Doses for Laboratory Animals based on Metabolic Rate

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The development and use of laboratory animal models - applied laboratory science - is based on the premise that animals of different species including man are more or less similar and thus can be compared.

It is well known that mammals in general have similar organ weights in proportion to their body size, and equally well known that the rate of function of the various tissues and organs varies from one species to another.

This variation renders it often difficult to estimate e.g. doses of anaesthetics or feed additives from one species to another.

In the many instances where metabolic functions are involved the problem of scaling may be simplified significantly, and simple guidelines for calculating e.g. drug dosage from body weight are easy to outline.

The metabolic rate refers to the energy metabolism per unit time. It can be calculated in different ways, the most frequently used being the determination of oxygen consumption per time unit.

It has been known since 1930, that the metabolic rate of all mammals is correlated to the body weight raised to the 0.75 power.

This correlation gives a straight line when the rate of oxygen consumption is plotted against body weight in a double logarithmic plot with a slope of 0.75.

Figure 1 (Schmidt-Nielsen 1975) shows the relationship between the rate of oxygen consumption per unit body mass of various mammals when plotted against body mass on logarithmic coordinates. Alternatively, the following equation may be used:

(1) $M = 3.8 \times W^{-0.25}$

where M is the metabolic rate (oxygen consumption in ml 0_2 per gram body mass per hour) and W is the body weight in grams.

In the following example we have tried to make use of the relationship between metabolic rate and body weight for the estimation of doses of pentobarbital in mammals of different size.

This has been done with the assumption that the dose depends on body size and metabolic rate in the following manner:

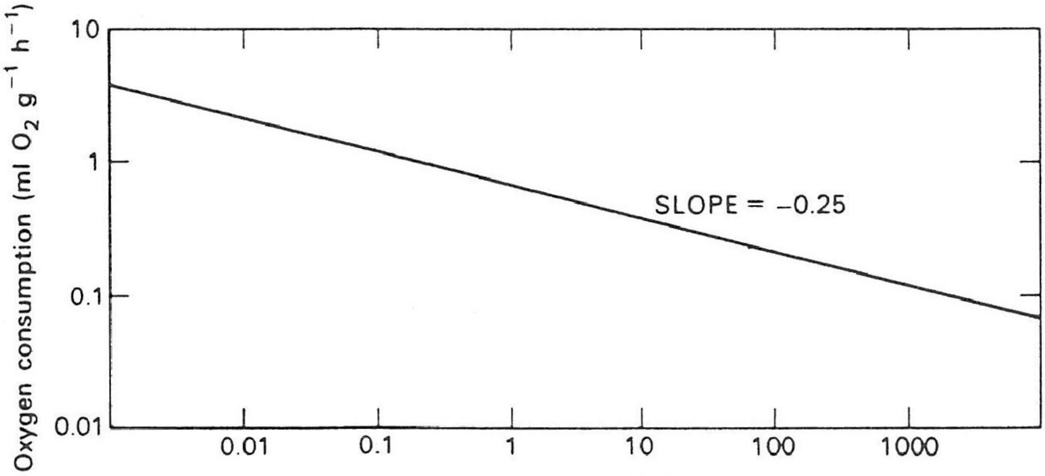

Figure 1. The rates of oxygen consumption of various mammals, when calculatedper unit body mass and plotted against body mass on logarithmic coordinates, tend to fall along a straight regression line with a slope of -0,25, (Schmidt-Nielsen 1975).

$$(2)\quad \frac{X_1}{X_2} = \frac{W_1^{-0.25}}{W_2^{-0.25}}$$

or

$$(3)\quad X_1 = X_2 \times \frac{W_1^{-0.25}}{W_2^{-0.25}}$$

As prototype we have chosen a monkey, body weight 10 kg and a pentobarbital dose of 25 mg/kg.
These data gives the equation

$$(4)\quad X_1 = 25/10^{-0.25} \times W_1^{-0.25}$$

Table 1 compares the doses of pentobarbital calculated by equation 4 with doses for various species reported in the literature. The doses calculated using the equation agree fairly well with the doses reported in the literature, exept for the dose for mice, which is much too high, when calculated by the formula. This is because the 0.50 power of body weight should be employed when dealing with animals having body weights below 100 g (Bartels 1982).

Table 1

Species/weight in g	Dose calculated by equation 4 in mg/kg	Dose from literature in mg/kg
Mouse (25)	112	60-90
Rat (350)	58	50-72
Guinea pig (900)	46	30-40
Rabbit (3000)	34	30-50
Cat (3500)	33	25-30
Monkey (10000)	25 by def.	25 def.
Dog (11000)	24	25-30
Goat (30000)	19	15-30
Pig (50000)	17	10-25

Doses of pentobarbital calculated by equation 4, compared with doses suggested by Green (1979), Svendsen and Hau (1981) and Ingebrigtsen and Erichsen (1985).

The formulas presented should be considered as guidelines only. Some species react with particular sensitivity towards one or more drugs and variations in the reaction or animals within a species occur due to differences in sex, age, strain, stock, nutritional state, time of day, stress level, type of bedding, ambient temperature etc.
It is however, our hope that this simple formula may be of assistance to laboratory animal veterinarians and scientists when they off the cuff have to estimate doses for mammals of various sizes and species.

Sammendrag

Forskellen i forskellige pattedyrs metabolske rater (M) gør det ofte vanskeligt at estimere dosis af anaestetika fra en art til en anden. Det er almindeligt kendt, at pattedyrs metabolske rate er relateret til kropsvægten (W), og relationen mellem kropsvægt og metabolsk rate kan udtrykkes ved formlen:

$$(1)\quad M = 3.8 \times W^{-0.25}$$

Under antagelse af, at dosis af f. eks. et anaestetikum alene afhænger af dyrets metabolske rate, kan et simpelt matematisk udtryk anvendes ved beregning af dosis fra en art til andre arter:

$$(2)\quad \frac{X_1}{X_2} = \frac{W_1^{-0.25}}{W_2^{-0.25}}$$

or

$$(3)\quad X_1 = X_2 \times \frac{W_1^{-0.25}}{W_1^{-0.25}}$$

Som eksempel anvendes formlen til beregning af den dosis af pentobarbital, der skal anvendes til en række forskellige dyrearter. De beregnede dosisværdier er i god overensstemmelse med de i litteraturen anbefalede doser for de pågældende arter. Formlen er muligvis generel anvendelig til hurtigt at estimere et anvendeligt dosisniveau, hvis dosis kendes for en eller flere pattedyrarter.

Summary

The differences in metabolic rates (M) of different mammals often make it difficult to estimate the dose of e.g. anaesthetics from one species to another. It is well known that the mammalian metabolic rate is correlated to the body weight (W), and the relationship between body weight and metabolic rate kan be expressed using the equation:

$$(1)\quad M = 3.8 \times W^{-0.25}$$

Using the assumption, that the dose of e.g. an anaesthetic only depends on the metabolic rate of the animal, a simple mathematic equation can be used in scaling the dose from one species to another:

$$(2) \quad \frac{X_1}{X_2} = \frac{W_1^{-0.25}}{W_2^{-0.25}}$$

or

$$(3) \quad X_1 = X_2 \times \frac{W_1^{-0.25}}{W_2^{-0.25}}$$

As an example the equation is employed for the calculation of the doses of pentobarbital for a series of different mammals of different size. The calculated doses agree well with the doses reported in the literature. The equation may be of generel usefulness for a quick calculation of a suitable dose level, when the dose level of another species is known.

Yhteenveto / Pelkonen

Erot eri eläinlajien aineenvaihduntanopeuksissa (M) vaikeuttavat usein esim. Nukutusainemäärien arviointia lajista toiseen. Tiedetään hyvin, että nisäkkäiden aineenvaihduntanopeus riippuu ruumiinpainosta (W) seuraavan kaavan mukaisesti:

$$M = 3.8 \times W^{-0.25}$$

Oletettaessa, että nukutusaineen annos riippuu vain eläimen aineen vaihduntanopeudesta, voidaan annos laskea lajista toiseen yksinkertaisen yhtälön avulla

$$X_1 = X_2 \times \frac{W_1^{-0.25}}{W_2^{-0.25}}$$

Esimerkin vuoksi yhtälöä on käytetty pehtobarbitaaliannosten laskemiseen erikokoisille nisäkkäille. Lasketut arvot sopivat kirjallisuudessa annettujen kanssa hyvin yhteen. Yhtälöstä voi olla yleisesti hyötyä haluttaessa tehdä nopea laskelma sopivasta annostasosta, kun toiselle eläinlajille tarvittava annos tunnetaan.

References

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