Clinical Topics

SI units and anticonvulsant drugs in paediatrics

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The concept of using SI units has now been accepted in principle by most medical practitioners in the United Kingdom, and laboratories now report most of their results in these units. During the transition period the use of conversion nomograms such as those produced by Baron¹ and Bold and Wilding² have proved invaluable in helping both clinician and laboratory worker to adjust to new reference ranges.

In drug monitoring the change has not been universal, and the reasons are so complex that uniformity in the near future seems unlikely. The lack of uniformity is not entirely due to the introduction of SI units, as several gravimetric units are in use—for example, $\mu\text{g/ml}$, $\text{mg}/100\text{ ml}$, mg/l . A medical student may have learnt to measure drugs in one of these units and then find that in the hospital where he does his resident posts SI or one of the other gravimetric systems is used.

We have constructed a conversion nomogram for gravimetric and molecular units to avoid the dangers of misinterpreting drug concentrations. The nomogram has been used in the paediatric department at Northwick Park Hospital for over a year.

Nomogram

The clinical biochemistry department at St Albans City Hospital offers a regional monitoring service for many of the

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more common drugs. This service is used by the paediatric department at Northwick Park Hospital. St Albans City Hospital reports the results in gravimetric units ($\mu\text{g/ml}$), as these are the most acceptable units to most of its users, whereas Northwick Park Hospital reports the results of all tests performed locally in molecular units ($\mu\text{mol/l}$). These results may be converted easily by the use of the nomogram (see figure).

A paediatric therapeutic range has been included on the nomogram so that the clinician can decide at a glance whether his treatment is appropriate at the same time as he converts the results. These ranges are based on considerable experience in dealing with specimens at St Albans City Hospital and have been substantiated by experience at Northwick Park Hospital. The recommended range for valproate is based on concentrations in specimens collected two to four hours after dosage.

SI conversion chart for therapeutic drugs. Shade area shows paediatric therapeutic range.

Guide to dosage levels

	Approximate blood concentrations from dose of 1 mg/kg	Frequency (times/day)	Starting dose (per 24 h)	Increments	Suggested upper limit of 24-h dose	Commonly accepted therapeutic ranges
Phenytoin*	1.0-3.0 $\mu\text{g/ml}$	1-2	4 mg/kg	1 mg/kg	8 mg/kg	10-20 $\mu\text{g/ml}$ (adults) 5-20 $\mu\text{g/ml}$ (children)
Phenobarbitone	7.5-15 $\mu\text{g/ml}$	2	1 mg/kg	0.5 mg/kg	2.5 mg/kg†	10-25 $\mu\text{g/ml}$
Primidone (phenobarbitone)		2	5 mg/kg†	2.5 mg/kg	12.5 mg/kg†	Judged by level of phenobarbitone
Ethosuximide	2.5-3.0 $\mu\text{g/ml}$	2	20 mg/kg	10 mg/kg	40 mg/kg	40-100 $\mu\text{g/ml}$
Carbamazepine	0.2-0.5 $\mu\text{g/ml}$	2	10 mg/kg	5 mg/kg	20 mg/kg	4-10 $\mu\text{g/ml}$
Valproate	1.0-2.0 $\mu\text{g/ml}$	3	20 mg/kg	10 mg/kg	50 mg/kg	30-70 $\mu\text{g/ml}$ (minimum level before dose) 60-100 $\mu\text{g/ml}$ (2-4 hours post dose)

*At a particular dose level, which varies between individuals, a small increase produces a disproportionate increase in serum concentration.

†The amount of primidone in mg/kg divided by 5 is about equivalent to the dose of phenobarbitone in mg/kg .

‡In children aged under 5 years the starting dose and upper limits may be more than doubled.

The other drugs reach a steady state, and the blood concentrations are therefore substantially independent of the time of collection. Primidone is metabolised to phenobarbitone and the therapeutic range is judged by the phenobarbitone concentration. Some centres may want to use other gravimetric units—mg/100 ml or mg/l—in which case the nomogram may be adapted easily.

Guidance on doses

The table gives practical guidance for drug dosage, although there are wide differences between the doses needed by individual patients to attain similar blood concentrations. This table may be used as a guide for both adult and child dosages, though where these are significantly different both are shown. The starting dose quoted is per 24 hours and not the amount taken at each administration. This dose is given at the beginning of a drug regimen that would normally be continued for about

two weeks. Should it be necessary to adjust the dose after that period the recommended dose change is shown in column headed increments.

The frequency of fits and the presence of side effects are the best guides to management, and blood concentrations of drugs provide only additional indicators of rational treatment. A few patients will be well controlled when their blood concentrations are below the lower limit of the range and some may have no side effects when their blood concentrations exceed the upper limit of the range; conversely, others may have side effects within this range.

References

- ¹ Baron, D N, *British Medical Journal*, 1974, **1**, 509.
- ² Bold, A M, and Wilding, P, *Clinical Chemistry Conversion Scales for SI Units with Adult Normal (Reference) Values*. Oxford, Blackwell Scientific Publications, 1975.

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Personal Therapeutics

Asthma

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Recognising asthma may present few problems, especially if the patient is young and has typical episodes of intermittent breathlessness precipitated by exposure to allergens or exercise. Some patients, however, appear to be normal when they attend the surgery or clinic, and have symptoms only at night or in the early morning, whereas other, older patients may be misdiagnosed as having chronic bronchitis or emphysema. A careful history and examination, chest radiography, and appropriate pulmonary function testing should point to the correct diagnosis. Although we do not yet know the nature of the basic defect in asthma, and are not clear about how some drugs produce their beneficial effects, we now have a potent armoury of effective remedies that can, with correct application, keep most patients fairly well most of the time.

It is crucial to assess the patient's disability objectively. The general practitioner can obtain important information if he has a peak flow meter in his surgery. Patients with pronounced and persistent symptoms often have a peak expiratory flow rate (PEFR) less than 200 l/min, and values less than 100 l/min indicate very severe airway narrowing. Inhaling a sympathomimetic usually produces an increase in PEFR of 20% or greater in the asthmatic patient. Lack of such a response, however, does not exclude asthma, and a trial of corticosteroids may be necessary to show that the airway narrowing is reversible. If the doctor is uncertain he should refer the patient to a pulmonary function laboratory.

Records in the notes of PEFR every time the patient attends prove useful. In addition, a chart of PEFR completed by the patient on three or four occasions during the day over several days may be most valuable in establishing the individual pattern of airway narrowing. To attempt to manage asthma without frequent objective measurements of the amount of airway narrowing is analogous to managing diabetes without testing the urine.

Management of asthma

PATIENT EDUCATION

Many problems arise because patients, and sometimes their doctors, do not appreciate the nature of asthma. The chronicity and variability of the condition should be explained, and if prophylactic treatment is being used the patient must understand the purpose and basis of such treatment. Emotional aspects should be minimised; psychological factors are rarely very important aetiologically, and, indeed, much anxiety and depression can be relieved when asthma is properly controlled. Although the dangers of some of the treatments—for example, overuse of sympathomimetic inhalers—should be explained, equal emphasis should be given to the dangers of ignoring the onset of an acute severe attack. Patients should be educated to seek medical advice promptly when their usual remedies fail to control their asthma.

AVOIDANCE OF TRIGGER FACTORS AND DESENSITISATION

Removal from working environments where there are dust and irritant fumes will help all asthmatic patients, and they should be discouraged from smoking. Avoidance of specific