Title : PHARMACOKINETICS OF SUFENTANIL IN THE ELDERLY

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INTRODUCTION

With increasing age, there are changes in body volumes and metabolism which might influence the kinetics of sufentanil, a new potent synthetic narcotic congener of fentanyl (1). Therefore we compared the kinetics of sufentanil (SF) in elderly subjects to those in young adults.

METHODS

After approval of the local ethical committee and informed consent, nine elderly subjects (71-82 years, one male) and nine young adults (19-45 years, five males) were studied. All were ASA I or II and underwent orthopedic surgery. Patients were premedicated by oral flunitrazepam 1-2 mg. Anesthesia was induced with thiopental 5-10 $mg.kg^{-1}$. Pancuronium 0.1 $mg.kg^{-1}$ was used to facilitate endotracheal intubation, and ventilation controlled to keep $PaCO_2$ at 35 mmHg. Anesthesia was maintained with 60 % N_2O in O_2. After induction of anesthesia, SF 3 $mcg.kg^{-1}$ was administered as a 3 min IV infusion. No further SF was used. If necessary thiopental or fentanyl were injected. Blood samples were collected from a radial canula at 1,3,5,10,15,30,60 min, every hour until the 9^{th} hour, then at the 24^{th} and 36^{th} hour. The samples were centrifuged and plasma separated, frozen and later assayed for SF concentration by radioimmunoassay sensitive to 0.05 $ng.ml^{-1}$. During anesthesia hepatic blood flow (HBF) was determined by measuring the indocyanine green plasma clearance. Two and three compartments models were fit to drug concentration versus time data using a weighted non linear least square regression. The following pharmacokinetic parameters were determined : clearance (Cl), volume of distribution of the central compartment (VC), volume of distribution (Vd), volume of distribution at steady state (Vdss), half lives for the initial two phases (tl/2 tl/2), elimination half life (tl/2).
Data are expressed as mean $\pm$ sem. Statistical analysis was by Student's t test for unpaired data and by analysis of variance ; $p<0.05$ was considered significant.

RESULTS

The mean pharmacokinetic data are listed in table I. The only significant difference between the two groups is the initial plasma concentrations (C_p). The delay of recovery was the same in the two groups. SF produced hypotension significantly greater in the elderly.

DISCUSSION

The pharmacokinetics of SF including clearance, half lives, VC, Vdss, do not show a significant correlation with age, a result which has been reported for other narcotics (2,3). Higher plasma concentrations of SF in the elderly for the first three minutes after injection do not cause a change in the duration of action, but may be a determinant of the hemodynamic changes in elderly.

Table I : Pharmacokinetics data

	Elderly n = 9	Young Adults n = 9
C_p at 1 min $ng.ml^{-1}$	9.78±5.28	5.92±2.24*
C_p at 3 min $ng.ml^{-1}$	5.16±1.97	3.84±1.46*
tl/2 α (min)	2.26±1.09	1.61±0.88
tl/2 α (min)	17.48±10.17	14.35±6.01
tl/2 β (h)	4.45±1.83	3.48±0.98
Vc (l)	0.316±0.150	0.370±0.168
Vdβ $(l.kg^{-1})$	4.27±1.49	3.18±0.70
Vdss $(l.kg^{-1})$	3.16±1.13	2.58±0.52
Cl $(ml.min^{-1}.kg^{-1})$	11.10±3.29	11.24±3.01
HBF $(ml.min^{-1})$	1030±238	1292±423

*p<0.05

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