MEDICAL PRACTICE

Contemporary Themes

Drugs taken by mothers in the puerperium: inpatient survey in Northern Ireland

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Abstract

In an inpatient survey the medication records of 2004 mothers both breast and bottle feeding were examined and the drugs taken in the early postnatal period recorded. No notable differences existed between the types of drugs prescribed for breast feeding and bottle feeding mothers. Iron, vitamins, and mild analgesics were taken routinely by the population, and antibiotics, laxatives, and hypnotics were frequently prescribed. A wide range of other drugs and preparations were taken or used. Although data were available for some of the drugs, there were many whose concentrations in breast milk and potential risk to the suckling infant were unknown.

Data are urgently required on hypnotics, narcotic analgesics, antiemetics, antihistaminics, and some antimicrobial agents with respect to their concentrations in breast milk and their safety for the suckling infant.

Introduction

During the past decade there has been a considerable increase in the number of mothers breast feeding their newborn; for example, a study in Harrow found an increase from 38% in 1972 to 69% in 1976.¹ A later report from Sheffield showed that the numbers had plateaued at about 69%.² The authors of that study concluded that the educational programme alerting mothers to the benefits of

breast feeding had been largely successful, although they cautioned that further progress could be made.

Unfortunately, some suckling infants react to specific substances excreted in human milk; these include food allergens, environmental pollutants, and drugs. Adverse effects attributed to drugs in milk vary in severity and include diarrhoea, irritability, sedation, convulsions, metabolic acidosis, anaemia, and allergic sensitisation to antibiotics.³

The problem of drug excretion in breast milk and the associated adverse effects in the suckling infant have received increasing attention over the past few years and several review articles have summarised the currently available information.³⁻⁵ The reviewers, however, emphasise that many of the early reports on drug excretion in milk were inadequate owing to poor assay techniques and that few pharmacokinetic based studies have been carried out. Clearly, therefore, many of the present recommendations on whether to breast feed or not during medication are based on isolated and often anecdotal case reports. Two reasons for the paucity of relevant studies are the complexities of obtaining serum and milk samples from new mothers and an apparent lack of interest on the part of clinicians.⁶

A further major problem is the complete lack of statistical information on the range of drugs taken by mothers in the immediate postpartum period. Information of this type is required so that a systematic approach may be made to further work. Our aim was therefore to obtain and document information and to highlight those drugs for which detailed data on breast milk excretion are urgently required.

Method

The survey was carried out in three major maternity units in Belfast: the Jubilee Maternity Hospital, the Royal Maternity Hospital, and the maternity unit of The Ulster Hospital, Dundonald. Approval for the survey was obtained from the ethical committee of the faculty of medicine, The Queen's University of Belfast, and data were collected with the full coopera-

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tion of the divisions of obstetrics and gynaecology and the medical records staff of the three Eastern Health and Social Services Board districts concerned.

The medical charts of mothers who had delivered live infants in July, August, and September 1982 were reviewed and the following information recorded for each birth: (a) the mother's hospital number, (b) dates of delivery and discharge, (c) method of feeding the infant, and (d) maternal drug treatment(s) after delivery, including the drugs administered, dosage regimen, and duration of treatment. The drug regimen was obtained from the charted medicine card index. The use of occasional medicines—that is, those given "as required": for example, mild analgesics and laxatives—and the method by which the infant was fed were obtained by reference to the nursing notes.

Results

Eastern Health and Social Services Board statistics showed that during the three months of the study there had been 2078 deliveries in the three maternity units surveyed. The number of charts reviewed totalled 2004; this number excluded stillbirths and a few charts which were not available. The number of charts from hospitals 1, 2, and 3 were 683, 841, and 480, respectively.

The total number of mothers in the three units who had breast fed their infants was 734 (31%, 41%, and 37% of mothers in the respective hospitals). Of the breast feeding mothers, however, 79 had started to bottle feed before discharge from hospital. The average number of medications taken or used by the study population was 3.6 (range 0-12), and 137 different drugs or drug preparations were administered. Only 14 mothers (<1%) received no drug treatment.

Tables I-X (miniprint) list the drugs taken by all mothers, both breast feeding and artificially feeding. For convenience the drugs are subdivided by pharmacological class.

Antibiotic or antibacterial treatment (table I) was received by 310 (15.5%) of the mothers surveyed, of whom 84 received a combination of two or more agents. The most frequent antimicrobial combinations were ampicillin and metronidazole (53 mothers) and cephalixin and metronidazole (13 mothers). Equal proportions of breast and bottle feeding mothers received ampicillin, metronidazole, cephalixin, and nalidixic acid, whereas a greater proportion of bottle feeding mothers received cotrimoxazole.

Analgesics (table II) were widely prescribed, most mothers receiving them "as required." Narcotic analgesics, when required, were given every

four to six hours for 24-36 hours after delivery. Table II lists the range of analgesics given; as with many other drugs, prescribing patterns varied widely among the three hospitals. An analgesic "cocktail" containing two Codis tablets (aspirin and codeine) dissolved in 30 ml mistura alkalina sedativa (Belfast Hospital formulary) proved popular and was taken by 531 mothers. Mistura alkalina sedativa contains sodium bicarbonate, bismuth carbonate, and liquor morphine hydrochloride in chloroform water. One mother received zomepirac (analgesic), which was later withdrawn from use. Hospital 1 did not appear to have the same reliance on minor analgesics; this may have been due to the regular use of chymotrypsin and trypsin by mothers who had episiotomies. Phenylbutazone, which was subsequently restricted to hospital use for the treatment of ankylosing spondylitis, had a remarkably high incidence of usage by the mothers in the survey (38 mothers).

A large proportion of mothers (36%) received hypnotics; many of them were breast feeding their babies (194 mothers). Nitrazepam and temazepam were the two hypnotics most frequently prescribed; temazepam was administered almost exclusively in hospital 3 (see table III). Other psychoactive drugs were less commonly administered to the postnatal mothers. Diazepam was the next most popular and was given to 46 mothers, 19 of whom were breast feeding. Diazepam was commonly prescribed only for short periods, however, and primarily to those mothers who had a history of hypertension.

One mother was given lithium; however, breast feeding had been stopped two days before treatment owing to her psychiatric condition, while a further mother receiving amitriptyline continued to breast feed during drug treatment.

Anticonvulsants were prescribed for only a small number of mothers (table IV). Phenobarbitone and sodium valproate were received by bottle feeding mothers only, while an equal number of breast and bottle feeding mothers received carbamazepine (three mothers in each group) and phenytoin (two mothers in each group). One mother receiving carbamazepine changed to bottle feeding on the advice of a paediatrician.

Preparations for the gastrointestinal tract were used when required for symptomatic relief of constipation, diarrhoea, vomiting, and haemorrhoids. Table V lists the agents used. From these data it was calculated that 19% of all mothers received a laxative preparation. A common comment on the nursing charts was "oral aperient given" or "suppositories given." Unfortunately, the preparations used could not be identified in the retrospective survey, and thus no entry of these was made in the present survey record sheets. There appeared to be a bias towards the use of anthraquinone preparations—for example, Dorebanex—for bottle feeding mothers and bulk laxatives—for example, Normacol—for the breast feeding mothers. Antiemetics, including cyclizine and perphenazine, were administered most frequently in combination with narcotic analgesics. A wide range of haemorrhoidal preparations were prescribed for both breast and bottle feeding mothers.

Cardiovascular drugs administered to the mothers included diuretics, β blockers, anticoagulants, and digoxin (table VI). Methyldopa and hydralazine were also used; treatment with hydralazine was usually confined to the early days after delivery.

Table VII groups together antihistaminics (systemic H_1 receptor blockers and topical preparations). With the exception of Benlylin and chlorpheniramine such products were rarely used, and then only for short periods.

Two steroidal products (table VIII) accounted for most of the prescribing within this pharmacological subgroup. The first of these was Hydrocort, a hydrocortisone-neomycin-bacitracin ointment, which was used exclusively in one hospital to treat cracked nipples. The second steroid was medroxyprogesterone acetate injection, which was used as a long term contraceptive; this was given to 14 breast feeding and 32 bottle feeding mothers. Further discussion on this use is given below.

Haematinic and vitamin preparations were widely prescribed (table IX), 1788 (89%) of mothers receiving iron supplements. A wide range of proprietary brands were used, the most popular being a combination of ferrous fumarate and folic acid (67% of all iron preparations prescribed). There were differences in prescribing patterns in the three hospitals. In hospital 1 multivitamin supplements were commonly given, in hospital 2 vitamin C was given to 95% of mothers, while in hospital 3 there was no record of vitamin supplementation.

Apart from the drugs mentioned above a miscellaneous group of preparations were also prescribed (table X). Bromocriptine was administered to bottle feeding mothers almost exclusively in hospital 3; this drug was given most commonly to those mothers who had attempted to breast feed, had gone on to bottle feeding, and had suffered breast engorgement.

Mothers who were not immune to rubella received rubella vaccine shortly after delivery and, because conception was contraindicated for three months after vaccination, medroxyprogesterone (Depo-Provera) was commonly given concurrently (see table VIII). Mothers who received the vaccine and not the injectable contraceptive were advised to begin oral

MINIPRINT TABLES I-V

TABLE I. Antimicrobials taken by breast feeding, B, and artificially feeding, A, mothers in postnatal survey.

Drug	Hospital 1		Hospital 2		Hospital 3		Total	
	B	A	B	A	B	A	B	A
Ampicillin				1				
Amoxycillin	18	28	64	9	21	57	103	94
Cephalexin		4		2	8	15	10	21
Cloxacillin		1		1				
Chloramphenicol		1		1				
Clindamycin			1					
Co-trimoxazole								
Doxycycline	14	3	6	1	7	4	26	8
Erythromycin	7	3	1					
Flucloxacillin								
Metronidazole		1						1
Nalidixic acid								
Neomycin		4				12		16
Penicillin V	15	11	24	9	12	83	52	57
Streptomycin								
Tetracycline								
Vancomycin								
Clotrimazole								
Fluconazole								
Griseofulvin								
Hydrocortisone								
Medroxyprogesterone								
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conjugation with fats, lipases, and steroids excreted in milk.¹⁹ Thus the excretion of progesterones in milk may increase the risk of neonatal jaundice, and monitoring for hyperbilirubinaemia would be a wise precaution. It may even be suggested that children should be monitored to puberty and beyond for side effects similar to those reported for intrauterine exposure to stilboestrol.²⁰

We were interested to note that bottle feeding mothers were much more likely to receive iron and vitamin preparations. No reason for this was found.

In conclusion, this survey has documented the range of drugs normally prescribed in the immediate postpartum period. In doing so, it has highlighted those drugs which require further study with respect to their concentrations in breast milk and their safety or hazard to the suckling infant. These drugs are hypnotics, narcotic analgesics, antiemetics, antihistaminics, and some antimicrobial agents.

It is well recognised, however, that this short list of drugs may represent only the "tip of an iceberg," many mothers perhaps receiving other prescribed or over the counter drugs after discharge from the maternity units. We think that retrieval of this latter information could be best achieved with the help of community midwives, health visitors, and general practice pharmacists. It is from those groups that we are currently seeking help for a complementary and ongoing outpatient study.

References

- 1 Coles EC, Valman HB. Breast feeding in Harrow. *Lancet* 1976;ii:583.
- 2 Taitz LS. Breast feeding trends in Sheffield 1976-82. *Br Med J* 1983;287:648.
- 3 Chaplin S, Sanders GL, Smith JM. Drug excretion in human milk. *Advances in Drug Reactions and Acute Poisons Review* 1982;1:255-87.
- 4 D'Arcy PF, McElroy JC. Drugs in milk. In: D'Arcy PF, Griffin JP, eds. *Iatrogenic diseases*. 2nd ed. Update 1983. Oxford: Oxford University Press, 1983:181-9.
- 5 Wilson JT, Brown RD, Cherek DR, et al. Drug excretion in human breast milk. Principles, pharmacokinetics and projected consequences. *Clin Pharmacokinet* 1980;5:1-66.
- 6 Knowles JA. Excretion of drugs in milk—a review. *J Pediatr* 1965;66:1068-82.
- 7 Postellon DC, Aronok K. Iodine in mothers' milk. *JAMA* 1982;247:463.
- 8 Traeger A, Peiker G. Excretion of nalidixic acid via mothers' milk. *Arch Toxicol* 1980;45:388-90.
- 9 Food and Drugs Administration. Metronidazole (Flagyl) box warning. *FDA Drug Bulletin* 1976;6:22-3.
- 10 Heisterberg L, Branebjerg PE. Blood and milk concentrations of metronidazole in mothers and infants. *J Perinat Med* 1983;11:114-20.
- 11 Joint Formulary Committee. Prescribing during breast-feeding. *British National Formulary*. No 7. London: British Medical Association, The Pharmaceutical Society of Great Britain, 1984:19-22.
- 12 Bailey DN, Weibert RT, Naylor AJ, Shaw RF. A study of salicylate and caffeine excretion in the breast milk of two nursing mothers. *J Anal Toxicol* 1982;6:64-8.
- 13 Berlin CM, Yaffe SJ, Ragni M. Disposition of acetaminophen in milk, saliva and plasma of lactating women. *Pediatr Pharmacol (New York)* 1980;1:135-41.
- 14 Bitzen PO, Gustafsson B, Jostell KG, Melander A, Wahlin-Boll E. Excretion of paracetamol in human breast milk. *Eur J Clin Pharmacol* 1981;20:123-5.
- 15 Findlay JW, De Angelis R, Kearney MF, Welsh RM, Findlay JM. Analgesic drugs in breast milk and plasma. *Clin Pharmacol Ther* 1981;29:625-33.
- 16 Knowles JA. Breast milk: a source more than nutrition for the neonate. *Clinical Toxicology* 1974;7:69-82.
- 17 Kok THHG, Taitz LS, Bennett MJ, Holt DW. Drowsiness due to clemastine transmitted in breast milk. *Lancet* 1982;ii:913-4.
- 18 Saxena BN, Shrimanker K, Grudzinskas JG. Levels of contraceptive steroids in breast milk and plasma of lactating women. *Contraception* 1977;16:605-13.
- 19 Thaler MM. Jaundice in the newborn. *JAMA* 1977;237:58-62.
- 20 Herbst AL, Scully RE. Adenocarcinoma of the vagina in adolescents. *Cancer* 1970;25:745-61.

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A layman's guide to grommets

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Introduction

The use of prostheses to establish and maintain ventilation of the middle ear cleft in patients suffering from secretory otitis media (also called seromucinous otitis and glue ear) is a remarkable feature of current otological practice compared with that of 25 years ago. The number of patients presenting with this condition may have increased sufficiently to stimulate the growth of an entire industry catering for the design and manufacture of ventilation tubes, but the problem was recognised, albeit on a smaller scale, by an earlier generation of ear, nose, and throat surgeons, whose attempts to treat persistent secretory otitis media were frustrated by the lack of suitable techniques for maintaining patency of myringotomy incisions. The efforts made by successive generations of otologists both to close some perforations and simultaneously to keep others from closing spontaneously must have caused a certain amount of amusement among non-otologists over the years. Indeed, the ingenuity displayed in attempting the second goal has been quite remarkable.

In 1801 Sir Astley Cooper obtained the Copley Medal of the Royal Society for his work on the value of myringotomy for the relief of deafness. Toynbee, the great 19th century otologist, described a method of punching out a circular hole in the eardrum, which he attributed to Fabrizzi. He also described his own method of raising a triangular flap in the tympanic membrane but acknowledged that the results would only be permanent in the presence of a functioning eustachian tube.¹ Ballin described the attempts of others to maintain

an artificial perforation.² Devices used included catgut, fishbone plugs, lead wires, silver cannulas, rubber plugs, and small gold tubes. Because these and other methods were unsuccessful the subject fell in to abeyance until interest was rekindled in 1954 by Armstrong,³ who used a vinyl plastic tube, 1.5 mm in diameter, left in situ for four weeks.

What ventilation tubes are available?

It is convenient to divide ventilation tubes into two types; those for medium term use, which are grommet shaped, and those for long term use—that is, for use in patients with permanent obstruction of the eustachian tube—which are tube shaped with a flange medial to the eardrum. The key to longevity is the size of the flange. All other things being equal, a tube with a large inner flange will remain in situ for a longer time than one with a small flange. Thus the length of time the tube ought to stay in place can, to an extent, be determined preoperatively.

The grommet most often used is the Shepard grommet (fig 1). It has three features of specific importance. The outer flange is thick to minimise deformation when it is grasped by crocodile forceps during insertion; the inner flange is thin to locate easily in the myringotomy incision; and a wire is attached to facilitate manipulation of the grommet in the confines of the external auditory meatus. Shepard grommets are also available without the wire and in a choice of four colours (red, blue, green, and white). The colour is of no significance. The Shah grommet (fig 1) has a larger flange than the Shepard grommet both to promote longevity and to aid insertion.

For the "average" case of secretory otitis media grommets similar to those described are quite satisfactory. The problem arises when, after meticulous attention to the nasopharynx and upper respiratory mucosa in general, the ear continues to deteriorate and grommets do not provide a suitable answer. At some arbitrary stage a decision is

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