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RESEARCH

Sedation with alfentanil and propofol for rhizotomies

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Background: Patient safety during sedation for closed rhizotomies is improved when analgesia is optimised, rather than relying on deep sedation for patient comfort. This retrospective study determined the appropriate effect-site concentration (Ce) for alfentanil, in combination with a constant propofol infusion, for optimal pain control during sedation for closed rhizotomies. Airway maintenance is ensured by keeping patients responsive to verbal commands, albeit at the price of inevitable ventilatory depression.
Method: The records of patients who received rhizotomies over a six-month period were studied retrospectively. Sixty-three outpatients were included. Patients rated the level of analgesia with each needle placement. If the Ce for alfentanil was adequate, it was kept constant. Otherwise, it was increased in 5 ng/ml increments with each needle placement until analgesia was effective, or up to the maximum Ce for alfentanil of 100 ng/ml. Propofol infusion at a constant Ce of 200 ng/ml was added.
Results: Forty-eight per cent of patients reported being comfortable at a Ce for alfentanil of 70–75 ng/ml. Only 5% of patients requested the maximum Ce for alfentanil of 100 ng/ml. All of the patients experienced ventilatory depression, but a patent airway was maintained. The haemodynamic observations were within normal limits. According to the ward records, 16% of the patients complained of nausea, and there was one incident of vomiting.
Conclusion: Combining alfentanil at a Ce for alfentanil of 70–100 ng/ml with propofol at 200 ng/ml is a safe and effective method for analgesia during sedation for closed rhizotomies.

Keywords: alfentanil, analgesia, procedural sedation, propofol, rhizotomy, target-controlled infusion

Introduction

Modern technology enables the use of noninvasive methods of treating painful pathological conditions. Therefore, the use of sedation is an attractive alternative to general anaesthesia for transcutaneous neurosurgical procedures, such as radiofrequency neurolysis or closed rhizotomy. These procedures are still painful and may necessitate deep sedation. Deep sedation borders on general anaesthesia,[1] and is accompanied by its own perils, of which airway obstruction and loss of airway are the most common.[1,2]

Deep sedation can be avoided by maximising analgesia, and keeping patients responsive to verbal commands. This benefits both the operator and patient. The operator can better locate the area of pathology with more exact needle placement through patient interaction. Patients maintain a patent airway and are able to respond to encouragement to take deep breaths if respiratory depression occurs. The patient's response to verbal commands serves as a guide to his or her level of consciousness, and alerts the sedationist in the event of the patient drifting into a deeper level of sedation. Patients can position themselves on the operating table, thereby reducing the chance of a pressure injury.

Alfentanil's short blood-brain equilibration half-time of 1.1 minutes[3] allows fast and easy titration against painful stimuli. Performing a rhizotomy takes approximately 20–30 minutes, and necessitates a short recovery time without delayed side-effects. Alfentanil's rapid terminal half-life of 1.6 hours[4] and favourable context-sensitive half-time[5] ensure rapid recovery. Even though it is haemodynamically friendly,[6,7] its undesirable side-effects, including respiratory depression, nausea, itching[8] and muscle rigidity,[9] necessitate careful titration in conscious patients. The addition of propofol at subhypnotic doses enhances sedation and analgesia through its synergistic effects with alfentanil,[10,11] and also acts as antiemetic.[11,12]

The purpose of this retrospective study was to define the appropriate targeted effect-site concentration (Ce) for alfentanil, to be administered in conjunction with a targeted propofol infusion of 200 ng/ml, in order to optimise analgesia and sedation for closed rhizotomies. Patient safety and operating conditions during the procedure were evaluated, as well as recovery afterwards.

Method

Approval was granted by the South African Medical Association Research and Ethics Committee. The records of patients who received a closed rhizotomy over a six-month period from June to November 2009 were reviewed. The reasons for patient exclusion are shown in Table 1. Patients aged 70 years and older were excluded because of the use of a lower initial targeted alfentanil concentration.

Patients were fasted and admitted as day cases. The same anaesthesiologist performed the pre-procedure medical history and examination, as well as sedation in all of the cases. Rhizotomies were performed in the operating room by the same neurosurgeon. Premedication was not used. Patients assumed the prone position on the operating table. Supplemental oxygen, at two litres per minute, was administered using nasal prongs containing a gas-sampling port, i.e. Salter Style® Nasal Cannula (Adult) (Salter Labs, Arvin, USA). Respiratory rate (RR) and end-tidal carbon dioxide ($EtCO_2$) were monitored with capnography, together with systolic noninvasive blood pressure (NIBPS) and

Table 1: Reasons for patient exclusion

Reason for exclusion	Number
Refused sedation	3
Additional procedures performed	7
Vasovagal attack before the start of sedation	1
Faulty infusion pump	1
Patient aged 70 years and older	9
Non-functional bispectral index	1
A different protocol was used	9
Language barrier	2
Weight out of range for the Schnider model	4
Patient with upper respiratory tract infection; refused postponement	1
Data not available	7
Total	**45**

diastolic noninvasive blood pressure, pulse oximetry [oxygen saturation (SpO_2)], pulse rate [heart rate (HR)] and bispectral index (BIS) (Philips Medizinsystems, Boeblingen, Germany).

An intravenous line was established, through which crystalloids and drugs were given. Baseline observations were recorded after the patient was settled and comfortable (observation point 1). Patients received 1 mg granisetron intravenously directly before the start of the sedation to prevent nausea and vomiting. Local analgesia was not used. Pajunk® Facet Denervation Needles 22 G x 100 mm (Pajunk, Geisingen, Germany) were used for the rhizotomy and a 20 G 3.5 inch Becton Dickinson® spinal needle (Becton Dickinson and Company, Madrid, Spain) for the caudal injection of betamethasone.

Two separate target-controlled infusion pumps, i.e. Alaris® PK Syringe pumps (Alaris Medical UK Ltd, Basingstoke, UK) were used. For the first pump, a 50 ml syringe was filled with alfentanil and diluted with normal saline to 100 µg/ml. Patient data were entered into the infusion pump software using the Maître pharmacokinetic parameter set for alfentanil.[13] The Ce was targeted to start at 70 ng/ml.

The second pump was fitted with a 20 ml syringe containing 1% propofol and set up using the Schnider pharmacokinetic parameter set[14] with a constant targeted Ce of 200 ng/ml. This infusion was started as soon as the calculated Ce for alfentanil was achieved. When the calculated Ce for propofol was reached, another set of observations were obtained (observation point 2), after which the first rhizotomy needle was placed. During each needle placement, observations were recorded together with patient movement and level of analgesia. Patient movement was scored by the operator as an indication of operating conditions as follows: 0 = no movement, 1 = a flicker of movement, 2 = tensing of the back muscles and 3 = movement interrupting needle placement. The number of incidents of movement was not taken into account.

The patient rated the quality of analgesia as being either sufficient or insufficient, and these responses determined the Ce for alfentanil for the next needle placement as follows: if analgesia was adequate, the Ce for alfentanil was kept constant, and the next needle was placed. Otherwise, the Ce for alfentanil was increased stepwise in 5 ng/ml increments with each following needle placement until the patient was comfortable or up to a maximum of 100 ng/ml. With each increase in Ce for alfentanil, there was a waiting period for the calculated alfentanil concentration to reach the set target before the next needle was placed. This was repeated with each needle placement. A consistent order and number of needle placements was used for the patients in each group: 10 needle placements (observation points 3–12) for cervical (C) rhizotomies right C7–C3 and left C3–C7; and nine needle placements (observation points 3–11) for lumbar (L) rhizotomies left L3–L5, left sacral (S)1, caudal, right L3–L5 and right S1.The lumbar procedure was performed first in patients who received a lumbar and cervical rhizotomy, followed by the cervical procedure with needle placement in the same order as that set out previously (19 needle placements, observation points 3–21).

BIS was used to monitor the level of sedation. Clinical sedation scores were not recorded. However, patients had to indicate whether or not the level of analgesia was sufficient at each observation point. The patients' responses to the verbal commands served as a clinical guide to their level of consciousness.

Both infusions were discontinued after the last needle placement. Supplemental oxygen was stopped with completion of the procedure. Patients were assisted in turning from the prone position on the operating table to the supine position on their beds. Recovery room staff performed standard postoperative monitoring and determined each patient's readiness for discharge to the ward. These records were used to evaluate post-procedure patient safety. Ventilation on room air was considered to be adequate if oxygen saturation (SpO_2) was equal to or above 90% and RR at least 10/minute. Intravenous naloxone 0.4 mg was available if the RR was below 10/minute, as well as intravenous ondansetron 4 mg for nausea and vomiting.

The ward records were scanned for possible late adverse effects.

The haemodynamic changes in HR and NIBPS were calculated for each patient as a percentage change from the previous observation point. Descriptive statistics were used to characterise these changes as an average percentage change for patients at each observation point.

Pearson's product-moment correlation co-efficient test was performed to determine whether or not there was a relationship between the Ce for alfentanil and movement. One-way analysis of variance was used to determine differences in the means of duration of stay in recovery against the maximum Ce for alfentanil reached, dose rate per kg and duration of the procedure.

The data were analysed using Statistical Software for Social Sciences® 19.0.

Results

During the six-month period, 108 rhizotomies were performed, of which 45 were excluded (Tables 1 and 2). The analgesic effect was rated according to the maximum Ce for alfentanil needed for patient comfort (Table 3). Forty-eight per cent of the patients were comfortable at a Ce for alfentanil of 70–75 ng/ml. Only three patients (5%) needed the maximum allowed Ce for alfentanil of 100 ng/ml. Of these, one patient was comfortable for the remainder of the procedure, while the other two continued to experience some discomfort during the needle placements.

All of the patients were able to respond verbally when questioned about their comfort level. The mean BIS for all of the observation points in the patients was 91.1 [standard deviation (SD) 4.95]

Table 2: Patient demographics

Number of patients	**Total (63)**	**Male (26)**	**Female (37)**
Number of patients per procedure	**Lumbar (23)**	**Cervical (30)**	**Lumbar and cervical (10)**
	Mean (SD)	**Minimum**	**Maximum**
Age (years)	43 (11.00)	23.00	70.00
Weight (kg)	77.6 (14.90)	45.00	115.00
Height (m)	1.70 (0.09)	1.55	1.94
Body mass index (kg/m^2)	28.01 (9.02)	16.90	36.00

Note: SD: standard deviation

Table 3: The alfentanil profiles during the procedure

Maximum Ce for alfentanil (ng/ml)	**70**	**75**	**80**	**85**	**90**	**95**	**100**
Number (%) of patients	17 (27)	13 (21)	10 (16)	6 (10)	9 (14)	5 (8)	3 (5)
Mean total dose alfentanil (µg); (SD, 95% CI)	2 101 (363, ± 124.5)	2 157 (448, ± 244)	2 242 (387, ± 240)	2 392 (413, ± 330)	2 449 (872, ± 697)	3 064 (925, ± 810)	3 077 (975, ± 1 103)
Mean duration of infusion (minutes)	21.2	18.7	20.2	21.8	24.1	23.2	24.6
Mean alfentanil dose rate per kg (µg/kg/minute)	1.30	1.50	1.50	1.56	1.59	1.58	1.6

Note: Ce: effect-site concentration, CI: confidence interval, SD: standard deviation

(Figure 1). Five patients had at least one BIS reading below 70. However, they responded verbally when prompted.

Haemodynamic changes during the procedure are shown in Figures 2 (HR) and 3 (NIBPS). The average percentage change in HR at each observation point for all patients varied between –4% and 6% (Figure 2). There was no incident of bradycardia (HR less than 50/minute). The average percentage change in systolic blood pressure at each observation point for all the patients varied between –2% and 4% (Figure 3).

As expected, the RR decreased after the induction of sedation (Figure 4), with one episode of witnessed apnoea (loss of CO_2 trace) that resolved immediately when the patient was prompted to take deep breaths. Figure 5 shows the gradual increase in $EtCO_2$ over time. The lowest SpO_2 recorded was 90%.

Twenty-eight patients (44%) did not move at all during the needle placements and the operating conditions were excellent

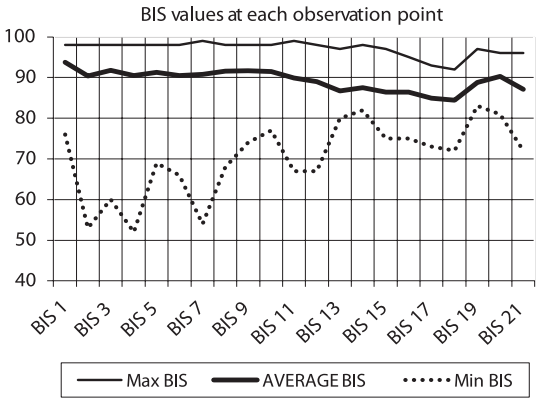

Figure 1: Bispectral index values

Note: BIS: bispectral index, max: maximum min: minimum

(Table 4). Twenty-one per cent (13 patients) moved to the extent that needle placement was interrupted. For half of these patients this only occurred once during the procedure, and was resolved when they were reminded to keep still. It is possible that factors other than pain contributed to incidents of movement, e.g. anxiety. One patient moved to some extent with each needle placement. This patient indicated that there was no need for more analgesia with each needle placement, and reached a maximum Ce for alfentanil of only 70 ng/ml. Statistical analysis showed no correlation between the maximum Ce for alfentanil and movement (Pearson's product-moment correlation coefficient = –0.026, $p = 0.825$).

Some patients exhibited wrist and finger flexion at the higher end of the dosage spectrum, as described by McDonnell et al.[15] It is uncertain whether or not this was part of the phenomenon of muscle rigidity during opioid use.

The recovery room sedation score, as determined by the recovery room staff, was 5/5 for all but two patients (Table 5). Of these two, one scored 4/5 because of the presence of pain, and the other scored 2/5, being "unresponsive to verbal commands", and scored 0 for muscle control and the presence of pain. All of the patients sustained adequate spontaneous ventilation. The lowest SpO_2 recorded was 92% on room air. No supplemental oxygen was required and naloxone was not needed. On discharge to the ward, the lowest recorded SpO_2 was 93%. The patients remained haemodynamically stable. Bradycardia and hypotension were not recorded. The average time spent in the recovery room was 16.5 minutes, from arrival until discharge to the ward. The correlation analysis showed that no variable (the maximum Ce for alfentanil reached, dose rate/kg and duration of the procedure) significantly correlated with the time spent in the recovery area ($p > 0.05$).

The ward records indicated that 10 (16%) patients reported nausea, one of whom vomited. Dizziness was mentioned in the records of four patients. One of these fell down when using the bathroom.

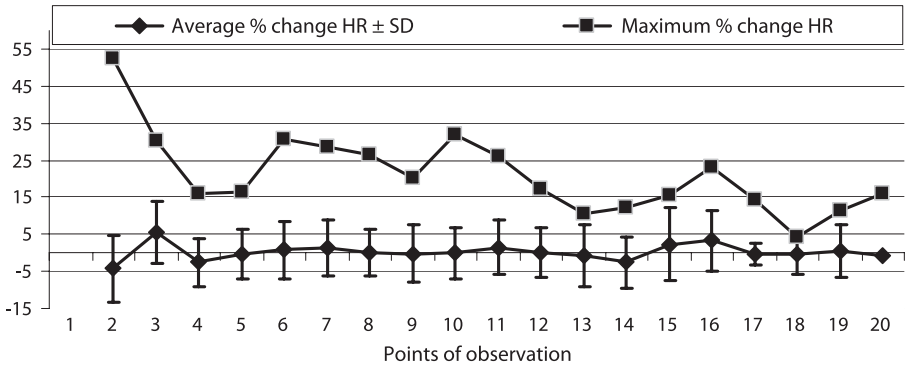

Figure 2: Percentage change in the heart rate from the preceding observation point.
Note: HR: heart rate, SD: standard deviation

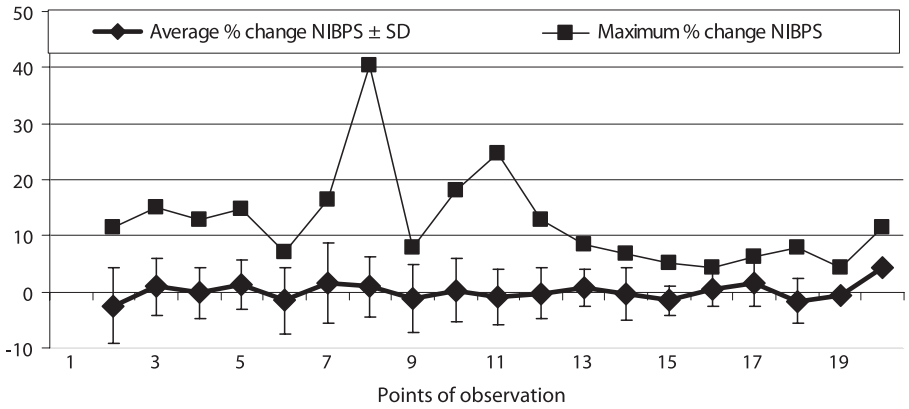

Figure 3: Percentage change in systolic blood pressure (noninvasive blood pressure monitors) from the preceding observation point
Note: NIBPS: non-invasive blood pressure systolic

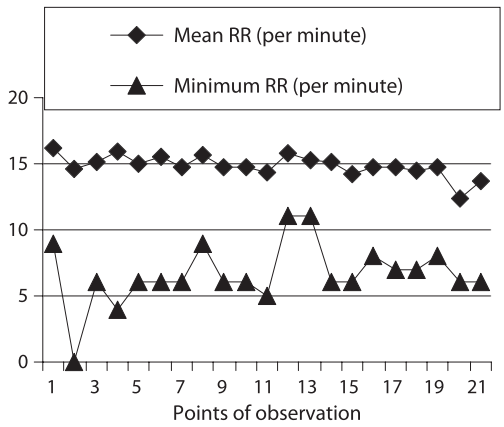

Figure 4: Mean and minimum respiratory rate
Note: RR: respiratory rate

Discussion

The purpose of this retrospective study was to define the appropriate targeted Ce for alfentanil in order to optimise analgesia for closed rhizotomies, without causing deep sedation. The therapeutic window for alfentanil was regarded as 70–100 ng/ml in the presence of a constant subhypnotic target-controlled infusion of 200 ng/ml propofol.

The optimal Ce for alfentanil should provide maximum pain relief with minimum side-effects. Alfentanil's analgesic effects are dose related[16] and vary between 40 ng/ml[10,17] and 110 ng/ml[8] for effective postoperative analgesia. Pavlin et al[10] found that combining propofol and alfentanil could produce sedation and analgesia that was greater than that observed with either drug alone. They stated that plasma propofol concentrations in excess of 800 ng/ml, especially when combined with alfentanil, were associated with "extensive sedation and tendency toward upper airway obstruction".[10] Their study demonstrated loss of "alertness and increased sedation" at target plasma propofol concentrations as low as 150 ng/ml, in the presence of a target alfentanil infusion of only 40 ng/ml. Vuyk et al[18] modelled the expected optimal propofol and alfentanil concentration combinations associated with adequate anaesthesia that would result in the most rapid recovery after termination of target controlled infusions of different durations. They estimated that the plasma alfentanil concentration at which awakening occurs vary between 64.6 ng/ml and 73 ng/ml in the presence of much higher propofol concentrations than that used in the current study.

Based on the Vuyk study[18] the Ce for alfentanil in our study, starting at 70 ng/ml, combined with a very modest target propofol concentration of 200 ng/ml, was chosen to ensure analgesia with some sedation without causing loss of consciousness.

Some studies also suggest that subhypnotic doses of propofol reduce sensitivity to pain.[10,19,20] Therefore, it is possible that propofol reduced pain by itself, apart from its synergistic analgesic effects

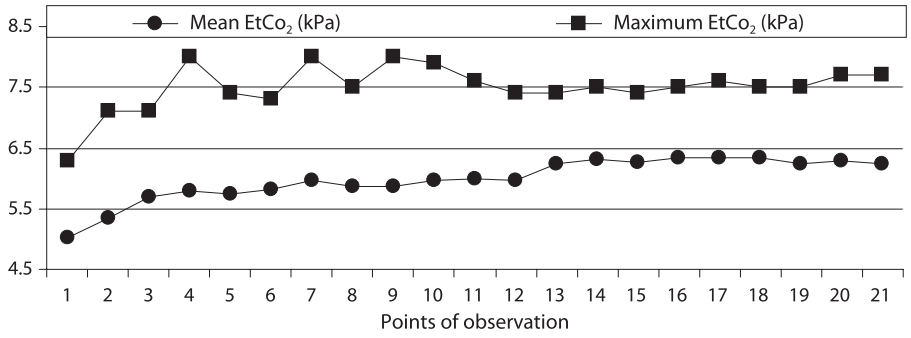

Figure 5: Mean and maximum end-tidal carbon dioxide.
Notes: $EtC0_2$: end-tidal carbon dioxide

Table 4: Maximum movement score observed

Maximum movement score observed*	**0**	**1**	**2**	**3**
Number (%) of patients	28 (44)	9 (14)	13 (21)	13 (21)

*: 0 = no movement; 1 = flicker of movement; 2 = tensing of back muscles; 3 = movement interrupting needle placement.

Table 5: Recovery room scoring system

Level of consciousness	Responsive to verbal commands	1
	Unresponsive to verbal commands	0
Systolic blood pressure	≥ 90 mmHg	1
	< 90 mmHg	0
Colour and perfusion	*Skin:* Normal and warm	1
	Skin: Pale, cold and cyanosed	0
Muscle control: Lift head for five seconds and grip hand firmly	Patient able to do this	1
	Patient unable to do this	0
Pain	Pain free	1
	Pain present	0
Score required for discharge to ward		**5**

when combined with alfentanil. Pavlin et al[10] reported that the analgesic synergism between propofol and alfentanil appeared to plateau at a plasma alfentanil concentration beyond approximately 100 ng/ml.

All of the patients remained conscious for the duration of the procedure, even though the alfentanil dose rate expressed as µg/kg/minute (Table 3) was high compared to the mean maintenance rate of 0.45 µg/kg/minute used in the study by Sherry,[21] and that of 0.3 µg/kg/minute (20 µg/kg/hour) by O'Connor et al.[8] Thirty patients (48%) were comfortable at a Ce for alfentanil of 70–75 ng/ml and 60 (95%) at a Ce for alfentanil of 70–95 ng/ml. Therefore, a Ce for alfentanil of 70–75 ng/ml can be regarded as a good starting point, and can be titrated upwards, if necessary. Only three patients (5%) required the maximum Ce for alfentanil of 100 ng/ml. After the maximum Ce for alfentanil was reached, two of the three patients continued to experience some discomfort during some of the needle placements. It is possible to enhance patient comfort in this small subset by increasing the Ce for propofol, taking into account that patients may drift into deep sedation with clinically important respiratory depression and loss of airway. To prevent this, patient responses must be monitored carefully throughout the procedure. Further studies are necessary to determine the optimal alfentanil and propofol combination to gain maximum analgesia without impeding consciousness.

Several studies demonstrated that the BIS is a sensitive measure of depth of sedation,[22,23] and also correlates with the observer's assessment of awareness and sedation scale (OAA/S) (5 = responds readily to name called in a normal tone to 1 = does not respond to mild prodding or shaking).[22,23] Data from the study by Liu et al suggested that a BIS value of 85–90 correlated with an OAA/S score of 3 (responds only if name is called out loudly or repeatedly). The OAA/S was not recorded in the present study. However, since all of the patients were able to respond when questioned about their level of analgesia, and none of them needed prodding or shaking in order for a response to be elicited, it can be assumed that they were sedated to a level of at least 3–5 using the OAA/S. This correlates with the mean BIS value of 91.1 (SD 4.95) in the present study. It is possible that patient arousal was caused by the painful stimulus of the needle placements, as well as the regular verbal questioning regarding the patient's level of analgesia, and might have affected the BIS. Furthermore, reports have suggested that BIS values may be influenced by the types of drugs used. The addition of fentanyl, nitrous oxide or alfentanil to a propofol anaesthetic increased the BIS value at which loss of response to voice command occurred.[24–26] The individual BIS scores also showed wide variability, as seen in the minimum BIS score recorded at each observation point (Figure 1). BIS values between 65 and 85 have been recommended for sedation, while values from 45–60 have been recommended for general anaesthesia.[27] The mean BIS values over all of the observation points indicated

that the BIS score remained well above the level of deep sedation and general anaesthesia (Figure 1).

Clinically important ventilatory depression was expected to occur at a Ce for alfentanil of 100 ng/ml, based on work carried out by O'Connor et al.,[8] and Andrews et al.,[28] who determined that moderate respiratory depression occurred at stable alfentanil plasma concentrations of 108 ng/ml and 120 ng/ml, respectively. The influence on spontaneous breathing, when an opioid and a hypnotic were combined, was obvious as witnessed by the decrease in RR (Figure 4) and increase in $EtCO_2$ (Figure 5). However, since the patients remained responsive to verbal commands, they were able to oblige requests to take deep breaths. More importantly, there were no cases of airway obstruction, and even at a higher Ce for alfentanil, intervention was not required to maintain a patent airway. There was also no need to reduce the rate of either infusion.

The lack of cardiovascular depression during the procedure confirmed the haemodynamic safety of the drug combination when carefully titrated to the desired Ce. Furthermore, the fairly constant mean HR and NIBPS over all of the observation points confirmed the ability of opioids, in this case, alfentanil, to blunt the autonomic responses that follow a noxious stimulation. It then seems that alfentanil, through its action on the opioid receptors in the spinal cord, successfully prevented the noxious stimulus from reaching the higher centres in the brain.

There was no relationship between the Ce for alfentanil reached in each patient and the movement score during the needle placements in patients who received either a cervical or lumbar rhizotomy. There was a clear relation between movement score and the Ce for alfentanil reached in patients who received both a lumbar and cervical rhizotomy. This may be explained by the longer duration of these procedures versus the individual lumbar or cervical procedures. Pavlin et al[10] found that when propofol and alfentanil were given in combination, a pharmacokinetic interaction occurred that led to an increased plasma concentration of both drugs. It is possible that owing to the longer duration of infusion during the combined procedure, the actual Ce of both the drugs was higher than that predicted by the infusion pump. This possibility is in line with the gradual decline observed in the average BIS values from observation point 13 onwards.

The postoperative period is very important as far as safety is concerned. Lingering drugs may cause patients to drift into deeper levels of sedation once the stimulation of the procedure has been withdrawn.[1,29] This was possibly the case for the one patient in the present study who scored 2/5 for being "unresponsive to commands" on arrival in the recovery room. However, the postoperative records indicate that the patient did not need airway intervention, breathing spontaneously at 16/minute and with a SpO_2 of 100% on room air. This patient's recovery room stay was 17 minutes, comparable to the average in this study. The importance of monitoring patients after sedation was underscored by this incident.

Recurrent respiratory depression after alfentanil infusion is one possibility with respect to late adverse effects. It has been described over a wide range of doses and duration of infusions,[29–31] occurring approximately 45 minutes after the infusion was stopped. According to the postoperative ward records, there were no cases of recurrent respiratory depression in any of the patients in the present study.

Propofol is useful for its antiemetic properties.[10] The plasma concentration of propofol for a 50% reduction in the nausea scores in a group of postoperative patients was 343 ng/ml.[32] The Ce for propofol of 200 ng/ml used in the present study is in line with that of Schulman et al,[33] who determined the plasma concentration of propofol for the successful treatment of nausea in a postoperative patient to be 197 ng/ml. In spite of the antiemetic prophylaxis with granisetron and the use of propofol in the infusion, a total of 10 patients (nine females and one male), i.e. 16% postoperatively, reported nausea, one of whom vomited. All of the cases resolved after a 4 mg bolus dose of ondansetron intravenously. It is interesting to note that all the cases of nausea, as well as the one case of vomiting, occurred when the patients were already back in the ward. It is uncertain if this related to food intake or mobilising the patients. The ward notes also indicated four cases of dizziness, with one patient falling down. It is unknown whether this was because of dizziness or owing to temporary muscle weakness after the lumbar rhizotomy.

The minimum alfentanil plasma or Ce at which muscle rigidity occurs is not known. Nauta et al[34] described the "ideal rate of alfentanil infusion in terms of minimising chest wall rigidity and induction time" as being 50 ug/kg/minute. Through computer simulation, it is estimated that an infusion rate of 50 ug/kg/minute alfentanil should result in steady state plasma and a Ce above 300 ng/ml. This is well above the maximum Ce for alfentanil of 100 ng/ml used in this study.

The use of opioids commonly causes pruritis.[17] The incidence of pruritus in this study was not recorded. An itchy nose was mentioned by some patients, but was not disruptive to the procedure.

There were limitations to this retrospective study. The plasma levels of alfentanil and propofol were not measured. It is possible that the actual plasma and the Ce for alfentanil and propofol were higher than the predicted values because of pharmacokinetic and pharmacodynamic interactions. Owing to pharmacokinetic variability, infusions must be titrated and adjusted for each individual patient. When generalising the findings to elderly and sick patients, it is essential to start the Ce for alfentanil at the lower end of the therapeutic window. As a safety precaution, the opioid should be started first in order to evaluate its sedative effects before propofol is added. It may be valuable to increase the Ce for propofol in patients who are not comfortable even at a higher Ce for alfentanil until the desired level of sedation and pain control is achieved. Patient responsiveness needs to be monitored carefully, as higher doses of propofol may cause excessive sedation, airway obstruction and delayed recovery.

Remifentanil often replaces alfentanil in sedation for painful procedures. Even though its pharmacokinetic profile is very similar to that of alfentanil,[35] its potency (20 times more potent than alfentanil)[35] and its rapid breakdown by tissue and blood esterases are its greatest assets. During sedation, a remifentanil infusion is often combined with a propofol infusion. Owing to remifentanil's ultra-short, context-sensitive half-time, a rapid return of consciousness is certain, even after a prolonged infusion.[18] More research is needed to determine the remifentanil dose range at which patients will be comfortable during rhizotomies.

The fact that remifentanil can be harmful in inexperienced hands has led to a recommendation in the South African Society of Anaesthesiologists sedation guidelines that it should not be used outside the hospital environment.[36]

Conclusion

The results of this retrospective study indicate that the combination of alfentanil, at a Ce for alfentanil of 70–100 ng/ml, and propofol at 200 ng/ml, is a safe and effective method for analgesia during sedation for closed rhizotomies. By effectively controlling the patients' pain during needle placement, it was possible to keep them responsive to verbal commands and to avoid deep sedation with airway compromise. Alfentanil should be carefully titrated upwards while patients are being adequately monitored.

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References

1. American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology. 2002;96:1004–17.
2. Nunn JF. Oxygen, applied respiratory physiology. 4th ed. Oxford: Butterworth-Heinemann; 1993. p. 247–305.
3. Scott JC, Ponganis KV, Stanski DR. EEG quantitation of narcotic effect. Anesthesiology. 1985;62:234–41. http://dx.doi.org/10.1097/00000542-198503000-00005
4. Stanski DR. The clinical pharmacology of alfentanil. Eur J Anaesth. 1987;S1:3–11.
5. Hughes M, Glass PSA, Jacobs JR. Context-sensitive half-time in multicompartment pharmacokinetic models for intravenous anesthetic drugs. Anesthesiology. 1992;76:334–41. http://dx.doi.org/10.1097/00000542-199203000-00003
6. De Lange S, Stanley TH, Boscoe MJ. Alfentanil-oxygen anaesthesia for coronary artery surgery. Br J Anaesth. 1981;53:1291–302. http://dx.doi.org/10.1093/bja/53.12.1291
7. Duggan M, Carey M. High dose alfentanil as sole anaesthetic induction agent for caesarean section in a patient with severe ischaemic heart disease. Int J Obstet Anesth. 2000;9:186–8. http://dx.doi.org/10.1054/ijoa.1999.0368
8. O'Connor M, Escarpa A, Prys-Roberts C. Ventilatory depression during and after infusion of alfentanil in man. Br J Anaesth. 1983;55S:217–22.
9. Ausems ME, Hug CC, de Lange S. Variable rate infusion of alfentanil as a supplement to nitrous oxide anesthesia for general surgery. Anesth Analg. 1983;62:982–6.
10. Pavlin DJ, Coda B, Shen DD, et al. Effects of combining propofol and alfentanil on ventilation, analgesia, sedation, and emesis in human volunteers. Anesthesiology. 1996;84:23–37. http://dx.doi.org/10.1097/00000542-199601000-00004
11. Avramov MN, White PR. Use of alfentanil and propofol for outpatient monitored anesthesia care: determining the optimal dosing regimen. Anesth Analg. 1997;8:566–72.
12. Borgeat A, Wilder-Smith OHG, Saiah M, et al. Subhypnotic doses of propofol possess direct anti-emetic properties. Anesth Analg. 1992;74:539–41.
13. Maitre PO, Vozeh S, Heykants J, et al.. Population pharmacokinetics of alfentanil. Anesthesiology. 1987;66:3–12. http://dx.doi.org/10.1097/00000542-198701000-00002
14. Schnider TW, Minto CF, Gambus PL, et al. The influence of method of administration and covariates on the pharmacokinetics of propofol in adult volunteers. Anesthesiology. 1998;88:1170–82. http://dx.doi.org/10.1097/00000542-199805000-00006
15. McDonnell TE, Bartkowski RR, Williams JJ. ED50 of alfentanil for induction of anesthesia in unpremedicated young adults. Anesthesiology.1984;60:136–40.http://dx.doi.org/10.1097/00000542-198402000-00010
16. Hill H, Walter MH, Saeger L, et al. Dose effects of alfentanil in human analgesia. Clin Pharmacol Ther 1986;40:178–86. http://dx.doi.org/10.1038/clpt.1986.161
17. Hill HF, Chapman CR, Saeger LS, et al. Steady-state infusions of opioids in humans: II. Concentration–effect relationships and therapeutic margins. Pain. 1990;43:69–79.
18. Vuyk J, Mertens MJ, Olofsen E, et al. Propofol anesthesia and rational opioid selection. Anesthesiology. 1997;87:1549–62. http://dx.doi.org/10.1097/00000542-199712000-00033
19. Wilder-Smith O, Borgeat A. Algesia with subhypnotic doses of thiopentone and propofol. Br J Anaesth. 1991;67:226–7. http://dx.doi.org/10.1093/bja/67.2.226
20. Anker-Møller E, Spangsberg N, Arendt-Nielsen L, et al. Subhypnotic doses of thiopentone and propofol cause analgesia to experimentally induced acute pain. Br J Anaesth. 1991;66:185–8. http://dx.doi.org/ 10.1093/bja/66.2.185
21. Sherry E. Admixture of propofol and alfentanil. Anaesthesia. 1992;47:477–9. http://dx.doi.org/10.1111/ana.1992.47.issue-6
22. Glass PS, Bloom M, Kearse L, et al. Bispectral analysis measures sedation and memory effects of propofol, midazolam, isoflurane, and alfentanil in healthy volunteers. Anesthesiology. 1997;86:836–47. http://dx.doi.org/10.1097/00000542-199704000-00014
23. Liu J, Singh H, White PF. Electroencephalographic bispectral index correlates with intraoperative recall and depth of propofol-induced sedation. Anesth Anal. 1997;84:185–9.
24. Kearse LA, Rosow C, Zaslavsky A, et al. Bispectral analysis of the electroencephalogram predicts conscious processing of information during propofol sedation and hypnosis. Anesthesiology. 1998;88:25–34. http://dx.doi.org/10.1097/00000542-199801000-00007
25. Iselin-Chaves IA, Flaishon R, Sebel PS, et al. The effect of the interaction of propofol and alfentanil on recall, loss of consciousness, and the bispectral index. Anesth Analg. 1998;87:949–55.
26. Mi WD, Sakai T, Singh H, et al. Hypnotic endpoints vs. the bispectral index, 95% spectral edge frequency and median frequency during propofol infusion with or without fentanyl. Eur J Anaesthesiol. 1999;16:47–52.
27. Johansen Jay W. Update on bispectral index monitoring. Best Pract Res Clin Anaesthesiol. 2006;20(1):81–99.
28. Andrews CJH, Sinclair M, Prys-Roberts C, et al. Ventilatory effects during and after continuous infusion of fentanyl or alfentanil. Br J Anaesth. 1983;55(S2):211–6.
29. Geerts P, Noorduin H, Vanden Bussche G, et al. Practical aspects of alfentanil infusion. Eur J Anaesth. 1987;S1:25–9.
30. Mahla ME, White SE, Moneta MD. Delayed respiratory depression after alfentanil. Anesthesiology. 1988;69:593–4. http://dx.doi.org/10.1097/00000542-198810000-00021
31. Jaffe RS, Coalson D. Recurrent respiratory depression after alfentanil administration. Anesthesiology. 1989;70:151–3. http://dx.doi.org/10.1097/00000542-198901000-00031
32. Gan TJ, Glass PSA, Howell ST, et al. Determination of plasma concentrations of propofol associated with 50% reduction in postoperative nausea. Anesthesiology. 1997;87:779–84. http://dx.doi.org/10.1097/00000542-199710000-00010
33. Schulman SR, Rockett CB, Canada AT, et al. Long-term propofol infusion for refractory postoperative nausea: a case report with quantitative propofol analysis. Anesth Analg. 1995;80:636–7.
34. Nauta J, De Lange S, Koopman D, et al. Anesthetic induction with alfentanil: a new short-acting narcotic analgesic. Anesth Analg. 1982;61:276–82.
35. Egan T, Minto C, Hermann D, et al. Remifentanil versus alfentanil. Anesthesiology.1996;84:821–33.http://dx.doi.org/10.1097/00000542-199604000-00009
36. SASA Sedation Guidelines 2010. S Afr J Anaesthesiol Analg. 2010;16(2):S11. http://sedationsa.co.za/images/Sedation%20Guideline%20adult%202010.FINAL.pdf.

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