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Associations of drugs routinely given in labour with breastfeeding at 48 hours: analysis of the Cardiff Births Survey

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Background Little is known about how breastfeeding rates are affected by drugs routinely administered in labour.

Objective To examine a large obstetric data set to investigate potentially modifiable associations between drugs routinely administered in labour and breastfeeding in healthy women and infants.

Design Retrospective cohort.

Setting The Cardiff (Wales UK) Births Survey.

Population A total of 48 366 healthy women delivering healthy singleton babies at term.

Methods Analysis of the Cardiff Births Survey.

Main outcome measure Association between intrapartum medications and breastfeeding at 48 hours postpartum.

Results At 48 hours, 43.3% (20 933/48 366) women were not breastfeeding. Regression analysis confirmed previously reported associations of lower breastfeeding rates with certain demographic indicators, epidural analgesia, intramuscular opioid analgesia and ergometrine. Novel associations were detected with oxytocin alone or in combination with ergometrine administered for prevention of postpartum haemorrhage (PPH), which were associated with reductions of 6–8%, (intramuscular oxytocin OR 0.75, 95% CI 0.61–0.91, intravenous oxytocin OR 0.68, 95% CI 0.57–0.82, oxytocin/ergometrine OR 0.77, 95% CI 0.65–0.91), and prostaglandins administered for induction of labour. The associations were maintained when subgroups, such as primiparous women, women whose labours were neither induced nor augmented, and women not receiving epidural analgesia were considered.

Conclusion Prospective studies on drugs in labour are needed to investigate potential causative associations between intrapartum medications and breastfeeding. Such studies will delineate the optimum balance between breastfeeding and maternal health, most importantly the risk of PPH.

Keywords Breastfeeding, ergometrine, oxytocin, third stage of labour, uterotonics.

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Introduction

Failure to breastfeed increases morbidity and mortality in both mothers and children in developed and developing countries.[1] The UK and the USA have breastfeeding rates 10–30% below other developed countries,[2] and are targeting annual increases of up to 2% *per annum*.[3,4] It is unlikely that these targets will be met without a full understanding of why women fail to establish breastfeeding. The main reasons cited are that there is insufficient milk and the baby does not suck.[5–7] Healthy women rarely start breastfeeding after 48 hours,[8,9] and, in developing countries, delayed breastfeeding is associated with increased infant mortality.[10]

Drugs are administered routinely in labour for a number of indications and fall into several pharmacological categories. The indications are, broadly: uterotonics for induction and augmentation of labour (prostaglandins and oxytocin) or prevention of postpartum haemorrhage (PPH) (oxytocin

and ergometrine) (Table 1); and pain control (opioids, nitrous oxide and local anaesthetics).

Based, in part, on data including our identification of the dose–response relationship between epidural fentanyl and absence of breastfeeding,[9] the need for further research into the impact of intrapartum analgesia on infant feeding was included in guidelines commissioned by NICE in 2007.[11] Currently, there is considerable international and national variation in management of third stage of labour.[12,13] The NICE guidelines recommend a change in UK standard practice for management of third stage of labour, from a combination of intramuscular oxytocin (5 units) plus ergometrine (500 μg)[14] to intramuscular oxytocin (10 units) alone, based on concerns that ergometrine is responsible for increased incidence of hypertension and nausea.[11] In addition, ergometrine may reduce breastfeeding rates.[15,16] Women in labour are thus increasingly exposed to exogenous oxytocin, the pulsatile endogenous secretion of which is closely associated with the establishment of breastfeeding.[17] There is a paucity of clinical trials of intrapartum medication with breastfeeding as the primary outcome, but interrogation of large retrospective data sets offers an alternative for the investigation of unsuspected adverse drug reactions,[18–21] such as the impact of drugs in labour. The Cardiff (Wales, UK) Births Survey is a large obstetric data set. The most recent decade available was 1989–1999 and routine obstetric practices have changed little since then: 48 366 cases were suitable for exploring the hypothesis that routinely administered intrapartum medication is associated with a reduction in the chances of breastfeeding in healthy women delivering healthy singleton babies at term. The data set is large enough to reveal effects of standard and nonstandard intrapartum medication on breastfeeding rates.

Methods

Following ethical approval and maternal consent, Cardiff Births Survey data were collected prospectively[22] and entered into the statistical package for the social sciences (SPSS Inc., Chicago, IL, USA) for windows, version 14. Uterotonics administered in the third stage of labour were analysed with five exclusive categories, and strategies for augmentation and induction were assigned four and six categories respectively (Table S1a, b). Intrapartum analgesics were each recorded as binary categorical variables, as their use is not mutually exclusive. Socio-economic status was accounted by the Townsend Index of Multiple deprivation and an adaptation of the Registrar General's groupings, based on the decennial census classifications of occupations of women or their partners; while these groupings do not readily translate into current National Statistics Socio-economic Classifications,[23] they continue to be useful predictors of income and long-term health. We analysed healthy women ordinarily resident in Cardiff and South Glamorgan[24] delivering healthy term singleton infants (gestation ≥37 weeks, birth weight ≥2500 g, 5 minutes Apgar score ≥4). We excluded infants with congenital anomalies or conditions requiring admission to special care, and women admitted to intensive care, losing >1 l of blood, remaining in hospital >7 days postpartum or with conditions indicative of ill-health likely to impede breastfeeding. Relatively few (1283/48 366, 2.7%) women were 'partially breastfeeding' (defined as infant receiving other liquids or foods in addition to breast milk).[5] A multinominal regression model was used to compare these women to the fully breastfeeding and formula feeding groups before combining them with those fully breastfeeding ($P = 0.312$ for intercept).[25] To guard against the possibility of failing to detect severe blood loss in any woman not receiving PPH prophylaxis, we also analysed blood loss and prophylactic uterotonics in women delivering in Cardiff and South Glamorgan who were unsuitable for inclusion in the main study on breastfeeding.

Breastfeeding (or not) at 48 hours, as recorded in maternal notes, was a binary outcome; accordingly, potential confounders were accounted for by logistic regression

Table 1. Uterotonics in childbirth

	Drugs	Route	Potential effect on lactation
Induction and augmentation of labour	Oxytocin	Intravenous (5 units/day)	May interfere with endogenous patterns of oxytocin secretion and sensitivity of oxytocin receptors
	Prostaglandins	*Per vaginam*	Dopamine agonists, suppress prolactin secretion and pro-inflammatory cytokines
Prevention of PPH in third stage of labour	Oxytocin	Intravenous or intramuscular (5 or 10 units)	Rapid administration may interfere with endogenous patterns of oxytocin secretion and receptor sensitivity
	Ergometrine (ergonovine)	Intravenous or intramuscular (500 μg)	Dopamine agonist, suppresses prolactin secretion and lactation
	Oxytocin/ergometrine	Intramuscular (5 units/ 500 μg)	Interaction with unknown outcome

analyses. Women expressing breast milk were not classed as breastfeeding. Table S1a, b list variables and numbers entered into the logistic regression analyses, with breastfeeding as the binary outcome variable. Explanatory variables were initially selected using a backwards likelihood ratio criterion; fitted models were then checked using analyses with enter and forward selection methods. Where data were missing, this was random;[26] therefore, where the model fitted without the affected variable, the cases were retained in the data set. Bivariate associations and trends were explored with chi-square tests and comparisons of means, as appropriate. The chi-square test for trend was based on the standard SPSS statistic for linear by linear associations.

Analyses were repeated excluding: potential outliers (women aged <16 and >50, babies with birth weights >4500 g); women from heterogenous social class categories (armed forces personnel, rank not specified, students and housewives);[27] women whose labours were induced or augmented; women receiving epidural and spinal analgesia; women partially breastfeeding; women who had delivered by Caesarean, as this may affect medication administration; and, to guard against ties in the data set, multiparous women. Data were re-analysed: including year of delivery; interaction terms for social class and analgesics; excluding Townsend Index and social class; and by social strata [non-manual occupations (classes I, II and IIIa), manual occupations (classes IV, V and armed forces) and not working (housewives and unemployed)]. Reference categories for the regression model were selected on clinical grounds, with the least invasive first, for ease of interpretation; analyses were repeated for medication administered during third stage with the largest category first. Women receiving ergometrine and no uterotonic in third stage were compared with the whole sample (Table S2a, b). Results were presented unadjusted and adjusted for potential confounders. *(For further details, see appendix S1.)*

Results

After exclusions, 48 366 women were entered into bivariate analyses and 44 641 and 18 165 into regression analyses (Figure 1A, B). At 48 hours, 43.3% (20 933/48 366) women and 37.4% (7437/19 900) primiparous women were not breastfeeding. Regression analyses confirmed previously described demographic associations with breastfeeding: breastfeeding rates increased with maternal age, parity, and social class and decreased as deprivation scores rose. In addition, when these were accounted for, there was a further independent association between intrapartum analgesia and breastfeeding (Table 2): previously described associations with breastfeeding, including intramuscular opioids and epidurals, were upheld. Inhaled nitrous oxide was associated with increased breastfeeding rates in primiparous women (Table 2, S3a, b).

The associations of uterotonics and analgesics with breastfeeding were cumulative, when the impact of social factors was accounted for. Oxytocin and ergometrine in the third stage of labour and prostaglandins for induction were associated with a significant reduction in breastfeeding rates. Unadjusted bivariate (Table S4a, b) and regression (Table 2) analyses suggested that reduced breastfeeding rates were associated with intramuscular oxytocin (5 units) in combination with ergometrine (500 μg), given to 79% of women in this cohort (adjusted OR 0.77, 95% CI 0.65–0.91, $P = 0.003$). Ergometrine alone was associated with the greatest reduction (Table S6a, b). Prostaglandins for induction were associated with reduced breastfeeding rates (adjusted OR 0.89, 0.83–0.96, $P = 0.001$ whole cohort, adjusted OR 0.85, 0.77–0.95, $P = 0.003$ primiparae only) (Table 2). Blood loss and need for transfusion were not associated with use of uterotonics in the third stage of labour, both in women in the main analysis (Table S4a, b), and when all women delivering in Cardiff and South Glamorgan were considered. Blood loss was linked to birth weight, and method of delivery.

Few women received oxytocin solely for induction (10) or augmentation of labour (18) or prostaglandins solely for augmentation (40). There was little overall change in the association between intrapartum medication and breastfeeding when regression analyses were repeated as outlined above (Table S6). Fitted models were robust with respect to the method for selecting explanatory variables: backward, forward and enter methods produced consistent results, with the same fitted models in all cases.

Discussion

Retrospective analysis of this large database revealed previously unsuspected associations between breastfeeding and intrapartum uterotonics, and confirmed associations with intrapartum analgesia and demographic factors. Routine prevention of PPH with oxytocin, either alone or in combination with ergometrine, was associated with reduction in breastfeeding rates of 6–8% at 48 hours. The association with oxytocin was strongest in women who received no previous interventions, such as induction, augmentation, epidural or spinal analgesia and those most likely to breastfeed. Other novel associations were reduced breastfeeding rates with prostaglandins administered for induction of labour, and, in primiparae, improved rates with nitrous oxide analgesia.

These findings have important potential implications and therefore warrant careful scrutiny to ascertain the extent to which they may be vulnerable to methodological constraints. Confounding by absence of direct data relating to

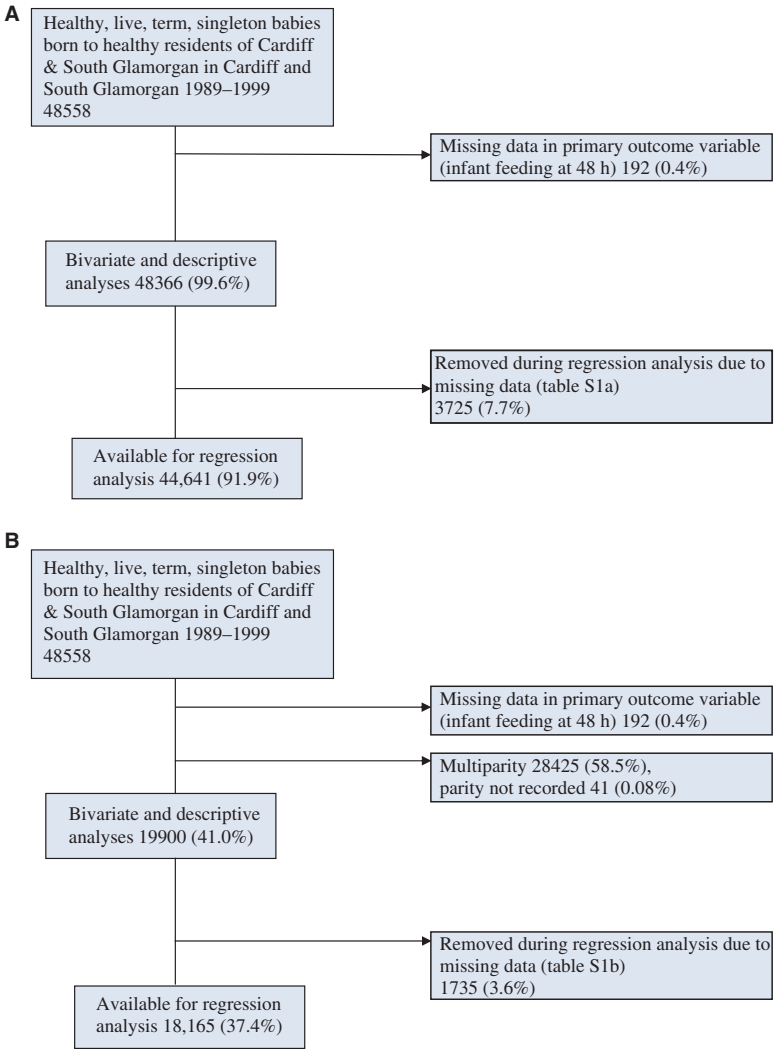

Figure 1. (A) Numbers in the analysis: multiparous and primiparous women. (B) Numbers in the analysis: primiparous women.

factors linked to breastfeeding can only be resolved by prospective observational studies, not reliant on self-reported behaviour. For example, in future studies, we would hope to record expression of breast milk in association with feeding difficulties as an indication of maternal intention and motivation. Ergometrine administration may have been confounded by perceived risk of postpartum blood loss: women who received ergometrine were older, of higher parity and more socially deprived than other participants (Table S2b). Latent, unknown or poorly defined confounders, such as biological constraints on lactation, maternal attitudes and cultural variables, can only be fully accounted by randomisation. The relatively low numbers of women receiving prophylactic ergometrine or no medication in third stage reflects current obstetric practice;[11] consequently, when the data set was subdivided, numbers in these groups fell further, reducing the power of the analysis to detect a relatively small, but clinically important, effect. Finally, the methods and quantity of data collection precluded direct observation of medication administration. Thus, it may be premature to discount the possibility that the findings might have occurred fortuitously and may not apply to other settings or to mothers suffering perinatal complications.

However, these findings merit further investigation by prospective studies, as the potential implications for infant and maternal morbidity and mortality of a reduction in breastfeeding rates by 6–8% are considerable. Certain findings reduce the likelihood of extensive confounding. Demographic differences between women receiving prophylactic uterotonics and other participants were small (Table S2a), and are unlikely to fully account for the difference in breastfeeding rates (Table 2, S4a, b). Although the proportion of women receiving no prophylactic uterotonic was

Table 2. Factors affecting breastfeeding at 48 hours of age: adjusted analysis

Variables in the equation	Whole sample (n = 44 641)		Primiparae only (n = 18 165)	
	Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*
Uterotonic for third stage		*<0.001*		*<0.001*
None, reference category	*1.00*		*1.00*	
Intramuscular oxytocin	*0.75 (0.61–0.91)*	*0.004*	*0.73 (0.52–1.04)*	*0.085*
Intravenous oxytocin	*0.68 (0.57–0.82)*	*<0.001*	*0.57 (0.41–0.80)*	*0.001*
Intramuscular oxytocin and ergometrine combined	*0.77 (0.65–0.91)*	*0.003*	*0.70 (0.51–0.96)*	*0.026*
Ergometrine intravenous or intramuscular	0.64 (0.48–0.85)	0.002	0.51 (0.26–0.98)	0.044
Induction of labour		<0.001		0.034
None, reference category	1.00		1.00	
Induction with no drugs	0.98 (0.89–1.08)	0.658	0.95 (0.82–1.11)	0.542
Induction (prostaglandins only)	*0.89 (0.83–0.96)*	*0.001*	*0.85 (0.77–0.95)*	*0.003*
Induction (oxytocin only)	0.94 (0.84–1.04)	0.207	0.88 (0.76–1.01)	0.076
Induction (both drugs)	0.98 (0.79–1.20)	0.809	0.84 (0.65–1.08)	0.169
Induction (elective section)	0.72 (0.64–0.81)	<0.001	0.86 (0.69–1.08)	0.204
Inhalational anaesthesia	Not significant in final model		*1.17 (1.06–1.30)*	*0.002*
Intramuscular opioids	0.86 (0.82–0.90)	<0.001	0.91 (0.85–0.98)	<0.001
Epidural	0.85 (0.81–0.90)	<0.001	0.87 (0.80–0.94)	<0.001
General anaesthetic	0.82 (0.73–0.92)	0.001	Not significant in final model	
Social class		<0.001		<0.001
Social class I, reference category	1.00		1.00	
Social class II	0.56 (0.50–0.63)	<0.001	0.58 (0.48–0.71)	<0.001
Social class IIIa	0.37 (0.33–0.42)	<0.001	0.35 (0.28–0.42)	<0.001
Social class IIIb	0.24 (0.21–0.27)	<0.001	0.25 (0.20–0.30)	<0.001
Social class IV	0.21 (0.19–0.24)	<0.001	0.22 (0.18–0.27)	<0.001
Social class V	0.14 (0.12–0.17)	<0.001	0.16 (0.13–0.21)	<0.001
Forces	0.36 (0.31–0.43)	<0.001	0.36 (0.28–0.48)	<0.001
Students	0.57 (0.48–0.67)	<0.001	0.39 (0.31–0.50)	<0.001
Housewives	0.16 (0.14–0.18)	<0.001	0.21 (0.14–0.30)	<0.001
Unemployed	0.14 (0.12–0.16)	<0.001	0.14 (0.11–0.18)	<0.001
Parity		<0.001	Not applicable	
Primiparous, reference category	1.00			
Parity (1 previous delivery)	0.50 (0.47–0.52)	<0.001		
Parity (2 previous deliveries)	0.38 (0.36–0.41)	<0.001		
Parity (3 previous deliveries)	0.29 (0.27–0.32)	<0.001		
Parity (4 or more previous deliveries)	0.23 (0.20–0.26)	<0.001		
Augmentation of labour	Not significant in final model		0.072	
None, reference category			1.00	
Artificial rupture of membranes only			0.91 (0.83–0.99)	0.028
Oxytocin administered			1.03 (0.93–1.13)	0.624
Prostaglandins administered			1.30 (0.71–2.23)	0.394
Mother's age	1.11 (1.10–1.11)	<0.001	1.12 (1.11–1.13)	<0.001
Townsend rank for deprivation	0.999 (0.999–0.999)	<0.001	1.00 (0.999–1.000)	<0.001
Constant	1.055	<0.001	0.666	0.071

New findings are italicized.
The variables entered into this regression model are listed in Table S1a, b.
Whole sample model: Hosmer and Lemeshow test: χ^2 = 15.46, df = 8, P = 0.051; Nagelkerke R^2 = 0.233; the model correctly predicts method of infant feeding for 68.6% of cases, 58.2% for formula feeding and 76.3% for breastfeeding.
Model including primiparae only: Hosmer and Lemeshow test: χ^2 = 15.88, df = 8, P = 0.044; Nagelkerke R^2 = 0.226; the model correctly predicts 70.8% of cases, 48.6% for formula feeding and 83.4% for breastfeeding.

higher among social classes I and II (Table S5), there was no difference between the groups in the deprivation scores (Table S2a). Conscious confounding by indication is unlikely as neither women nor clinicians would have been aware of the association between reduced breastfeeding rates and routinely administered drugs,[28–30] and we

excluded women with a clinically significant haemorrhage, which may have a negative effect on breastfeeding. When the data set was stratified, the associations between intramuscular opioids and epidural analgesia and reduced rates of breastfeeding were consistent in nearly all subgroups (Table S6). The association between prophylactic uterotonics and breastfeeding was strengthened when women not receiving epidurals, spinals, augmentation or induction and women of non-manual occupation were considered alone (Table S6). 'Difficult'[31] labour is unlikely to be an important confounder, as augmentation and induction of labour were not linked to breastfeeding, with the exception of prostaglandin induction. To minimise the threat of latent confounders to the analysis, we achieved a relatively homogeneous population by including only healthy dyads ordinarily resident in our catchment area.[24]

Although this is a retrospective analysis, large cohort studies represent a powerful method of identifying unsuspected possible adverse drug reactions.[18–21] The data set is sufficiently large to reveal independent associations of drugs administered in labour that are concealed by the more obvious impact of social class on infant feeding.[5] It is an indication of the strength of the associations uncovered here that they have emerged despite some limitations in the data, including: absence of drug doses,[18] incomplete coding for social class[23,27] and observational design. The use of drugs in labour, and the incidence of breastfeeding, described here are similar to the most recent reports:[5,13,32] at 1 week, 45% of UK women are exclusively breastfeeding.[5] Our findings are entirely consistent with previously described demographic, obstetric and pharmacological predictors of breastfeeding,[5,9,15,33–36] and there are physiological mechanisms, whereby opioids,[9] exogenous oxytocin[37] and ergometrine[16] might reduce breastfeeding (Table 1).

Ergometrine[16] and prostaglandins[38] are dopamine agonists, reducing prolactin secretion (Table 1). Prostaglandins administered *per vaginam* are systemically absorbed and metabolites remain in the circulation for several hours (duration depends on dose), and are transferred to the fetus.[39] Exogenous oxytocin has the potential to interrupt initiation of lactation by: disruption of endogenous pulsatile secretion and fluctuating concentrations when crucial changes in neuronal architecture are occurring;[40,41] augmentation of the stress response, which replaces pulsatile secretion with continuous secretion and inhibits lactation;[37,42,43] desensitisation and downregulation of myooepithelial receptors[44] and local feedback mechanisms;[45] and, more speculatively, infant or maternal behaviour.[46–48] In addition, some clinical studies report reduced breastfeeding following oxytocin administration.[7,36,49–51] (for a full account, see appendix S3). In primiparous women, nitrous oxide (with oxygen) improved breastfeeding rates. This is congruent with its short half-life and analgesic effects. Pain is a likely source of stress which may impair endogenous oxytocin release.[37,43] However, this protective effect was not seen when all women were considered, as in the Infant Birth Survey.[5] Association between third stage drugs and breastfeeding was strongest in women of non-manual occupation. We suggest that the biological impact of drugs in labour is most apparent in those who intend to breastfeed:[9] in smaller databases, where drug doses were not recorded, the impact of drugs in labour has only emerged where high proportions of women intend to breastfeed.[36,52]

Recommendations for the routine administration of uterotonics for prevention of PPH[11,14,53] are, in part, based on a systematic review demonstrating their beneficial effects on blood loss (mean difference between expectant and active management of third stage, 79 ml, 95% CI 64–94 ml).[54] This review included two randomised controlled trials,[55,56] that did not detect an effect on breastfeeding (total $n = 3142$, relative risk 0.92 (95% CI 0.82–1.04).[54] However, infant feeding was a secondary outcome, and these studies suffered cross over from the expectant to active management arms of the trials.[55,56] Trial settings may differ from routine practice:[57] some 36%,[55] and 23%[56] of women delivering in the trial hospitals participated; this may explain why the exclusive breastfeeding rates at discharge (74%, 75%,[55] 70%, 73%[56] expectant and active arms respectively) were higher than in our study and the UK Infant Feeding Surveys 2000,[23] 2005.[5] The entry criteria for these trials were clear and rigorous, and led to the exclusion of several important groups of women, such as those receiving intravenous oxytocin, which we and others[7,36,49,50] found to be associated with reduced breastfeeding rates.

If, as intimated by this analysis, the universal administration of oxytocin or oxytocin combined with ergometrine reduces breastfeeding rates, by around 7%, up to 50 000 infants in the UK and 300 000 in the USA may be affected each year, potentially accounting for over a 1000 cases of obesity and 2000 to 3000 cases of asthma in the first 9 years of life in the UK.[58] Women able to avoid third stage medication and use only inhalational analgesia might increase their chances of breastfeeding. These changes in breastfeeding rates would achieve US targets to increase the number of women initiating breastfeeding by 11% by 2010,[4] and UK targets of 2% *per annum*.[3,5] The resulting decrease in the prevalence of obesity in children could be as high as 1–3%,[59] benefitting up to 200 000 children in the US.[60] Similarly, infant hospital admissions for diarrhoea and lower respiratory tract infection might fall by up to 3.7% and 1.9% per month, respectively,[61] and breast cancer might affect 1 in 200 fewer women.[62] Therefore, these new findings should be considered in future reviews of universal routine prophylactic administration of uterotonics in the third stage of labour.[11,53]

These findings may also have implications outside the developed world. They are not directly transferable to developing counties where breastfeeding is subject to different cultural constraints, and death in the first 6 months of life is ten times more likely in formula-fed infants.[1] Any potential reduction in breastfeeding, as identified here, should be considered if prophylactic uterotonics, including prostaglandins,[63] are to be widely recommended. Our novel findings present a new dilemma: a potential conflict between realisation of the fourth (improving child mortality) and fifth (reducing maternal mortality) UN Millennium Development goals.[64]

Our findings await confirmation from prospective studies; however, their potential implications in developed[58] and, possibly, developing countries[1,10] merit consideration. Our findings might appear to strengthen arguments for physiological management of the third stage of labour in low-risk women whose labours have been neither induced nor augmented; however, in the absence of prospective studies, it would be unacceptable to risk an increase in morbidity and mortality from PPH by using our findings alone to change current recommendations. Active management shortens the third stage of labour, and is associated with increased nausea, vomiting and hypertension (diastolic BP > 100 mmHg) and, in low-risk women, manual removal of placenta (relative risk 2.05, 95% CI 1.20–3.51).[54] When oxytocin alone is compared to expectant management in randomised trials only, the reduction in PPH >1 l is not statistically significant (relative risk 0.72, 95% CI 0.49–1.05, 41/619 women lost >1 l in the oxytocin groups versus 62/654 in the comparator groups), and there is no difference in incidence of blood transfusion.[65] Closely observed expectant management of the third stage of labour is regarded as safe for low-risk women in parts of Europe and the USA,[13,53,66,67] may not be associated with increased blood loss or incidence of 500 ml or 1 l haemorrhage,[68] and may be supported, providing risk factors, including induction,[68] prolonged second stage and epidural analgesia,[69] are absent.[11] We found associations between prophylaxis for PPH and breastfeeding were weaker or absent among women whose labours had been medicated, and for whom expectant management would be ill-advised (for example those receiving epidural or spinal analgesia, induction or augmentation of labour).

Conclusion

We concur with the recommendations of the NICE guidelines[11] that associations between intrapartum medications and breastfeeding uncovered in cohort studies merit further research, including exploration of the dose–response relationship.[18] In view of the relatively modest advantages of active management of third stage,[54,65] an adequately powered randomised controlled trial to compare expectant management of third stage with prophylactic oxytocin (10 units) in low-risk women only is needed to fully address the question of latent and ill-defined confounders and provide the evidence needed to achieve the optimum balance between the competing risks of maternal PPH and failure to breastfeed. Pending this, additional resources should be allocated to support women identified in our analysis as being at high risk of breastfeeding failure, most particularly women receiving ergometrine alone. Associations uncovered in observational research cannot be deemed causative; however, were our hypothesis to be correct, where initiation of breastfeeding is proving difficult, mothers and babies might benefit if the time needed for intrapartum medications to be eliminated from mother and infant could be taken into consideration.

Disclosure of interest

All authors declare that they have no financial or other competing interests.

Contribution to authorship

Sue Jordan and Simon Emery designed the study, Sue Jordan, Alan Watkins and John Evans analysed the data, Sue Jordan, Gareth Morgan, Simon Emery, Alan Watkins, Melanie Storey wrote the manuscript and all authors have seen and approved the final version.

Details of ethical approval

Ethical approval for the Cardiff Births Survey was granted at its inception in 1965 (Evans 2005). This study used only anonymised data where consent had already been given.

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Supporting information

The following supplementary materials are available for this article:

Appendix S1. Full details of methods

Appendix S2. Data Tables S1a–S6

Appendix S3. Uterotonics and breastfeeding

Additional Supporting Information may be found in the online version of this article.

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Commentary on 'Association of drugs routinely given in labour with breastfeeding at 48 hours: analysis of the Cardiff Births Survey'

In the above article Jordan *et al.* (BJOG 2009: DOI: 10.1111/j.1471-0528.2009.02256.x), the authors are right: associations uncovered in observational research—even their well-conducted retrospective cohort study on a large database—cannot be deemed causative; their findings await confirmation from prospective studies or, ideally, randomised controlled trials. In particular, it would be important to look at the association between drugs routinely given in labour and breastfeeding in settings where the rates of initiation of breastfeeding are 90% or higher, such as Baby Friendly Hospitals in countries with breastfeeding rates well above those recorded in the UK.

The authors correctly discuss some of the limitations of their study, including the possible effects of obvious confounders and of their specific setting, in addition to the study design. They did not, however, exclude women, who did not initiate breastfeeding, from their analysis. Also, they did not adjust, because of lack of data, for support to breastfeeding provided in the first 48 hours to women who did breastfeed: time of first breastfeed, rooming-in, breastfeeding on demand, avoidance of teats and pacifiers and, most important, help for good latching and effective suckling. Finally, it is not clear whether the breastfeeding outcome refers to the whole 48 hours period or to the last recorded feed. If the latter is true, one cannot exclude that breastfeeding will resume, if adequately supported: this would add a further difficulty to the interpretation of the findings.

Posing the dilemma of a potential conflict between realisation of the fourth and fifth UN Millennium Development goals is nevertheless correct. How can the possible negative consequences of this conflict be prevented? On the maternal and routine medication sides, the suggestions for action and research put forth by Jordan *et al.* seem adequate. On the infant and breastfeeding sides, it seems obvious to recommend that all measures shown to be effective to initiate and establish exclusive breastfeeding be put in place. These include: proactively offered skilled breastfeeding support, peer or professional; preventing the provision of discharge packs containing formula-feeding information and samples; unrestricted feeding and mother–baby contact (skin-to-skin) from birth onwards; and avoiding supplementary fluids and prelacteal feeds unless medically indicated (Renfrew *et al.*, London: National Institute for Health and Clinical Excellence, 2005; Shealy *et al.*, Atlanta: Centers for Disease Control and Prevention, 2005).

All these measures, with others meant to promote the initiation of breastfeeding in pregnancy and at community level (Protheroe *et al.*, London: Health Development Agency, 2003; Dyson *et al.*, Cochrane Database of Systematic Reviews, 2005;2:CD001688), should be targeted to all women, but as a priority to those identified as being at high risk of breastfeeding failure. As the odds ratios for not breastfeeding estimated by Jordan *et al.* were much worse for social classes II to V than for any of the drugs given as uterotonic or for induction of labour, upstream policies aimed at reducing inequalities should go hand in hand with effective interventions for the protection, promotion and support of breastfeeding.

Disclosure of interest

I declare that I have no conflict of interests. ■

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Editor's Commentary

In the above article Jordan *et al.* (BJOG 2009: DOI: 10.1111/j.1471-0528.2009.02256.x), the authors have reported an interesting observation—association of postpartum use of oxytocic drugs and a lower breastfeeding rate. Is this reliable data, and could the association be causative? The observation is based on a large cohort—data collected meticulously from 48 366 pregnant women. The association was maintained even with subgroup analysis and is unlikely to be spurious.

However, the data cannot be interpreted as 'use of uterotonic agents causes a reduction in breastfeeding' and the authors have acknowledged this. The main reason for the caution is the presence of multiple confounders. For example, 1.7% of the mothers did not receive uterotonics for the third stage in this study. Why did these women not receive uterotonics despite a national recommendation (Intrapartum care, NICE clinical guideline 55, September 2007)? There is evidence of influence of social class on the likelihood of not receiving uterotonics. More women in social class 1 and 2 received no uterotonics, than those from social class 3–6 in this study. Is it possible that some women declined them? Is it possible that these belong to a distinct group of well-informed women who are highly motivated to breastfeed? One can only speculate, but it is impossible to be certain. It is also not clear why women undergoing induction of labour with oxytocin did not show a reduction in breastfeeding rate similar to those receiving oxytocin for prophylaxis of postpartum haemorrhage.

The manuscript also reports an association between induction of labour using prostaglandins and reduction in the rate of breastfeeding. It is well known that breastfeeding rates are associated with the type of analgesia in labour (Wiklund *et al.*, *Midwifery* 2009;25:e31–8,). However, epidural analgesia is commoner with induction of labour. It is uncertain if prostaglandins, the drugs used for epidural analgesia, the fact that labour was induced, women's mindset or a totally separate but unknown other factor is primarily responsible for reduction in the breastfeeding rate.

Retrospective observational studies are useful for identifying associations and generating hypotheses, but confirmation of hypotheses needs more robust evidence such as randomised trials. A Cochrane review based on two randomised trials involving 3142 women (Active versus expectant management in the third stage of labour. Cochrane Database of Systematic Reviews 2000; Issue 3) did not detect any influence of uterotonic drugs on the rate of breastfeeding. Given the limited external validity of RCTs, coming up with an appropriate design to investigate the potential causative association between intrapartum or postpartum medications and breastfeeding will be hugely challenging to say the least.

Disclosure of interest

I declare that I have no conflict of interest. ■

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