Serum creatinine concentration of patient (case 1) rose until start of dialysis. During this time topical treatment with piroxicam stopped, and renal function rapidly improved

the risk increases tenfold.² Risk factors include age, volume depletion, pre-existing renal impairment, and other high renin states such as heart failure and cirrhosis. Inhibition of tonic prostaglandin dependent renal vasodilatation reduces the glomerular filtration rate and may lead to acute renal failure. Other effects include sodium and water retention, hyperkalaemia, hypertension, and medullary ischaemia, sometimes sufficient to cause papillary necrosis.

Nephrotic syndrome can occur with or without interstitial nephritis, but the combination is characteristic of the use of non-steroidal anti-inflammatory drugs.³ Allergic features such as rash, eosinophilia, or eosinophiluria are usually absent. Prognosis is good if the drug is stopped, and in a review of 56 cases steroids gave no clear benefit.³ The development of nephrotic syndrome does not seem dose dependent, and most non-steroidal anti-inflammatory drugs, including piroxicam, have been implicated.⁴ In healthy volunteers daily topical treatment with 2 g of 0.5% piroxicam gel for 14 days gave a blood concentration that was 5% of that achieved by the standard oral dose.⁵ Elderly patients might achieve higher blood concentrations because of reduced drug clearance, thin skin, and frequent application of the drug over large areas.

The first case demonstrates that topical non-steroidal anti-inflammatory drugs may cause considerable systemic side effects. The renal lesion seen is highly specific for non-steroidal anti-inflammatory drugs and strongly suggests that the piroxicam was responsible. A complete drug history must include questions on the use of topical preparations.

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Formal measurement of clinical uncertainty: prelude to a trial in perinatal medicine

R Lilford for the Fetal Compromise Group

morbidity would be halved by immediate delivery, and an answer of 2 that it would be doubled. Respondents were then asked what they would regard as a surprisingly good or bad result in the hypothetical trial—that is, when they believed that there was only a one in 40 (2.5%) chance of a result being equally or more extreme. These ranges of expected results gave a measure of the respondents' confidence in their own beliefs. To familiarise participants the answers were displayed during the practice scenario, but they were concealed for the three substantive scenarios.

For each scenario the mean result considered to be most likely was close to 1, with a wide scatter in the individual results—for example, from a 75% decrease to a 25% increase in the risk to a fetus delivered early in the practice scenario (figure). This shows that the scenarios caused collective uncertainty. The mean of all the estimates of surprisingly good and bad results was roughly a reduction and increase in risk of around 50% respectively. All 10 respondents had individual ranges of expected results that included 1 on scenario 1. One was included for six respondents on scenario 2 and for eight respondents on scenario 3.

Comment

These results show that experts do not agree about the benefit of delivery for preterm fetuses that are failing to thrive but are not thought to be near to death. For babies such as those described there is collective and reasonably balanced uncertainty²—the main requirement for a randomised trial.³ It is fortunate that clinicians given the same inconclusive information form different views because these differences provide the impetus for clinical trials. Our results also show, however, that some clinicians are in two minds when others have strong expectations of either benefit or harm. This makes agreement on fixed entry criteria unlikely and suggests that individual balanced un-

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Clinical trials are ethical when there is collective and balanced uncertainty about the best treatment among informed clinicians. This uncertainty can be identified either by observing differences in practice or, as explored here, by formal measurement of clinical belief.

Fetomaternal medicine is largely concerned with timing delivery of preterm fetuses that are failing to thrive. Delivery is indicated when prematurity is judged preferable to continued intrauterine life, but often the relative risks of these alternatives are unknown.¹ During the planning of a trial to compare early with delayed delivery under different circumstances 10 specialists in fetomaternal medicine were interviewed about their beliefs.

Methods and results

The specialists were presented with four scenarios, one practice and three substantive, in each of which the decision between immediate and delayed delivery was difficult (see figure). They recorded their opinions on an analogue dial connected to a microcomputer. For each scenario respondents were asked what they thought the relative risk of permanent morbidity was most likely to be in a hypothetical and infinitely large randomised trial in similar patients. An answer of 1 indicated that their best guess was that such a trial would show no difference between immediate or delayed delivery, an answer of 0.5 that the chance of

Risk to fetus of immediate delivery in four given circumstances as assessed by 10 experts. *Data entry error

Practice scenario

Singleton pregnancy, 32 weeks' gestation; blood pressure 160/100 mm Hg; proteinuria 1 g/l; no maternal symptoms; normal cardiotocogram; no end diastolic flow in umbilical artery on Doppler ultrasonography; liquor volumes slightly reduced (amniotic index = 6); other biophysical variables normal; steroids taken for 48 hours; regional neonatal unit available

Scenario 1

As in practice scenario but reduced end diastolic flow in umbilical artery on Doppler ultrasonography (systolic/diastolic = 4:5) and liquor volume slightly reduced (amniotic index = 6)

Scenario 2

As in practice scenario but 26 weeks' gestation; cardiotocogram showing unreactive fetus; no end diastolic flow on Doppler ultrasonography; liquor volumes severely reduced (amniotic index = 3); fetal limb movements and breathing reduced; fetal tone abnormal

Scenario 3

As in practice scenario but 28 weeks' gestation; reduced end diastolic flow in umbilical artery on Doppler ultrasonography (systolic/diastolic = 4:5); liquor volume reduced (amniotic index = 5); fetal limb movements and breathing reduced; fetal tone abnormal

certainty should be the entry criterion, a method already adopted in some major trials.⁴ The measurement of experts' previous belief and their confidence in this previous belief is also suitable for bayesian analysis of clinical trials, which takes account of opinions based on information external to the trial.⁵

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Correction

A randomised controlled trial to test equivalence between retinyl palmitate and β carotene for vitamin A deficiency

An authors' error occurred in this paper by C Carlier *et al* (30 October, pp 1106-10). In the abstract and the fourth paragraph of the results section the 95% confidence interval for the difference between children taking retinyl palmitate and those taking β carotene (1.2%) should be -6.2% to 8.6% (not 0.8% to 1.6% as published). This does not affect the conclusions of this study; the two treatments remain statistically equivalent.