the best-fit BMI of values derived from Janmahasatian’s equation for LBW was 25.92 for men and 21.38 for women (Fig. 1).

As there is a direct relationship between body weight and height for a given BMI,4–7 a simplified formula has been proposed to estimate IBW, that is, IBW = BMI h2.5 6 Some authors have found that a BMI of 22 represents the best generic value for both men and women to replace BMI in this simplified formula.5 6 Unfortunately, the BMI value of 22 identified by these earlier reports is not gender-specific, which is important given the differences in fat and lean mass between men and women.8 9 Instead, we propose that a BMI value of 21 should be used for women and a BMI value of 23 should be used for men when estimating IBW.

Interestingly, there are no data available for a simplified means to estimate LBW in MO patients. From our results, we suggest using a BMI of 22 in the simplified formula for females and a BMI of 26 for males. The gender-specific values that should replace the BMI in the new simplified formula for estimating LBW are greater than those used for the estimation of IBW, which is appropriate. While in normal-weight patients, the IBW and LBW are similar,1 2 this is not the case in MO patients, where LBW increases with increasing TBW.1 2 In addition, for a given BMI, men have higher lean mass and more visceral and hepatic adipose tissue, whereas women in particular have elevated general adiposity and subcutaneous adipose tissue.8 9 We suggest that our formulas provide an easy, quick, reproducible, and gender-specific estimation of IBW and LBW in MO patients.

Declaration of interest

None declared.

M. Carron*  
S. Guzzinati  
C. Ori  
Padova, Italy  
E-mail: michele.carron@unipd.it


doi:10.1093/bja/aes368

Brain microdialysis distribution study of cefotaxime in a patient with traumatic brain injury

Editor—Following on from our recent review of microdialysis studies of antibacterial agents in the brain,1 we report a case of a 56-yr-old woman (78 kg, normal renal function) admitted for severe traumatic brain injury (TBI), with a Glasgow coma scale score of 5, a contaminated temporal craniocerebral wound, and multiple haemorrhagic contusions. She was managed according to the TBI guidelines and received cefotaxime i.v. (4 g/8 h) to prevent central nervous system (CNS) infection. On admission, routine monitoring included intracranial pressure (Micro-sensor ICP; Codman & Shurtleff, Raynham, MA, USA), partial pressure brain tissue oxygen tension (Licox; Integra Neurosciences, Lyon, France), and cerebral microdialysis (CMA-70; CMA, Stockholm, Sweden). The probe was placed into healthy brain tissue, perfused at 0.3 ml min–1 with CNS perfusion fluid (CMA), and dialysates were analysed for metabolic parameters. This microdialysis monitoring allows us to determine unbound concentrations of therapeutic agents in brain extracellular fluid (ECF) and only few microdialysis studies have characterized antibiotics’ brain distribution in humans.2–5 After informed consent from relatives, cefotaxime brain ECF distribution was explored after the 12th dose, on Day 4. After baseline samples, cefotaxime (4 g) was infused over 30 min and nine brain dialysates were collected every 30 min during 3 h, then hourly to the 7th hour. One blood sample was collected at 30 min and ultrafiltered to determine unbound plasma cefotaxime peak concentration (Cu max,p). Cefotaxime assays used high-performance liquid chromatography with UV detection. In vivo probe recovery was determined using the retrodialysis-by-drug method as previously described.6 A non-compartmental analysis of brain ECF concentrations was performed (Phoenix WinNonlin 6.2, Pharsight, USA). Time over minimal inhibitory concentrations (t->MIC) was estimated at two MIC values (2 and 4 μg ml–1), corresponding to intermediate and resistant strains of Streptococcus pneumoniae.6 7 The mean probe recovery was estimated at 67 (0.25)% and even if in vivo recovery was not always determined in the past,2 4 5 this observation attests to the absolute necessity of careful assessment of in vivo probe recovery in each individual patient.

The Cu max,p was equal to 118.8 μg ml–1 and the maximal brain ECF concentration was clearly lower (C max,b =11.4 μg ml–1). C max,b was achieved at t max=85 min, 55 min after...
the end of infusion. The concentration vs time profile in brain ECF is shown in Figure 1. This limited brain distribution of cefotaxime may be explained by the blood–brain barrier which is known to express efflux transporters like P-glycoprotein (P-gp) or multidrug resistant-associated protein (MRP). To circumvent this problem, antibiotic doses are increased for the prevention or treatment of CNS infections. Without severe side-effects, cefotaxime doses may be increased from 6 g up to 24 g per day for meningitis.

Cefotaxime t>MIC in the brain were, respectively, equal to 78% (6.2 h) and 46% (3.7 h) for MIC values of 2 and 4 µg ml\(^{-1}\). To get effective bacteriostatic and bactericidal effect in vivo, \(t>MIC\) should, respectively, be 40 and 70% of the dosing interval, suggesting a bacteriostatic effect even for the highest MIC (4 µg ml\(^{-1}\)) and a bactericidal effect only for MIC values of 2 µg ml\(^{-1}\). Cefotaxime dosing regimen for adult’s meningitis treatment is 4 g every 4–6 h, but this case indicates that 4 g every 8 h could provide sufficient brain tissue concentration for preventing infections of resistant pneumococcal strains and treating intermediate ones.

In conclusion, the ECF brain concentrations indicate that an adequate exposure to cefotaxime is achieved in prevention and treatment of most CNS infections.

**Acknowledgement**

We thank Pharsight Corporation for the free supply of WinNonLin through the PAL programme.

**Declaration of interest**

None declared.

**Funding**

This work was support by a grant (PHRC) from the French Ministère de l’Education et de la Recherche.

---


**Differential effect of phenylephrine and ephedrine on cerebral haemodynamics before carotid cross-clamping during carotid endarterectomy**

Editor—Internal carotid artery stenosis is often associated with impaired cerebral autoregulation, implying that cerebral blood flow depends on arterial pressure.\(^1\)\(^–\)\(^3\) To preserve cerebral perfusion and to prevent ‘watershed’ stroke during carotid endarterectomy (CEA), hypotension before and during cross-clamping needs to be avoided.\(^4\) Several short-acting agents, such as phenylephrine or ephedrine, are commonly used to correct intraoperative hypotension, but have different haemodynamic effects. Phenylephrine, an

---

D. Frasca*
C. Dahyot-Fizelier
W. Couet
B. Debaene
O. Mimoz
S. Marchand
Poitiers, France
*E-mail: denis.frasca@univ-poitiers.fr

---

doi:10.1093/bja/aes369