Dosage Precision of Cytostatic Agents in Oncology

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Key Words

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Summary

The cytostatic dosage is calculated by Du Bois' formula, which is based on the body surface. In individual cases this may involve overdosage or underdosage. It therefore seems advisable to base the dosage on the metabolic body mass and the general nutritional state.

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Zusammenfassung und Schlüsselwörter

Die Zytostatika-Dosis wird nach der Formel von Du Bois berechnet, welche sich auf die Körperoberfläche stützt. Im Einzelfall bleibt hierbei unklar, ob eine Über- oder Unterdosierung vorliegt. Es wird empfohlen, für die Dosierungsberechnung das metabolische Körpergewicht und den Ernährungszustand zugrunde zu legen.

Chemotherapie · Dosierungsberechnung ■ Zytostatika

600 mg/m²

40 mg/m²

600 mg/m²

Cytostatic agents have a very limited therapeutic range. The therapeutic regimen must therefore be strictly observed. The potentially life-threatening side-effects of chemotherapeutic agents enforce a dosage corresponding to their individual extent. The dosage is therefore frequently modified in the course of therapy, putting in question the efficacy of the cytostatic agents.

One example in gynecologic oncology is breast cancer, which is most frequently treated with – depending on the TNM classification – either adjuvant or palliative polychemotherapy, e.g. with CMF, according to Bonadonna [1]. If possible, a maximal dosage is applied over six cycles. The following dosages are recommended:

Cyclophosphamide

Methotrexate

Fluorouracil

The recommended dosages apply to the body surface of an adult. It is calculated by the patient's height in cm and mass in kg according to Du Bois' formula (1916):

$$0.725 \times 71.84$$

$$\times L$$

$$O = M^{\frac{1}{4}}$$

the patient's metabolic body mass. Frequent use is made of the metabolic body mass, the $\frac{3}{4}$ exponent of the real body weight, as a calculation parameter in comparative medicine based on animal studies. This parameter makes the different body masses of highly different species and individuals comparable, at the same time taking into account the isokinetic behavior of substances in the organism. In cylindrical and round bodies, an increase in mass leads to a shift of the surface-volume ratio in favor of the contents. Kleiber [3] reported in detail on the theoretical basis of this relationship. Thus, the metabolic body mass in stout patients with athletic build is relatively large, whereas patients with extensive depot fat only appear to have a large body mass.

The examples calculated on the basis of the metabolic body mass are given on the assumption that a patient weighing 80 kg with a height of 180 cm and a balanced weight-height ratio has been given the right dosage also based on the body surface as a calculation parameter according to Du Bois. The examples show that relatively tall patients with a relatively low body weight are easily overdosed.

It is therefore advisable to pay more attention than has been common practice so far to the patient's nutritional condition when assessing dosages.

(O = body surface, M = body mass, L = body height)

In the clinical setting, the body surface is determined by nomograms from which the above data can be obtained. When the individual dosages are determined by use of this formula, both the body weight and the body height are taken into account. However, the metabolic body mass of a very short patient can be almost equivalent to that of a tall patient, regardless of the body weight. Thus, the length of the extremities exerts an overproportional influence on the dosage to be applied.

The question must be asked, therefore, whether undesired overdosages could not be avoided by paying more attention to

Table 1. Examples which illustrate the discrepancies in dosage according to different calculation parameters

Example no.

1

2

3

4

Body mass

50 kg

50kg

80 kg

80 kg

Body height

180 cm

160 cm

180 cm

160 cm
Body surface (m²)
1.6349
1.5011
1.9960
1.8330
according to Du Bois

Dosage (600 mg/m²)
980
900
1197
1099
kg body mass ^{0.75}
18.8
18.8
26.7
26.7
Suggested dosage (mg)
842.8
842.8
1197
1197
186
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References

Bonadonna G, Valagussa P, Rossi A, et al: Multimodal therapy with CMF in resectable breast cancer with positive axillary nodes: The Milan Institute Experience, in Salmon SE, Jones SE (eds): Adjuvant therapy of cancer III. New York, Grune & Stratton, 1981, p 435.

DuBois EF: The mechanism of heat loss and temperature regulation. Stanford University Press, 1937.

3 Kleiber M: Der Energiehaushalt von Mensch und Haustier. Hamburg, Parey. 1967. pp 174–183.

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