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RECOVERY OF COGNITIVE FUNCTIONS AFTER ANAESTHESIA WITH DESFLURANE OR ISOFLURANE AND NITROUS OXIDE†

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SUMMARY

We studied recovery in 25 adult patients, ASA I, undergoing elective orthopaedic procedures after anaesthesia with 0.65 MAC desflurane (n = 16) or isoflurane (n = 9) with 60% nitrous oxide in oxygen. Early emergence from anaesthesia was assessed in the operating room by measuring time to spontaneous movement, cough, response to painful pinch, tracheal extubation, opening of the eyes and stating correct age, name and body parts. The return of cognitive functions in the late recovery phase was assessed in the post-anaesthesia care unit (PACU) by post-anaesthesia recovery scores (PARS), the Trieger dot test (TDT), and the digit substitution test (DST). In the early recovery phase, time to tracheal extubation, opening eyes, telling correct name, age and body parts occurred significantly faster in the desflurane group than in the isoflurane group ($P < 0.05$). The mean "triple orientation" time (to name, age, body parts) was 10.9 (SEM 0.9) min for desflurane, compared with 18.6 (2.5) min for isoflurane ($P < 0.01$). In the late recovery phase, desflurane patients had significantly greater PARS, more correct responses to the DST and fewer error responses to the TDT. Recovery times were not increased by increased duration of desflurane anaesthesia. The desflurane patients showed no delirium, minimal sedation and less shivering during the entire postoperative course. We conclude that desflurane anaesthesia was superior to isoflurane anaesthesia, not only in emergence, but also in the recovery of cognitive functions.

KEY WORDS

Anaesthetics, volatile: desflurane, isoflurane. Recovery: cognitive function.

Isoflurane ($CF_2H–O–CClH–CF_3$) has a blood:gas solubility coefficient of 1.40 at 37 °C—less than that of enflurane or halothane [1, 2]. This accounts for the rapid return of consciousness after isoflurane anaesthesia. Desflurane ($CF_2H–O–CFH–CF_3$) is a new, promising volatile anaesthetic. The fluorine substitution of the single chlorine atom of isoflurane markedly decreases the blood:gas solubility coefficient of desflurane, to 0.42 [3]. Rapid emergence and faster awakening from desflurane anaesthesia have been observed in the rat [4] and in earlier clinical studies [5]. In this study we have evaluated the different phases of recovery from 0.65 MAC desflurane or isoflurane anaesthesia with 60% nitrous oxide in oxygen.

PATIENTS AND METHODS

We studied 25 male patients, aged 18–42 yr, weighing 73 (SD 10) kg, undergoing elective orthopaedic surgery on the limb. The study was approved by the Research and Education Institute and informed consent was obtained. Only ASA I patients were enrolled. To compare the recovery between these two agents, we measured the time to early recovery of consciousness in the operating room and used a modified post-anaesthesia recovery score (PARS) of Aldrete and Kroulik [6] (including the count-down test) (table I), the Trieger dot test (TDT) [7] and the digit substitution test (DST) [8] for assessment of the late recovery of cognitive functions in the post-anaesthesia care unit (PACU). In the TDT, a figure was outlined in a series of 41 dots and the patient was asked to join the dots without missing any. We standardized a time allowance of 40 s to complete the test. Scoring was made by counting the dots missed. In the DST, the patient was asked to substitute 20 single digits, 0–9, each with its specific symbol. The correct matching of the symbols with the corresponding digits completed in a 90-s period of time was counted. In the count-down test, the patient was asked to count backwards from 10 to 0 as quickly as possible, 30 s allowed. Before operation, the TDT, DST and the count-down test were explained to the patients and baseline values obtained. Patients failing any item in any test were excluded.

Premedication comprised midazolam 1–2 mg given in divided doses i.v. Eighteen patients were assigned to desflurane ($n = 9$) or isoflurane ($n = 9$) by a randomized table. Seven patients were added later to the desflurane group to satisfy the requirement of the study outlined in table IV. Patients were monitored

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TABLE I. *Post-anaesthesia recovery score (PARS)*

	Score
Consciousness	
Easily arousable, alert	3
Arousable, oriented, not alert	2
Arousable, not oriented	1
Not responding	0
Ventilation	
Normal	2
Not perfect, but requires no support	1
Airway requires support	0
Circulation (mean, supine and sitting)	
Arterial pressure difference	
<10%	2
10–20%	1
>20%	0
Heart rate difference	
<10%	2
10–20%	1
>20%	0
Horizontal nystagmus	
Follow command—no nystagmus	2
Follow command—nystagmus	1
Fail to follow command	0
Count-down test (backward from 10 to 0)	
Succeed right away	2
Succeed in 30 s	1
Fail in 30 s	0

with an arterial pressure device (Datascope Accutorr IA), electrocardiograph (Physiocontrol VSMI), pulse oximeter (Nellcor), nasal temperature probe and Puritan–Bennett Datex 254 airway gas monitor for measuring inhaled and exhaled concentrations of desflurane or isoflurane.

Anaesthesia was induced with thiopentone 5 mg kg^{-1} i.v., followed by 2 mg kg^{-1} in 2 min. Anaesthesia was then deepened with desflurane or isoflurane via a face mask to a level of approximately 2 MAC, for intubation of the trachea without using neuromuscular blocking agents. The trachea was sprayed with 4% lignocaine 4 ml. After intubation of the trachea, the anaesthetic agents were adjusted to maintain a stable exhaled concentration of 0.65 MAC (4.7% desflurane or 0.8% isoflurane) combined with 60% nitrous oxide in oxygen throughout surgery. Ventilation was controlled to maintain end-tidal carbon dioxide at 4.3–4.7 kPa. Oesophageal temperature was maintained at 36–37 °C by placing the patient on a warming mattress. During operation, atracurium was the only neuromuscular blocking drug used, and all patients had neuromuscular transmission restored fully to a train-of-four ratio of 1 towards the end of surgery, by antagonizing any residual neuromuscular block with neostigmine. Fentanyl 50 μg was administered approximately 30 min before the anticipated discontinuation of anaesthesia. Normal end-tidal carbon dioxide was ascertained at the end of surgery.

At the end of surgery, the anaesthetics were discontinued. The duration of inhalation anaesthesia was noted. The patient's lungs were ventilated with 100% oxygen with a fresh gas flow of 6 litre min^{-1}. The times to the first spontaneous motion and cough were noted. Response to painful pinch and to verbal command to open eyes, and orientation to age, name and body parts (left *vs* right, mouth *vs* eyes, toe *vs* hand) were assessed in a uniform method at 1-min intervals until all three orientations ("triple orientation") were completed. The modified PARS (table I) was measured every 15 min for 2 h. Recovery of cognitive functions was evaluated by the count-down test, the DST and the TDT every 15 min until complete recovery was observed. All anaesthesia was administered by one designated investigator; recovery was assessed by another. The patient was observed continuously for any shivering or delirium, the latter defined as incomprehensible or disoriented behavioural or verbal expression. Results are presented as mean (SE). Desflurane and isoflurane groups were compared with Student's t or chi-square test. Subgroups of desflurane patients receiving anaesthesia of various durations were compared by ANOVA. $P < 0.05$ was considered statistically significant in either case.

RESULTS

Patient characteristics and duration of anaesthesia were similar for the desflurane and isoflurane groups (table II). Desflurane patients showed faster emergence and awakening in the early recovery phase (table III). Time to respond to verbal command by opening eyes was 7.8 (0.7) min after desflurane and 14 (1.9) min after isoflurane ($P < 0.05$). The triple orientation time to age, name and body parts was 10.9 (0.9) min in the desflurane group and 18.6 (2.5) min in the isoflurane group ($P < 0.05$). There was no significant difference in time to first cough, spontaneous movement or reaction to painful pinch. There was no correlation or trend between recovery time and the duration of desflurane anaesthesia, which was less than 100 (86 (4)) min in five patients, 100–150 (125 (5)) min in six patients and greater

TABLE II. *Demographics of patients (mean (range or SE)). No significant differences*

Group	Age (yr)	Weight (kg)	Anaesthesia duration (min)
Desflurane ($n = 16$)	28	75 (3.0)	146 (17)
Isoflurane ($n = 9$)	26	73 (3.1)	149 (23)

TABLE III. *Recovery from 0.65 MAC desflurane or isoflurane anaesthesia with 60% nitrous oxide in oxygen (mean (SE)). *P < 0.05, desflurane vs isoflurane*

	Recovery time (min)	
	Desflurane ($n = 16$)	Isoflurane ($n = 9$)
Spontaneous activity		
Cough	5.6 (0.7)	8.5 (1.1)
Motion unrelated to cough	5.8 (0.8)	7.9 (1.3)
Response to		
Painful pinch	6.1 (0.7)	8.7 (1.3)
Verbal command	7.8 (0.7)*	14.0 (1.9)
Orientation to		
Age	10.5 (0.9)*	17.6 (2.5)
Name	10.9 (0.9)*	17.9 (2.4)
Body parts	10.0 (0.9)*	18.1 (2.4)
All three	10.9 (0.9)*	18.6 (2.5)
Extubation	7.4 (0.7)*	11.1 (1.3)

TABLE IV. *Recovery from desflurane–nitrous oxide anaesthesia independently of duration of anaesthesia (mean (SE)). No significant differences*

Duration of anaesthesia:	Recovery times (min)		
	< 100 min (86 (4)) ($n = 5$)	100–150 min (125 (5)) ($n = 6$)	> 150 min (229 (26)) ($n = 5$)
Spontaneous movement	5.6 (0.9)	7.0 (1.6)	4.4 (0.6)
Reaction to painful pinch	6.8 (1.3)	6.2 (1.3)	5.4 (0.6)
Response to verbal command	8.2 (1.1)	8.7 (1.4)	6.2 (0.7)
Orientation to			
Age	10.4 (1.7)	12.0 (1.8)	8.8 (0.6)
Name	11.4 (1.5)	12.0 (1.8)	9.0 (0.8)
Body parts	10.4 (1.3)	12.0 (1.9)	8.4 (0.7)
All three	11.4 (1.5)	12.0 (1.8)	9.0 (0.7)
Extubation	8.2 (1.1)	7.8 (1.6)	6.2 (0.8)

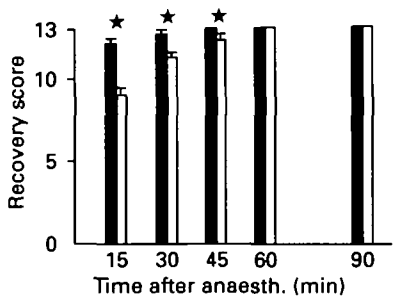

FIG. 1. Mean (SE) PARS after 0.65 MAC desflurane (■) or isoflurane (□) anaesthesia with 60% nitrous oxide in oxygen. *$P < 0.05$.

than 150 (229 (26)) min in another five patients. Their times to response to verbal command were 8.2 (1.1) min, 8.70 (1.4) min and 6.2 (0.7) min, respectively; their times to triple orientation were 11.4 (1.5) min, 12.0 (1.8) min and 9.0 (0.7) min ($P > 0.05$) (table IV).

In the PACU, desflurane patients had significantly greater recovery scores during the first 45–60 min (fig. 1). Desflurane patients demonstrated significantly fewer error responses on the TDT, and more correct responses on the DST (fig. 2). The time to tracheal extubation was also significantly shorter after desflurane anaesthesia (7.4 (0.7) min *vs* 11.1 (1.3) min) ($P < 0.05$). Desflurane patients had no delirium, whereas 44% of isoflurane patients had delirium of varying degree ($P < 0.05$). Shivering occurred in 12.5% of the desflurane group and in 56% of the isoflurane group ($P < 0.05$).

DISCUSSION

It is desirable to have a fast recovery from anaesthesia, especially after day-case surgery. Our data showed that after termination of anaesthesia, the desflurane patients had greater PARS scores for 45–60 min and reached complete scores earlier than the isoflurane patients. Additionally, the desflurane patients had a better performance on both the TDT and the DST.

Rapid emergence from desflurane anaesthesia is a result of its low blood:gas partition coefficient of 0.40, which is similar to that of nitrous oxide (0.44) and significantly smaller than that of isoflurane (1.40) [1,3,9]. The finding that desflurane patients did not cough, move spontaneously or respond to painful pinch earlier than isoflurane patients is not necessarily surprising. In addition to emergence from anaesthesia, many factors affect the cough reflex and response to noxious stimulation. Spontaneous motion indicates wakefulness or emergence excitement, and early spontaneous motion may imply either rapid emergence from anaesthesia or slow emergence through the excitement stage.

The isoflurane patients often appeared drowsy even after they had become oriented to age, name and body parts. This residual drowsiness probably accounted for delay in recovery of cognitive functions. Furthermore, commenting upon the cognitive function tests, several isoflurane patients stated that they perceived distortion of the symbols and numbers of the DST even after they had managed to pass the TDT. It appears, therefore, that the DST was the most sensitive test for the residual cortical depression. Suitability of the DST as a sensitive measurement of the late-stage recovery of cortical function has been demonstrated previously by Boerner and colleagues [8] after prolonged infusion of alfentanil. Fletcher and colleagues [10] recently described complex psychomotor performance tests for the assessment of recovery from desflurane anaesthesia. Our results substantiated their findings, although our methods are simpler and easier to use.

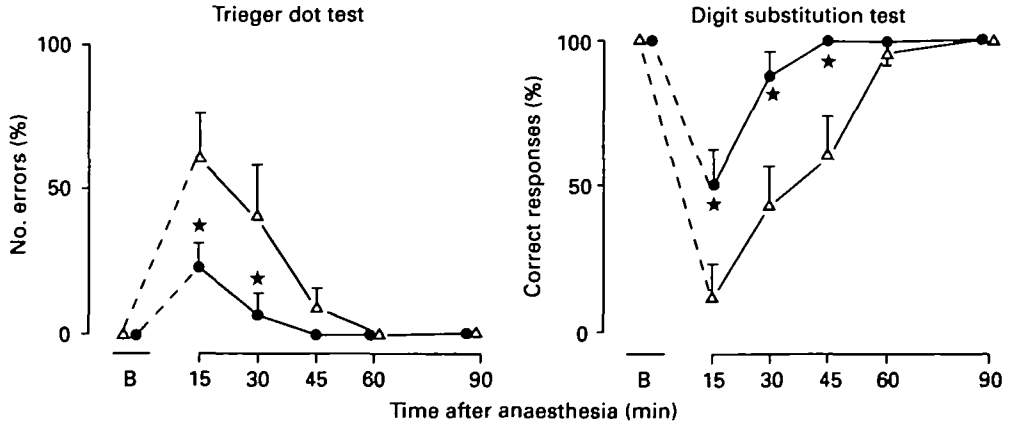

FIG. 2. Mean (SE) TDT and DST before (B) and after 0.65 MAC desflurane (●) ($n = 16$) or isoflurane (△) ($n = 9$) anaesthesia with 60% nitrous oxide in oxygen. *$P < 0.05$.

In addition to having minimal postoperative sedation, the desflurane patients also demonstrated no delirium and less shivering. Postoperative delirium is related to age, pain and drug effects [11]. As our patients did not differ in these factors, the absence of delirium in the desflurane group can be attributed to rapid transition from anaesthesia to consciousness. Shivering increases tissue oxygen consumption by as much as 400–500% [12] and initiates other undesirable side effects, such as accentuated cardiac work and hypoxaemia. Because the desflurane and isoflurane patients had similar oesophageal temperatures and were managed identically, a lesser incidence of shivering during emergence from desflurane anaesthesia is possibly related to the rapid return of central thermoregulatory mechanisms.

An increase in the duration of desflurane anaesthesia did not delay recovery of consciousness. Because of its low solubility, desflurane equilibrates rapidly between body compartments. As a result, an increase in the duration of anaesthesia does not significantly increase the amount of anaesthetic stored in the body.

REFERENCES

1. Cromwell TH, Eger EI II, Stevens WC, Dolan WM. Forane uptake, excretion and blood solubility in man. *Anesthesiology* 1971; **35**: 401–408.
2. Munson ES, Eger EI II, Tham MK, Embro WJ. Increase in anesthetic uptake, excretion, and blood solubility in man after eating. *Anesthesia and Analgesia* 1978; **57**: 224–231.
3. Eger EI II. Partition coefficients for I-653 in human blood, saline, and olive oil. *Anesthesia and Analgesia* 1987; **66**: 971–973.
4. Eger EI II, Johnson BH. Rates of awakening from anesthesia with I-653, halothane, isoflurane and sevoflurane: A test of the effect of anesthetic concentration and duration in rats. *Anesthesia and Analgesia* 1987; **66**: 977–982.
5. Smiley R, Ornstein E. Emergence from desflurane anesthesia is more rapid than from isoflurane. *Anesthesia and Analgesia* 1990; **70**: S378.
6. Aldrete JA, Kroulik D. A postanesthetic recovery score. *Anesthesia and Analgesia* 1970; **49**: 924–934.
7. Newman MG, Trieger N, Miller JC. Measuring recovery from anesthesia—A simple test. *Anesthesia and Analgesia* 1969; **48**: 136–140.
8. Boerner TF, Bartkowski RR, Goldberg ME, Torjman M, Odoriso L, Deluca P. Cognitive recovery after prolonged alfentanil infusion: Midazolam and diazepam. *Anesthesia and Analgesia* 1990; **70**: S27.
9. Stoelting RK, Eger EI II. The effect of ventilation and anesthesia solubility on recovery from anesthesia: An *in vivo* and analog analysis before and after equilibrium. *Anesthesiology* 1968; **30**: 290–296.
10. Fletcher JE, Sebel PS, Murphy MR, Smith CA, Mick SA, Flister MP. Psychomotor performance after desflurane anesthesia: A comparison with isoflurane. *Anesthesia and Analgesia* 1991; **73**: 260–265.
11. Eckenhoff JE, Kneale DH, Dripps RD. The incidence and etiology of postanesthetic excitement. *Anesthesiology* 1961; **22**: 667–673.
12. Ray J, Nunn JF, Prys-Roberts C. Factors influencing arterial Po_2 during recovery from anaesthesia. *British Journal of Anaesthesia* 1968; **40**: 398–407.