Do old pharmacokinetic parameter estimates predict new data?

Editor—Investigators may report different parameter estimates to describe the pharmacokinetics of a drug used in children. A number of parameter sets exist for describing propofol time–concentration data in children, often predicting quite different profiles in a typical child. These differences may be attributed to different patient populations, administration (single dose vs infusion), study duration, and differing analysis methodologies. Similarly, parameter sets for i.v. paracetamol are reported that differ.

An alternative to comparing predicted time–concentration profiles using differing parameter sets for a typical child is to ascertain if parameter estimates from an earlier study can predict concentrations similar to those reported in a new study is to use a modelling tool known as the visual predictive check. Concentration prediction intervals from an earlier study are graphically superimposed on those intervals determined from observed concentrations in the new study. Simulation is performed with parameter estimates from the earlier study using 1000 subjects with characteristics taken from new patients. For data such as these where covariates such as dose, weight, and height are different for each patient, a prediction-corrected visual predictive check is used; observations and simulations are multiplied by the population baseline value divided by the individual-estimated baseline. Figure 1 shows a graphical representation. The median predictions and observations graphically lie on top of each other. Observed concentration intervals are narrower than predictions, reflecting limited subjects (n=33) in the new study.

The earlier study (n=144) was performed using a prodrug of paracetamol (procetamol) that is rapidly metabolized to paracetamol (F=0.5) by plasma esterases. This graphical validation supports parameter estimates for i.v. paracetamol determined using the prodrug.

Declaration of interest

None declared.

B. J. Anderson1*
J. McLay2
K. Allegaert3
T. Engelhardt2

1 Auckland, New Zealand
2 Aberdeen, UK
3 Leuven, Belgium

* E-mail: briana@adhb.govt.nz

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Fig 1. Prediction-corrected visual predictive check using parameter estimates from an earlier study5 and observations from the new study. All plots show the median and 90% intervals (solid and dashed lines). (a) shows all prediction-corrected observed concentrations. (b) shows prediction corrected percentiles (10%, 50%, and 90%) for observations (lines with symbols) and predictions (lines) with 95% confidence intervals for prediction percentiles (green-shaded areas).
Videolaryngoscopy allows a better view of the pharynx and larynx than classic laryngoscopy

Editor—Videolaryngoscopy plays an increasingly more important role in airway management, a ‘core’ business of all anaesthetists.1 During direct laryngoscopy, the larynx is viewed from outside the oral cavity. The distance between the vocal cords and the laryngoscopist’s eye is substantial (30–40 cm). This reduces the angle of view to 15° with a classic laryngoscope. During videolaryngoscopy, the digital camera and light source are mounted very close (2–3 cm) to the tip of the videolaryngoscope and close to the larynx. The laryngoscopist obtains a much wider angle of view as captured on the camera monitor. In Figure 1, a blade size 4 of the C-MAC™ Storz® videolaryngoscope (Karl Storz, Tuttlingen, Germany) is shown with an angle of view of 80°. However, the 80° view angle provided by the lens is not visible in total because the anterior view is restricted by the tip of the blade itself, resulting in a visual angle of 60°. The anterior view angle is enhanced by using the more curved Mac 4 blade compared with Mac 2 and 3 blades. In contrast to most Europeans, Americans prefer to use the Mac 4 blade in daily routine practice, especially in obese patients. The success of the Macintosh Classic laryngoscope is attributable to the versatility of the human head and eyes’ ability to travel rapidly across three-dimensional space such that the 15° angle of view can be applied from a variety of vantage points. The D-blade was designed for the remaining 2–5% ‘most difficult’ cases. It allows only indirect visualization of the glottis, because the D-blade is much more curved compared with all Mac blades. It is recommended for use in difficult airways with a more anteriorly placed glottis (with reference to the line of vision from the top incisors to the laryngeal cords).2 3 Additionally, much less force is needed for glottis visualization with both the D-blade and the videoscopes when compared with other Mac blades.

Fig 1 Vertical visible angle of view (60°) with a Mac blade size 4 and a D-blade C-MAC™ videolaryngoscope, compared with 15° with a classic laryngoscope.