AIMS For a better birth...

Misoprostol - Letters in The Lancet

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The following letters, one promoting the continued use of misoprostol and one warning of its dangers, have appeared in the 30th June 2001 edition of the medical journal THE LANCET.

Misoprostol and the politics of fear

Sir - If a drug was proven by scientific study to be the equivalent of another drug but nearly 100 times cheaper, it would make sense to use the cheaper drug. If the manufacturer warned that they would not support use of the cheaper drug for an indication for which there was ample data from clinical trials about its efficiency, one might expect to know why.

The drug in question is misoprostol, and the indication is induction of labour. In our National Health Service Trust, as in all Trusts, we are organising our spending plans for the coming financial year. Use of misoprostol instead of other prostaglandins for the induction of labour would save a lot of money. We would be able to meet government-set cost-improvement plans and to plough some money back into other clinical areas.

Searle, the manufacturers of misoprostol, do not support its use in obstetrics and gynaecology. They support its use only as an anti-ulcer medication. Misoprostol is widely used worldwide for induction of labour, induction of abortion, and the treatment of postpartum haemorrhage. The company wrote to all the obstetricians and gynaecologists in the USA to say that they do not support the use of misoprostol for these indications. Searle's position seems to be a response to anti-abortion pressure groups in the USA. The American College of Obstetricians and Gynaecologists has written to the US Food and Drug Administration to critically challenge the letter.

Goldberg and colleagues[1] concluded that, although there were no published estimates of the extent to which misoprostol was currently used for obstetric and gynaecological indications, more than 200 studies involving at least 16,000 women had assessed the drug's effectiveness, and results supported its continued use. Searle have, however, maintained their position in the USA.

So, what is to stop an obstetric unit in the UK using misoprostol for induction of labour in selected patients? Clinical risk advisers tell us that if we do so, we will be exposed from the clinical-risk angle should any unforeseen complication arise. Searle's fear probably stems from the activities of minority pressure groups in the USA concern about bad public relations; our fear stems from the what-if scenario increasingly heard in clinical practice.

The losers are patients and, directly, the financial resources of the National Health Service. And the winners are?

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Reference

1 Goldburg AB, Greenburg MB, Darney PD. Misoprostol and pregnancy, N Engl J Med 2001; 344: 38-47.

Misoprostol and the politics of convenience

Sirs - In earlier correspondence[1], misoprostol for induction of labour was urged as efficacious and cheap. But the author never mentions the risks of misoprostol induction. Searle, the manufacturers of misoprostol, wrote to all obstetricians and gynaecologists in the USA urging them never to use misoprostol for induction, not, as suggested, because of pressure from antiabortion groups but because of pressure from the FDA which has never approved misoprostol induction and has received over fifty reports of serious consequences from misoprostol induction including many cases of uterine rupture and some cases of neonatal death and maternal death.

Between 1990 and 1999 the rapid acceleration of misoprostol induction in the USA before adequate data on safety had tragic consequences. A paper in 19992 documented a 5.6 per cent rate of uterine rupture with misoprostol induction during vaginal birth after caesarean section (VBAC), a 28-fold increase in rupture rate compared with VBAC without induction. But it is easy to reliably estimate that use of this drug for this purpose before such data appeared resulted in thousands of women having misoprostol VBAC induction, hundreds of these women with uterine rupture (a grassroots organization of women with uterine rupture already has over one hundred members) and dozens of dead babies. These women were (and are) not told the risks and lack of FDA approval.

While data are still inadequate on risks of misoprostol uterine induction with unscarred uterus, since rupture in misoprostol VBAC induction is at least double rupture in VBAC induction with other prostaglandins, it is likely misoprostol is also less safe than other prostaglandins for the unscarred uterus.

Mackenzie [1] stresses cost savings with misoprostol induction but fails to factor in the great expense of increasing uterine rupture, increasing operative births, increasing neonatal special care and many cases of litigation after misoprostol induction.

While Goldberg and colleagues[3] state over 200 studies have assessed the drug's effectiveness, the majority of those studies were not of misoprostol induction but misoprostol for medical abortion or postpartum hemorrhage. None of the studies of misoprostol induction have large enough sample size to assess the more rare but serious risks such as uterine rupture and death and wide variations in methodologies exclude valid meta-analysis, leading Goldberg and colleagues to state "the relative risk of rare adverse outcomes with the use of misoprostol for labor induction remains unknown". The Cochrane

database has reviewed misoprostol induction and recommends it not be used for this purpose because of insufficient data on risks.

Misoprostol is rarely or never used for labour induction in Western Europe, Australia, and other industrialized countries. Their drug regulatory agencies agree with FDA, not approving such use because of inadequate data on safety. But misoprostol induction is widespread in the USA in spite of lack of approval from the FDA, the drug manufacturer and the scientists. Why such vigilante obstetrics - not waiting for the judge? Data from CDC [4] show an increase in induction of labour in the USA during the 1990s from 10 per cent to 20 per cent, after misoprostol induction spread, and during the same decade a significant increase in the trend for births to be more frequent Monday through Friday. ACOG and many American obstetricians approve the use of misoprostol induction without adequate data on safety because of convenience. In a country where highly qualified surgeons, i.e. obstetricians, attempt to attend most or all low-risk births, the return of daylight-weekday obstetrics takes priority over safety.

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References

1 Mackenzie WE, Misoprostol and the politics of fear, Lancet 2001; 357: 1296
2 Plaut M, Schwartz M, Lubarsky S, Uterine rupture associated with the use of misoprostol in the gravid patient with a previous cesarean section, Am J Obstet Gynecol 1999; 180: 6, 1535-40
3 Goldberg AB, Greenberg MB, Darney PD, Misoprostol and pregnancy, N Engl J Med 2001; 344: 38-47
4 www.cdc.gov/nchs/births.htm