Desflurane accelerates patient response during the wake-up test for scoliosis surgery

[Le desflurane hâte la réponse du patient pendant le test de réveil pendant le test de réveil d'une intervention chirurgicale pour scoliose]

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Purpose: To evaluate if desflurane possesses a shorter wake-up onset time and less incidence of recall than fentanyl-based anesthesia.

Methods: Forty ASA class I–II adolescents, were enrolled into either a desflurane (DES) group, or a fentanyl (FEN) group for scoliosis surgery. Bispectral index (BIS) was monitored continuously in all patients throughout the procedure; the relationship between the wake-up time and BIS value was evaluated.

Results: Patients in the DES group had a significantly shorter wake-up onset than patients in the FEN group (4.1 ± 0.6 vs 8.9 ± 2.1 min, $P < 0.01$). No recall occurred during the wake-up test in the DES group, while five patients had recall in the FEN group, including two patients who recalled a given colour. Extubation time was significantly shorter in the DES group than in the FEN group (7.2 ± 0.6 vs 16 ± 11.9 min, $P < 0.01$).

BIS values were significantly higher in the FEN group than in the DES group during anesthesia. (62 ± 4.5 vs 42 ± 5.3 , $P < 0.05$) BIS after the wake-up test was similar in both groups (90 ± 2.9 vs 93.8 ± 2.5). There was a latency period (3.3 ± 1.2 min) between the maximal BIS value and wake-up time in the FEN group but not in the DES group.

Conclusions: DES provides a significantly shorter onset time during the wake-up test and a rapid emergence after scoliosis surgery. BIS monitoring during the wake-up test was more informative when anesthesia was maintained with DES compared to FEN infusion.

Objectif: Vérifier si l'anesthésie avec du desflurane présente un réveil plus hâtif et moins d'incidence de souvenir que l'anesthésie avec du fentanyl.

Méthode : Quarante adolescents d'état physique ASA I–II ont fait partie des groupes desflurane (DES) ou fentanyl (FEN) pour l'opération d'une scoliose. L'index bispectral (BIS) a été enregistré en continu chez tous les patients tout au long de l'intervention ; la relation entre le délai de réveil et la valeur du BIS a été évaluée.

Résultats : Le retour à la conscience des patients du groupe DES a été significativement plus court que celui des patients du groupe FEN ($4,1 \pm 0,6$ vs $8,9 \pm 2,1$ min, $P < 0,01$). Pendant le test de réveil, aucun patient du groupe DES n'a eu de souvenir, mais cinq patients du groupe FEN en ont eu, y compris deux patients qui ont pu nommer une couleur donnée. Le moment de l'extubation a été significativement plus tôt avec le DES qu'avec le FEN ($7,2 \pm 0,6$ vs $16 \pm 11,9$ min, $P < 0,01$).

Pendant l'anesthésie, les valeurs du BIS ont été plus élevées avec le FEN qu'avec le DES ($62 \pm 4,5$ vs $42 \pm 5,3$, $P < 0,05$). Après le test de réveil, le BIS était similaire dans les deux groupes ($90 \pm 2,9$ vs $93,8 \pm 2,5$). Il y a eu un temps de latence ($3,3 \pm 1,2$ min) entre les valeurs maximales de BIS et le moment du retour à la conscience dans le groupe FEN, mais non dans le groupe DES.

Conclusion : Le DES permet un réveil significativement plus hâtif, révélé par le test de réveil, et un retour rapide à la conscience à la suite de l'opération d'une scoliose. Le monitoring du BIS pendant le test de réveil est plus informatif quand l'anesthésie est maintenue avec une perfusion de DES plutôt que de FEN.

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THE wake-up test has been used routinely to monitor neurological deficits during scoliosis surgery.^{1,2} Anesthesia for scoliosis surgery is commonly performed using balanced anesthesia with a fentanyl (FEN) infusion and nitrous oxide. Providing a rapid onset of wake up is a challenge for the anesthesiologist during scoliosis surgery. Desflurane (DES) has the advantage of rapid recovery due to a lower blood: gas solubility coefficient.³⁻⁶ We evaluated the onset time of wake up during DES and balanced anesthesia for scoliosis surgery. The bispectral index (BIS) correlates with consciousness during adult anesthesia, but limited data on the correlation of BIS with consciousness are available during the wake-up test for scoliosis surgery. A secondary objective of this study was to evaluate BIS during the wake-up test in scoliosis surgery.

Methods

Patients

With informed consent and approval of the Institutional Committee on Human Investigation, 40 ASA class I–II patients undergoing surgical correction of scoliosis were enrolled. Patients were excluded if they had any neurological disability, impaired hearing, epilepsy, or were taking antiepileptic, sedative, or stimulant medication. Prior to the study, we educated and explained the wake-up test procedure to the patients: they would be asked to move their fingers first then to move their toes and finally to remember a given colour during the test. The surgical technique was similar for all patients. An independent study nurse recorded all data.

Anesthesia

After premedication with midazolam ($0.08 \text{ mg}\cdot\text{kg}^{-1}$), anesthesia was induced with propofol ($2 \text{ mg}\cdot\text{kg}^{-1}$, *iv*) and FEN ($5 \text{ }\mu\text{g}\cdot\text{kg}^{-1}$, *iv*); atracurium was used to facilitate endotracheal intubation. The patients were divided randomly into two groups of 20. The randomization schedule was computer generated by a biostatistician (not otherwise involved in the study). The randomization schedule specified the group (I or II) to which each prospective patient would be allocated upon enrollment in the trial. An opaque envelope containing the patient number and group assignment was prepared, sealed, and numbered for each patient. In the DES group, anesthesia was maintained with DES (end-tidal 6–8%) and N_2O ($2 \text{ L}\cdot\text{min}^{-1}$) in O_2 ($1 \text{ L}\cdot\text{min}^{-1}$). In the FEN group, anesthesia was maintained with a FEN ($3 \text{ g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$) continuous infusion and N_2O ($2 \text{ L}\cdot\text{min}^{-1}$) in O_2 ($1 \text{ L}\cdot\text{min}^{-1}$). Intraoperative monitors included pulse

oximetry, electrocardiogram, non-invasive blood pressure, end-tidal anesthetic concentration and end-tidal capnography. Right radial arterial and jugular vein cannulation were performed and pressure was measured continuously. Rectal temperature was maintained at 37°C by using a warming blanket. The compound electromyogram of the adductor pollicis muscle was recorded using a Datex neuromuscular transmission monitor. Neuromuscular block was elicited by an intermittent *iv* bolus injection of atracurium to maintain one twitch of the train-of-four during anesthesia. Arterial oxygen saturation, mean arterial blood pressure (MAP), central venous pressure, respiratory rate and heart rate (HR) were also recorded simultaneously.

A disposable BisSensor (Aspect Medical Systems, Newton, MA, USA) was applied to the forehead of each patient before the induction of anesthesia and connected to a bispectral index (BIS) Model A-2000 monitor (Aspect Medical Systems, Newton, MA, USA). The BIS was monitored continuously in all patients throughout the procedure. T_1 was defined as the time before starting the wake-up test; T_2 was the time of maximal BIS value. T_3 was the time when the patient followed the verbal command to move his/her fingers and toes. Mean blood pressure was maintained at 80 mmHg by the infusion of nitroglycerin as required.

Wake-up procedure

Thirty minutes before the wake-up test, the administration of atracurium was interrupted, allowing the train-of-four count to recover gradually. Small doses of a reversal agent (edrophonium and atropine) were given if the train-of-four count did not recover to four. When the wake-up test was begun, either DES or the FEN infusion was terminated. The patient was first asked to move his/her fingers and this was repeated every 15 sec until the patient responded. The patient was then instructed to move both his/her fingers and toes and, finally, was asked to remember a given colour.

When the wake-up test was completed, patients were reanesthetized with a bolus of propofol and anesthesia maintained with either DES (end-tidal 6–8%) or a FEN infusion ($3 \text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$) as before. Neuromuscular blockade was re-established. By the end of surgery, the anesthetics were discontinued and the patient's lungs were ventilated with 100% oxygen with a fresh gas flow of $6 \text{ L}\cdot\text{min}^{-1}$. The time to the first spontaneous motion was recorded. Response to verbal command to open the eyes, and orientation to body parts (left *vs* right, mouth *vs* eyes, toes *vs* hands) were assessed in a uniform method at one-minute intervals.

TABLE I Demographics and baseline hemodynamic variables

	DES group (n = 20)	FEN group (n = 20)
Age (yr)	15.4 ± 2.4	15.3 ± 2.9
Weight (kg)	49.8 ± 5.6	44.3 ± 5.7
Height (cm)	158 ± 10	156 ± 11
Baseline mean arterial pressure (mmHg)	85 ± 18	83 ± 10
Baseline mean HR (beats/min)	86 ± 13	84 ± 17

Values are mean SD. DES = desflurane; FEN = fentanyl.

TABLE II Changes in BIS and hemodynamic variables during the wake-up test

	DES group (n = 20)	FEN group (n = 20)
Anesthesia duration before wake up (T ₀ -T ₁ , min)	340.3 ± 96.2	300.7 ± 78.5
Onset of wake up (T ₁ -T ₃ , min)	4.1 ± 0.6	8.9 ± 2.1*
Latency (T ₂ -T ₃ , min)	0.0 ± 0.2	3.3 ± 1.2*
BIS value		
at T ₁	42 ± 5.3	62 ± 4.5*
at T ₃	90.0 ± 2.9	93.8 ± 2.5
MAP (mmHg)		
at T ₁	63.6 ± 5.4	58.4 ± 8.2
at T ₃	85.5 ± 5.5	
	80.2 ± 8.7	
HR (beats·min ⁻¹)		
at T ₁	99.6 ± 13.1	85.9 ± 13.6
at T ₃	98.4 ± 14.1	97 ± 10.3

Values are mean ± SD. **P* < 0.05. DES = desflurane; FEN = fentanyl; T₀ = time of induction; T₁ = start of wake-up test; T₂ = time of maximal BIS value; T₃ = time when patient responds to verbal command and orientated; BIS = bispectral index; MAP = mean arterial pressure; HR = heart rate.

TABLE III RECALL FOLLOWING THE WAKE-UP TEST

	DES group (n = 20)	FEN group (n = 20)
Recall of Intraoperative events (before and after wake-up test)	0	0
Recall during wake-up test		
Total	0	5 (25%)*
Recall of colour	0	2 (10%)*
Pain during wake-up test	0	0

DES = desflurane; FEN = fentanyl; **P* < 0.05.

TABLE IV ORIENTATION AND EXTUBATION TIME

	DES group (n = 20)	FEN group (n = 20)
Spontaneous movement (min)	4.4 ± 0.5	4.2 ± 0.7
Response to verbal command (min)	4.5 ± 0.7	8.4 ± 1.8*
Orientation to Body parts (min)	6.4 ± 0.8	14.4 ± 2.3*
Time to extubation (min)	7.2 ± 0.6	16 ± 11.9*

DES = Desflurane; FEN = fentanyl. Values are mean ± SD. **P* < 0.05.

All patients were extubated before they were sent to the postanesthesia care unit.

On the day following surgery, the patients were interviewed to ascertain whether they remembered intraoperative events including pain, voice or the given colour during the wake-up test. All patients in both groups received *iv* morphine patient controlled analgesia (PCA) for postoperative pain control. The loading dose of *iv* PCA was morphine 0.05 mg·kg⁻¹, with a continuous infusion of 0.015 mg·kg⁻¹. The PCA dose was 0.02 mg·kg⁻¹ with a lockout interval of ten minutes and a four-hour maximum dose of 10 mg morphine.

For statistical analysis, the wake-up time and the BIS values at T₁ and T₃ were compared within each group using a paired Student's *t* test and between each group using an unpaired Student's *t* test. Time to response (T₃-T₁) was analyzed by the Kaplan-Meier method. Values were considered significant when *P* < 0.05. Results are presented as mean ± SD. The power of the study was calculated.

Results

Demographic data were similar between the two groups. All demographic and baseline hemodynamic data are shown in Table I.

Duration from induction of anesthesia to start of the wake-up test was not significantly different between the two groups (Table II). Onset of wake up was significantly shorter in the DES group than in the FEN group (4.1 ± 0.6 *vs* 8.9 ± 2.1 min, *P* < 0.01). There were significant increases in BIS, MAP, and HR from T₁ to T₃ in both groups. Changes in mean BIS value, MAP, and HR during the wake-up test are shown in Table II. Before the wake-up test, the BIS value was significantly higher in the FEN group than in the DES group during surgery, but the BIS value at the end of the wake-up test was similar in both groups (Table II). The time required to reach T₃ was longer in FEN patients compared to DES patients. In addition, there was a latency period (T₂ to T₃) (3.3 ± 1.2 min) between the maximal BIS value and wake-up in the FEN group but not in the DES group (Table II and Figures 1-3).

There were nine patients in the FEN group who required a nitroglycerin infusion to maintain a mean blood pressure of 80 mmHg compared to none in the DES group.

During the postoperative follow-up, there was no recall during the wake-up test in the DES group compared to five patients who had recall in the FEN group (Table III).

Patients in the DES group recovered more rapidly from anesthesia than patients in the FEN group (Table IV).

FIGURE 1 Typical recording of bispectral index in a desflurane patient. T_1 to T_3 was four minutes (T_1 = start of wake-up test; T_3 = time when patient responds to verbal command and orientated). T_2 (time of maximal BIS value) corresponds to T_3 .

FIGURE 2 Typical recording of bispectral index in a fentanyl patient. T_1 to T_3 was nine minutes. There is a delay between T_2 and T_3 .

Discussion

In our study, we demonstrated a significantly shorter onset time of patient response during the wake-up test with DES anesthesia. This shorter onset time is consistent with DES's low solubility in blood and body tissues, and low blood: gas partition coefficient of 0.4.³⁻⁶ Our results are also compatible with a previous report that an increase in the duration of anesthesia does not significantly delay recovery of consciousness.⁶

Our results also showed that no patient in the DES group but 25% patients in the FEN group had recall with two remembering the colour given during the

FIGURE 3 Kaplan-Meier curves of onset of response during the wake-up test for desflurane and fentanyl groups.

test. The BIS value of these five patients was not different from that of the other FEN patients. The incidence of recall in our study is comparable to that reported by McCann *et al.*⁷ who observed that 17.5% of patients with FEN anesthesia had recall. This result suggests that DES may be superior to FEN during maintenance of anesthesia for the wake-up test during scoliosis surgery.

Bispectral analysis is a well known mathematical technique of signal processing that quantifies the degree of phase coupling between different frequency components within a signal. The BIS yields the best combination of sensitivity and specificity of any commercially available depth-of-anesthesia monitoring device,^{8,9} and has been reported to be an alternative technique for the wake-up test.⁷ Our data show that BIS values were lower during DES anesthesia than during FEN anesthesia. BIS values do not appear to be independent of the anesthetic agent administered,¹⁰⁻¹³ therefore, comparable BIS values achieved with different agents may not represent the same depth of anesthesia.¹¹⁻¹⁴ The current BIS algorithm was derived from patients anesthetized with predominantly hypnotic drugs, such as propofol and inhaled anesthetics.¹⁴⁻¹⁸ Therefore, the BIS value for adequate anesthesia or wake up will vary among patients and among anesthetic regimens. The effect of narcotics on BIS level is not as clear as with other drugs. In our study, BIS values were high in the FEN group (> 60) during maintenance of anesthesia, but without recall of intraoperative events. This suggests that BIS values in opioid-based anesthesia may be different than with other techniques.¹⁷

The wake up from anesthesia has to ensure not only that the patient responds to verbal command but also that the patient is orientated to body parts (moving the toes). The recovery time from anesthesia for these two categories of response varies with different anesthetic agents. The slow response to orientation was responsible for the latency period between the maximal BIS value and patient awakening. Our results show that the final BIS value was greater than 90 when the patient woke up and that there was a latency period between the maximal BIS value and patient awakening in the FEN group but not in the DES group. Patients in the FEN group did not respond to the command to move their toes for few minutes when BIS values were greater than 90. This would imply that the maximal BIS value adequately reflects the time of awakening in DES patients but not in FEN patients. It has been shown previously that DES anesthesia is associated with a rapid emergence and faster response to verbal command and orientation.⁶

In conclusion, DES provides a significantly shorter wake-up time and a rapid emergence from anesthesia. BIS monitoring during the wake-up test was more informative when anesthesia was maintained with DES compared to FEN infusion.

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