Proportional Criterion of Metabolic Activity and Fundamentals of Drug Dosage

I. I. Turkovskii and A. N. Kuznetsov

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A method for determining the drug dose is proposed, according to which the dose of injected drug is proportional to body weight to the power $^2/_3$. The dosage of narcotic analgesic ketamine is in good agreement with the proposed relationship.

Key Words: *metabolic activity; dosage; body surface area; narcosis*

The drug dose is usually estimated per unit of body weight [1,3], but sometimes it is more correct to determine the dose proceeding from body surface area, because this parameter better correlates with the intensity of metabolic processes in the organism [2]. A theoretical argument supporting this thesis is the fact that heat is an obligatory product of metabolic processes, and heat emission is always proportional to body surface area [4].

Our method for estimating the individual dose (D_{IND}) is based on a linear coefficient of body similarity (LCBS). Neglecting the age and individual constitution, human (and animal of the same species) bodies can be considered as geometrically similar. If this be true, LCBS is equal to cube root of the ratio of their volumes, or (due to approximately the same density) weights: $(M_1/M_0)^{1/3}$, where M_1 is body weight of the individual and M_0 standard human body weight (70 kg). The ratio of areas is equal to squared LCBS: $(M_1/M_0)^{2/3}$.

The standard dose (D_0) is determined by reference data (by multiplication of specific dosage by M_0), and D_{IND} is calculated by the formula:

$$D_{IND}=D_0(M_1/M_0)^{2/3}.$$

The purpose of this study was experimental verification of this method for calculating the individual drug dose.

Military Medical Academy, St. Petersburg; Russian University of Peoples' Friendship, Moscow

MATERIALS AND METHODS

Eight mongrel dogs weighing 25.0±2.1 kg, 10 Chinchilla rabbits weighing 1.50±0.13 kg, and 40 male Wistar rats aged 1 year (0.200±0.012 kg) were used. Single dose of ketamine was chosen experimentally by injecting increasing doses at 5-7-min intervals. The dose was considered sufficient, if there were no reflex response to painful stimulus in the presence of spontaneous respiration.

Doses selected experimentally were compared to doses estimated by the common and our original method.

RESULTS

Doses estimated by our method differed from experimentally selected by no more than 28%, while the dose calculated per body weight and empirical dose

TABLE 1. Estimated and Empirical Doses of Ketamine for Dogs, Rabbits, and Rats for Adequate Narcosis

Animal (body weight, kg)	Ketamine dose, mg		
	per body weight	per body area	empirical
Dog (25.0±2.1)	200	280	300
Rabbit (1.50±0.13)	12	45	60
Rat (0.200±0.012)	1.6	11	15

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varied greatly (Table 1). Hence, the method of dose estimation conforms to the "surface rule" for, at least, narcotic analgesics and, though there is no absolute similarity in the shape of different organisms, our method is simple and sufficiently accurate, bearing in mind the differences in sensitivity between individuals and species. Further studies are needed for more accurately defining the sphere of application of this method.

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