P 31 DRUG DOSE ADJUSTMENTS IN OBESE PAEDIATRIC PATIENTS

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Aim To review the pharmacokinetic principles and data related to drug dosing in obese paediatric patients in order to develop a guideline to standardise practice throughout the Trust.

Method A literature search was performed on Embase with search terms: childhood obesity/or obesity and drug dose. Medline was searched using search terms: obesity and dose-response relationship, drug. The search was limited to all ages under 18. Other paediatric hospitals were contacted to establish their practice and identify any additional data. National published adult guidelines were reviewed. The results

were used to develop a drug dosing guideline. There is currently no nationally agreed definition of obesity. The guideline was developed using the general consensus that a body mass index of >98th centile is defined as obese.

Results Demand for the guideline—The prevalence of childhood obesity is increasing.[1 2] Obesity causes physiological changes which alter drug pharmacokinetics.[3] This may result in toxicity or reduced therapeutic effect.[1 3] However, there is limited published data available to guide drug dosing.[1] Data is often extrapolated from adults.

Pharmacokinetic principles—Absorption is not altered in obese adults.[1] Drug distribution is altered, as fat mass and lean body increase.[1 2] 75% of excess weight is fat, increasing the volume of distribution (VD) of lipophilic drugs.[1 2 3] Changes in protein binding are not clinically significant.[2] Evidence does not demonstrate any modification to hepatic metabolism.[2] The clinical data regarding drug clearance is conflicting, however animal studies have demonstrated increased kidney weight, renal blood flow and glomerular filtration.[2]

Drug physicochemical properties determine dose adjustments required. The VD for hydrophilic drugs should theoretically be based on ideal body weight (IBW). Those which partially distribute into fat, such as gentamicin, would be based on IBW plus a proportion of actual body weight (a correction factor) and lipophilic drugs, such as amphotericin B, would be based on actual body weight (ABW).[2] The necessity to achieve therapeutic levels should be balanced against drug toxicity.[2]

Sufficient data on 27 drugs were identified. These were grouped into four categories; antimicrobials, anticonvulsants, sedation and analgesia, and miscellaneous. Three weights to base doses on were included; IBW, adjusted body weight using a correction factor and ABW. There are no standardised methods to estimate IBW.[1 2] The most common method uses the 50th percentile for height.[1] A diagram was included in the guideline illustrating this.

Conclusion This research resulted in a guideline summarising the available data on drug dosing in obese paediatric patients. There is limited information available so where there is a lack of clinical data, it is necessary to consider pharmacokinetic principles. This guideline was subsequently approved by the Trust's Drugs and Therapeutics committee and is now in clinical use.

REFERENCES

1 Kendrick JG, Carr RR, Ensom MHH. Pharmacokinetics and drug dosing in obese children. *J Pediatr Pharmacol Ther* 2010;15:94–109.
2 Mulla H, Johnson TN. Dosing dilemmas in obese children. *Arch Dis Child Educ Pract Ed* 2010;95:112–17.
3 Siu D. "Weighing in" on antibiotic dosing in obese patients. *Drug Therapy Topics* 2006;35:9–11.