University of Hong Kong CRCG Small Project Fund (200807176008).

Conflict of interest
None declared.

Appendix 1

Grade of operating conditions

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>Patient co-operates, operating conditions good</td>
</tr>
<tr>
<td>Fair</td>
<td>Patient moves due to over- or under-sedation, co-operation is obtained only with constant reminders and operation is difficult</td>
</tr>
<tr>
<td>Poor</td>
<td>Patient moves due to over- or under-sedation, no co-operation even with constant reminders and operation is very difficult</td>
</tr>
<tr>
<td>Very poor</td>
<td>Operation is impossible due to over- or under-sedation</td>
</tr>
</tbody>
</table>

References

6 Angst MS, Ramaswamy B, Davies MF, Maze M. Comparative analgesic and mental effects of increasing plasma concentrations of dexmedetomidine and alfentanil in humans. *Anaesthesia* 2004; 101: 744–52
29 Cheng SS, Yeh J, Flood P. Anesthesia matters: patients anesthetized with propofol have less postoperative pain than those anesthetized with isoflurane. *Anesth Analg* 2008; 106: 264–9