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Aging prolongs recovery of psychomotor functions at emergence from propofol-alfentanil anaesthesia

Purpose: To compare recovery of psychomotor function in elderly and young surgical patients at emergence from propofol-alfentanil anaesthesia.

Methods: Ten elderly (> 70 yr) and 10 younger (< 40 yr) patients scheduled for orthopaedic surgery of less than three hours, were anesthetized with nitrous oxide, propofol and alfentanil. Propofol and alfentanil cumulative doses, time from cessation of propofol infusion to eye opening (EO) on verbal command and to extubation were recorded. Psychomotor performance was assessed by the Mini-Mental State (MMS) performed the day prior to surgery and postoperatively at 30, 60, and 120 min. following extubation. Propofol blood concentrations were measured at EO and at each MMS task.

Results: Elderly patients were comparable with young patients for preoperative MMS scores, surgery and anaesthesia duration, propofol and alfentanil cumulative doses. Postoperative MMS scores were lower at 30, 60 and 120 min. in elderly patients. Propofol blood concentrations were not different between elderly and young patients at EO, 30, 60 and 120 min.

Conclusion: Psychomotor performance is impaired in elderly compared with young patients at emergence from propofol-alfentanil anaesthesia. These differences are not likely to be related to propofol accumulation in elderly subjects.

Objectif : Comparer la récupération de la fonction psychomotrice chez des patients âgés et de jeunes patients lors du réveil après une anesthésie au propofol et à l'alfentanil.

Méthode : Dix patients âgés (> 70 ans) et 10 jeunes patients (< 40 ans), dont la chirurgie orthopédique de moins de trois heures avait été prévue, ont reçu une anesthésie avec du protoxyde d'azote, du propofol et de l'alfentanil. On a enregistré les doses cumulatives de propofol et d'alfentanil, le temps entre l'arrêt de la perfusion de propofol et l'ouverture des yeux (OY), d'après une commande verbale, et le moment de l'extubation. Le rendement psychomoteur a été évalué par le test MMS de Folstein et coll. (Mini-Mental State) administré le jour précédent la chirurgie et, après la chirurgie, 30, 60 et 120 min. après l'extubation. Les concentrations sanguines de propofol ont été mesurées à l'OY et à chaque tâche du test MMS.

Résultats : Les rendements au MMS préopératoire, la durée de la chirurgie et de l'anesthésie et les doses cumulatives de propofol et d'alfentanil étaient comparables entre les jeunes patients et les patients âgés. Les rendements MMS postopératoires ont été plus bas à 30, 60 et 120 min chez les patients âgés. Les concentrations sanguines de propofol n'étaient pas différents entre les deux groupes de patients à l'OY, et à 30, 60 et 120 min.

Conclusion : Le rendement psychomoteur est altéré chez les patients âgés par rapport aux jeunes patients au moment du réveil après l'anesthésie au propofol et à l'alfentanil. On ne peut probablement pas relier ces différences à l'accumulation de propofol chez les patients âgés.

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Supported by INSERM and the Délégation à la Recherche Clinique, Assistance Publique des Hôpitaux de Paris, Paris, France (grant AOM 95024).

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Presented in part at the Annual Meeting of the American Society of Anesthesiologists, New Orleans, Louisiana, October 19-23, 1996.

Accepted for publication September 26, 1998

AGING is associated with a decrease in requirement for intravenous anaesthetics.^{1,2} However, little is known of the influence of aging on the time-course of recovery of cognitive functions after anaesthesia and surgery. In a previous study, neuropsychological function was found to be impaired on the first postoperative day following intraabdominal surgery, but this cognitive dysfunction was transient and similar in young and elderly patients.³ In the present study we compared psychomotor performance at emergence from anaesthesia between young and elderly patients undergoing elective orthopaedic surgery under propofol-alfentanil anaesthesia.

Methods

After institutional approval and written informed consent, 20 patients, ASA 1 or 2 physical status scheduled for elective orthopaedic surgery (< 3 hr) were prospectively allocated to an elderly (> 70 yr) or young (< 40 yr) group. Exclusion criteria were outpatients, unstable angina, severe myocardial dysfunction, a history of anaphylactic reaction during previous anaesthesia and the inability to perform MMS (0 - 32 score)⁴ (see appendix) because of language barrier or a score < 25/32.

Patients received no premedication and atropine was not administered, since anticholinergic medication has been associated with postoperative confusion.⁵ Anaesthesia was induced by propofol (20 mg·kg⁻¹·hr⁻¹ for 5 min.) and 5 µg·kg⁻¹ alfentanil. Succinylcholine (0.08 mg·kg⁻¹) was used to facilitate orotracheal intubation, and no other neuromuscular blocking agent was given. Mechanical ventilation (O₂ 60% -N₂O 40%) was initiated to keep P_{ET}CO₂ between 30 and 35 mmHg. Esophageal temperature was controlled to 37°C by surface warming (Bair Hugger devices). The maintenance rate of propofol infusion was based on a stepwise infusion regimen (12 mg·kg⁻¹·hr⁻¹ for 10 min., and 6 mg·kg⁻¹·hr⁻¹ until the end of the procedure). These infusion rates were modified to maintain MAP and/or HR within -30% and -10% of the baseline values when appropriate. Additional alfentanil boluses, 5 µg·kg⁻¹, were given when necessary except during the last 30 min of anaesthesia. Propofol infusion was stopped after skin closure and tracheas were extubated when the spontaneous breathing was restored (respiratory rate > 10 min⁻¹).

The data recorded were age, weight, pre-, intra- and postoperative blood pressure and HR, propofol and alfentanil cumulative doses, time from cessation of propofol administration to EO and extubation, duration of surgery and anaesthesia defined as the times from induction of anaesthesia to skin closure and

extubation, respectively. Psychomotor performance was assessed by the MMS the day prior to surgery. The MMS, sedation and pain scores (see appendix) were performed in the postoperative care unit, at 30, 60, and 120 min after extubation. At these times and at EO, five ml arterial blood samples were drawn for determination of propofol blood concentration. Postoperative analgesia was achieved with intravenous propacetamol and morphine was not given. The occurrence of nausea and vomiting, hypoxaemia (one or more episodes of oxygen saturation 80% for two minutes) and severe hypotension (MAP decrease > 30% of the preinduction value over five minutes) was also noted.

Statistics

Results are expressed as mean ± SEM. Statistical analysis was performed using the Mann-Whitney-Wilcoxon test, a *P* value < 0.05 being considered significant.

Results

Patients were comparable for weight and duration of anaesthesia and surgery. No difference was observed in propofol and alfentanil total intraoperative requirements between the groups (Table I). No major difference was observed between the two groups with respect to HR or MAP (Table II).

Postoperative MMS scores were lower in elderly patients at 30, 60 and 120 min. after extubation, while the sedation scores were similar between the two groups at the same times (Table III). Pain scores at these times were also comparable. No major side effect, particularly nausea or vomiting, was observed in the recovery room in the two groups. Propofol blood concentrations were not different between the two groups at any time.

TABLE I Demographic and intraoperative DATA.

	<i>Elderly</i>	<i>Young</i>	<i>P</i>
Number (n)	10	10	
Age (n)	76 ± 2	29 ± 1	0.0004
Weight (kg)	67 ± 3	65 ± 4	NS
Duration of surgery (min)	99 ± 21	59 ± 13	NS
Duration of anaesthesia (min)	118 ± 19	76 ± 16	NS
P total dose (mg·kg ⁻¹ ·hr ⁻¹)	10 ± 1	13 ± 2	NS
A total dose (mg·kg ⁻¹ ·hr ⁻¹)	24 ± 6	36 ± 6	NS
Time to EO (min)	18 ± 5	17 ± 3	NS
Time to extubation (min)	19 ± 5	17 ± 3	NS

Data: mean ± SEM

P = propofol, A = alfentanil, EO = eye opening.

TABLE II Intraoperative hemodynamic variations in young and elderly patients.

Time	MAP (mmHg)	Elderly P vs control for MAP	HR (b.min ⁻¹)	P vs control for HR	MAP (mmHg)	Young P vs control for map	HR (b.min ⁻¹)	P vs control for HR
Control	111 ± 7		79 ± 3		94 ± 4		76 ± 6	
+ 2 min	86 ± 7	0.02	75 ± 4	NS	80 ± 3	0.009	68 ± 5	0.03
+ 4 min	78 ± 7	0.007	70 ± 4	NS	76 ± 4	0.005	69 ± 7	0.01
+ 6 min	84 ± 4	0.005	68 ± 4	0.02	84 ± 4	0.02	72 ± 5	NS
+ 10 min	81 ± 4	0.01	72 ± 4	NS	78 ± 8	0.01	80 ± 10	NS
+ 15 min	87 ± 5	NS	72 ± 5	NS				
Incision	84 ± 5	0.019	65 ± 4	0.011	78 ± 6	0.005	63 ± 4	0.028
+ 2 min	84 ± 3	0.012	63 ± 4	0.007	85 ± 7	NS	66 ± 4	NS
+ 5 min	83 ± 4	0.019	66 ± 6	0.03	83 ± 8	NS	66 ± 4	NS
+ 10 min	78 ± 5	0.012	67 ± 5	NS	85 ± 7	NS	60 ± 4	0.007
Extubation	99 ± 7	NS	72 ± 6	NS	97 ± 5	NS	87 ± 6	NS
+ 10 min	100 ± 7	NS	72 ± 5	NS	91 ± 4	NS	80 ± 7	NS
+ 30 min	101 ± 6	NS	71 ± 4	NS	94 ± 4	NS	66 ± 4	0.02
+ 60 min	101 ± 5	NS	71 ± 4	NS	89 ± 4	NS	66 ± 4	NS
+ 120 min	96 ± 3	NS	76 ± 6	NS	86 ± 3	NS	71 ± 4	NS

Data are expressed as mean ± SEM

MAP = mean arterial pressure, HR = heart rate, control values were obtained just before induction of anaesthesia.

TABLE III Psychomotor performance of patients at emergence from anaesthesia and propofol blood concentrations.

		Elderly	Young	P
SS (0-4)	30 min	3 ± 0.3	4 ± 0.2	NS
	60 min	3 ± 0.2	4 ± 0.2	NS
	120 min	4 ± 0.2	4 ± 0.2	NS
MMS (0-32)	pre-op	30 ± 1	31 ± 0.4	NS
	30 min	16 ± 5	30 ± 1	0.018
	60 min	25 ± 3	31 ± 0.5	0.012
	120 min	26 ± 2	31 ± 0.4	0.011
P blood conc. (ng.ml ⁻¹) EO		1560 ± 101	1717 ± 305	NS
	30 min	1038 ± 223	1467 ± 178	NS
	60 min	736 ± 115	844 ± 95	NS
	120 min	557 ± 146	538 ± 50	NS

Data: mean ± SEM

SS = sedation scores, MMS = Mini Mental State, P. blood conc. = propofol blood concentrations,

EO = cyc opening.

Discussion

The main observation made in this study was that psychomotor performance in elderly and young patients differed at the time of emergence from propofol-alfentanil anaesthesia.

Several hypotheses can be proposed to explain this observation. Age-related differences in sensitivity to alfentanil seem unlikely, since alfentanil pharmacodynamics have been found to be similar in elderly and in

younger patients.⁶ Also, postoperative hypotension and hypoxaemia, which could contribute to confusion,⁵ were not noted in the postoperative care unit. Pain management was standardized and was unlikely to have influenced patient outcome in this study.

It could be argued that elderly patients exhibited altered postoperative psychomotor performances because they were maintained at higher intraoperative blood concentrations. However, propofol cumulative doses were not different between the two groups. Although we did not use the bispectral index of the EEG to measure depth of anaesthesia, no differences in intraoperative hemodynamic variations were observed between groups. A slower clearance of propofol in the elderly group is also not supported by our data since no elevation of arterial propofol blood concentrations was observed in patients aged > 70 yr at EO and at each MMS trial.

More likely, differences in the response of elderly patients to the same effect site concentration could contribute to this postoperative cognitive dysfunction. Interestingly, elderly-related changes in the sensitivity of specific carriers located on presynaptic GABA (a major target of anesthetics in the brain) nerve endings have been recently demonstrated in the rat.⁷ It can be speculated that these or other related pharmacodynamic responses to propofol might apply to elderly patients.

In conclusion, our results support the hypothesis that aging alters recovery of psychomotor function at emergence from propofol-alfentanil anaesthesia.

Acknowledgment

Authors thank Dr Frédérique Servin for insightful discussion.

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Appendix

Modified version of "Mini-Mental State" evaluation

Score

Orientation:

- / 5 * What is the (year) (season) (date) (day) (month)?
- / 4 * Where are we (state) (town) (hospital) (ward)?

Recall:

- / 4 * *Anterograde amnesia:* look at 4 pictures taken out of a children's game of "memory", 1 every second. 5 minutes later, find the pictures amongst 20 others.
- / 3 * *Retrograde amnesia:* On the first evaluation, the patient memorizes any 3 events he chooses (eg: I came to the hospital in a blue taxi; the nurses are kind, my room mate snores ...). On the following evaluations, he is asked to recall them.

Attention:

- / 2 * Spell backwards a simple five letters word (a different one every time).

0 if no response

1 if incorrect

2 if correct

Reasoning:

- / 5 * look at a paper on which are written 2 letters (eg: A-B) and answer by true or false the following sentences:

A is after B B is before A

B is not followed by A A is before B

A is not before B

(letters and sentences are different every time)

Language:

- / 2 * Name two usual objects (pen, key...)
- / 2 * Repeat the following: "no ifs, ands or buts" (0 if does not repeat, 1 if non accurate, 2 if accurate)
- / 1 * Read and obey a simple command (ex: CLOSE YOUR EYES)
- / 2 * Write down the previous command
- / 2 * copy a simple drawing
- / 32 Total score

Pain score: 0 = no pain, 1 = mild, 2 = moderate and 3 = severe.

Sedation score: 0 = asleep, not arousable, 1 = asleep, but arousable, 2 = drowsy, 3 = awake and quiet calm, 4 = fully awake and responsive.