LETTERS TO THE EDITOR

Outcome in antenatally diagnosed renal pelvis dilatation

EDITOR,—Dr Nicholl raises some pertinent points in his letter regarding our paper.1 The nub of the matter is whether antenatally diagnosed vesico-ureteric reflux (VUR), detected as a result of antenatal ultrasound findings is clinically important or not. The answer to this question is not yet known and will require a trial that looks at what, if any, difference treatment makes to outcome, as judged by the development of renal scars.

Until this matter is resolved, however, we feel it appropriate to look for VUR when there has been antenatal pelvis dilatation, and treat accordingly. As stated in our study,1 this judgement is partly based on the fact that the prevalence of asymptomatic VUR is around 1%, as described by Bailey, in contrast to an incidence of 20% in our study, implying that our findings were significant.

We accept that in a review of the published findings, from which Bailey acquired his data, the radiological techniques used may have differed from those currently in use, but as can be imagined, it is not easy to acquire information about the incidence of VUR in healthy children, and Bailey’s work is, to our knowledge, the currently accepted reference.1

With regard to the specific points raised by Nicholl around 50% of the babies with VUR in their study, have now undergone further imaging at the age of 3 years. Their reflux had resolved and, more importantly, no renal scar had been incurred. In those babies where both postnatal ultrasonography and the microureteric cystogram were normal, the infants were discharged from further follow up, as we saw no further indication for continuing their surveillance.

The fact that only one baby required surgical intervention reflects that VUR, which is generally treated medically, was the most common finding, and a more conservative approach is now adopted in cases of pelviureteric junction obstruction. In table 1 of our study we included, under the diagnosis of “idiopathic dilatation” only those infants in whom persisting renal pelvis dilatation was > 10 mm, because in those (n=22) in whom it was 5–10 mm and the microureteric cystogram was normal, we did not feel an MAG III renogram was indicated; therefore, they did not strictly fulfil our criteria for this diagnostic label.

Mervyn S Jaswon
Department of Paediatrics
The Whittington Hospital
Highgate Hill
London N19 5NF

Unlicensed and off label drug use in neonates

EDITOR,—Most papers in this journal have a commendable clear “take home” message, but this was not really true of the recent paper by Conroy et al.2 They described a 13 week, one unit study in Derby as finding that two thirds of all neonatal prescriptions for 44 out of 455 involved the use of a drug in a way that the manufacturers had no license to recommend. The authors do not say what should be done about it.

They note that 84 prescriptions for vitamins and 77 for penicillin or an aminoglycoside used a dose other than the one mentioned in the drug data sheet. But they must be aware, surely, that at the time these were written that was in nature. Secondly, an immense amount of information has been published on these issues since the data sheets were first prepared. The authors note that 36 prescriptions for caffeine, morphine, or parenteral nutrition had to be made up in the local pharmacy aseptic service unit, and the products were therefore classified as unlicensed. They do not suggest, however, how they would prefer to see the prescribing and dispensing of these drugs handled.

What was the intended message when arranging the paper for the news media to latch on to this report before most clinicians had had their chance to read the paper for themselves? Were headlines such as “Doctors raise alarm over drugs given to babies,” and “Babies used drug groups?” really what you hoped to generate? Coming only a week after an article in the Scoop Scientific,7 inspired by a steer from the Derby clinicians, the journal article led the BBC to report that “Doctors are calling for stricter controls to ensure children are not given dangerous doses of adult drugs.” Such manipulation of the news media does a serious disservice to a serious subject. Professor Aynsley-Green’s subsequent letter,3 contrasting the lack of support for paediatric pharmacology in the UK with the establishment of 13 such centres in North America, rather suggests that it was a simple bid for money.

Readers who turned to Professor Sir David Hull’s commentary in the same issue will have found little enlightenment. His main message seemed to be that one should buy Medicines for Children. However, any suggestion that this would be the first reference text to clearly identify unlicensed and off label paediatric drug use in the UK would be misleading. Even should that be the case, it wouldn’t get us very far: the new consensus driven text may tell us what “we” can do. What is needed is sensible, sustained, and constructive dialogue between the profession, the licensing authorities, and the manufacturers, to get drug sheets revised at regular intervals, so that they reflect all the additional information that becomes available in the years after the product first comes on the market. My message is, that it is up to the profession to start the ball rolling.

E Hey
Department of Child Health, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP

NEW PAPERS


Drs Conroy et al respond:

We welcome the opportunity to clarify our “take home” message. This is actually very simple: drugs used in children should be tested scientifically to ensure that age dependent changes in pharmacokinetics and pharmacodynamics are known, the likely side effects are anticipated, and that the minimum effective dose can be given.

We expect the Medicines Control Agency to ensure that neonates receive drugs that are as carefully evaluated for efficacy, safety, and quality as the drugs given to adults. We also expect the pharmaceutical industry to provide drugs that are appropriate for use in neonates and children as well as in adults. We accept that health professionals involved in the care of neonates have a responsibility to contribute to this process. It requires a joint effort between healthcare staff caring for children, the industry, and the government. Dr Hey states that data sheet information is “advisory” but this is the only information that the pharmaceutical manufacturer will take responsibility for, anything else is on the head of the prescriber.

There may be few published reports of renal or other few reports of the use of these drugs in neonates, as it is difficult to definitely attribute such problems to the drug. However, this does not mean that gentamicin does not cause such problems. We note that renal insufficiency is not a feature of the use of gentamicin in neonates, and it is difficult to definitely attribute such problems to the drug. However, this does not mean that gentamicin does not cause such problems. We note that renal insufficiency is not a feature of the use of gentamicin in neonates, and it is difficult to definitely attribute such problems to the drug. However, this does not mean that gentamicin does not cause such problems. We note that renal insufficiency is not a feature of the use of gentamicin in neonates, and it is difficult to definitely attribute such problems to the drug.
have many other potentially contributory problems. Research is needed to establish the dose and frequency required to provide therapeutic, non-toxic serum concentrations of this drug for babies of all gestations.1

We were surprised by the media interest in our paper and responded to requests for interviews accordingly. Unfortunately, we cannot be held responsible for the headlines or tone of the published newspaper reports.

The extent of drug toxicity from unlicensed and offtarget drug use in neonates is unknown. We know that severe adverse drug reactions in children are more likely to occur with unlicensed and offtarget treatment than licensed drugs. The scientific study of drug treatment in neonates has been relatively neglected by both doctors and pharmacists in the UK and Europe. However, there are positive developments: the British Forum for the Use of Medicines in Children and the European Network for Drug Investigation in Children are trying to both encourage and coordinate clinical trials in this area.2

It is clear that many health professionals now accept the need for research in paediatric therapeutics. We are not simply bidding for money but trying to raise the profile of a neglected area of research. Historically, research has been centred on disease in specific areas—for example, cystic fibrosis, leukaemia, cardioducardiac defects, etc. When seeking funding for research on the extent and risk of unlicensed and offtarget drug use in children3 we were told by a major children’s charity that they did not consider it an appropriate area for research and that they would not even consider an application for funding. We hope that the studies documenting the extent of unlicensed and offtarget prescribing3 and the consequences of such prescribing4 will convince the Department of Health and the major charities that this is an important area of research, and that the use of drugs in the neonate should be evidence based.


CORRECTION

Please note that the authors of Gilbert et al (Role of Ureaplasma urealyticum in lung disease of prematurity: 1999;81:F162-7) have noted a discrepancy in the reference list for this article. Reference 2 should read:


From there on all references should be renumbered accordingly.