

Title: INFLUENCE OF AGE AND GENDER ON INDUCTION DOSE OF THIOPIENTAL

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Introduction. It is generally agreed that the induction dose of thiopental is reduced in elderly patients^{1,2}. It has been suggested that this can be explained on a pharmacokinetic rather than a pharmacodynamic basis^{2,3} although the nature of this is not clear⁴.

In clinical practice the combination of pathologic states and ageing can engender acute sensitivity to thiopental in the geriatric patient. We here report a large clinical study confined strictly to ASA 1 and 2 post-puberty patients in an attempt to evaluate the influence of ageing alone on thiopental dosage avoiding the added effect of associated pathologic states. The requirements of thiopental in the two sexes were also compared.

Method. The study, which was approved by the University Medical Ethical Research Committee was carried out on fit, unpremedicated patients scheduled for elective operations under general anesthesia, for which thiopental was the induction agent of choice. All were non-drinkers or drank only on rare occasions. Weights ranged from 40-85 kg.

Thiopental 2.0 mg kg⁻¹ was injected into a large forearm vein over 20 s. At 15 s intervals thereafter 25 mg increments were given until the eyelash reflex was abolished or contact lost with the patients, the total dose of thiopental administered being taken as the induction dose¹. All observations were made by one of the three authors. Results were analysed using analysis of variance on log-transformed data. In comparing the influence of sex, independent 't' tests were carried out on log-transformed data.

Results. Table 1 shows a highly significant (P < 0.001) reduction in thiopental requirements with age in both sexes

F for 7 and 246 df = 10.3 for women

F for 7 and 174 df = 14.2 for men

In both sexes the larger standard deviation of the mean in the younger patients indicates a greater scatter of induction doses.

Table 1. Mean±SD induction dose of thiopental (mg kg⁻¹) by decades of age in men and women.

yr	MALE	n	FEMALE	n
-19	4.94±1.663	25	4.36±1.000	21
-29	4.75±1.189	25	4.35±1.308	39
-39	4.93±1.058	11	3.88±1.101	42
-49	4.80±0.971	15	4.11±1.027	31
-59	3.83±1.214	23	3.93±0.769	29
-69	3.28±0.868	35	3.35±0.798	45
-79	2.96±0.678	28	3.02±0.757	33
-89	3.04±0.736	20	2.67±0.632	14

Analysing the difference in thiopental requirements in men and women by decade of age shows a significantly lower dosage for women in the 30-39 age group (P < 0.01) and 40-49 age group (P < 0.05) only. As there was a sharp drop off in dosage over the age of 50, Table 2 gives the data for patients below and above this age. There was a very highly significant difference in doses in 'young' men as compared with 'young' women (P < 0.001), but this did not apply to the more elderly patients (P < 0.6).

Table 2. Mean ± SD induction dosage of thiopental (mg kg) in patients above and below 50 yr.

yr	Males	Females
< 50	4.80±1.082	4.11±1.167
> 50	3.27±0.934	3.32±0.857

Discussion. This carefully controlled study, carried out in clinical conditions on a broad spectrum of patients, demonstrates a reduction in thiopental requirements with age in both sexes. It also shows that young men require more drug than women of the same age.

It differs from two large published series^{1,2} in avoiding observer variability and using a standard method of administering thiopental, as well as excluding pathologic conditions which might influence distribution and/or its metabolism.

This was not a pharmacokinetic study and we cannot confirm or refute the view that reduced dosage in the elderly was associated with differences in drug distribution^{2,3}. However, it should be noted that the decreased tolerance of ageing brain to benzodiazepines cannot be accounted for on such a basis⁵.

References.

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