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 cephalexin and metronidazole (13 mothers). Equal proportions of breast and bottle feeding mothers received ampicillin, metronidazole, cephalexin, and nalidixic acid, whereas a greater proportion of bottle feeding mothers received co-trimoxazole.

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, Dorbanex—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 Benylin 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 Hydroderm, 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

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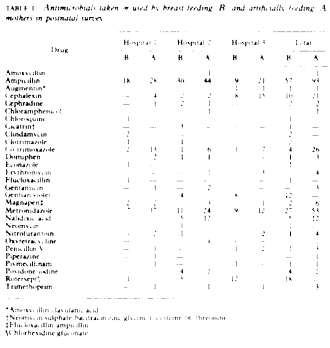
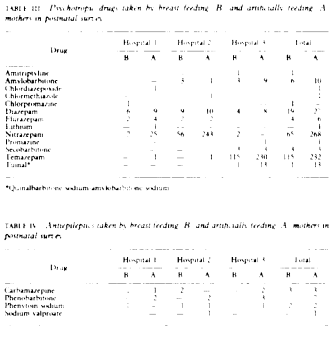
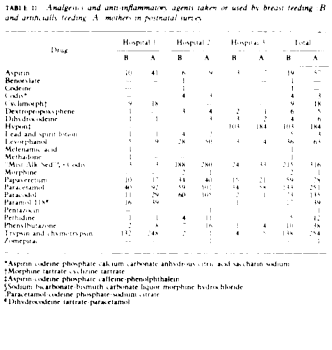
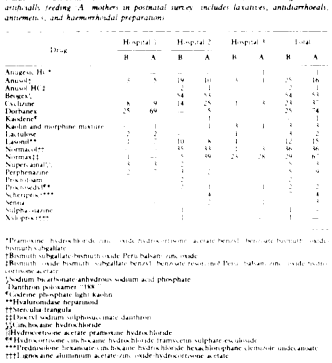
MINIPRINT TABLES I-V









contraceptives six weeks after delivery (progesterone only preparations for lactating mothers) and to continue with these for two months.

The pharmacological classes shown in tables I-X were further subdivided for statistical analysis by χ^2 test for significance of differences. There was a significant difference ($p<0{\cdot}001$) between the numbers of breast and bottle feeding mothers taking hypnotics; the greater use was in the bottle feeding group. There was also a significant difference between breast and bottle feeding mothers receiving iron and vitamin supplements ($p<0{\cdot}001$), with a greater frequency of administration to bottle feeding mothers. No statistically significant differences were found in the proportion of mothers from the two groups receiving mild and narcotic analgesics, non-steroidal anti-inflammatory drugs, laxatives, or antibacterials. Statistical analysis was confined to these drug groups since they were judged to be those used by sufficiently large numbers of mothers to make statistical evaluation reliable.

Discussion

Overall the present data indicate that with the sole exception of hypnotic drugs and iron and vitamin preparations there was no appreciable difference in the range or quantity of drugs prescribed for breast and bottle feeding mothers. The difference with hypnotics was most likely due to mothers wishing to breast feed their babies during the night and so refusing the drugs. Haematinics excepted, few drugs were taken routinely by mothers over a prolonged period. Only about 2% of the study population required long term treatment for organic disease—for example, epilepsy, cardiovascular or respiratory disorders, diabetes mellitus, and thyroid disorders. A further 2% of mothers received a medroxyprogesterone injection, and several breast feeding mothers would be expected to take oral progestogens as contraceptives. Thus at least 4% of the study population (and therefore roughly 4% of breast feeding mothers) received long term medication.

The relatively high incidence of both short term and long term medication and the wide range of drugs taken by nursing mothers highlight the need for evaluation of their potential adverse effects in the suckling infant.

The concentrations in milk of many antibiotics have been estimated both theoretically and experimentally and, although these amounts have been found to be subtherapeutic, they may cause sensitivity reactions.[3,5] Many of the breast feeding mothers (17%) in this survey received antibiotics.

A single case report of raised serum and urine concentrations of iodine in an infant whose mother had been receiving povidone-iodine has been reported.[7] Although the mother had been using 200 mg pessaries for six days, compared with the occasional wound soaks received by mothers in our survey (see table I), it may be advisable to monitor infant serum or urine iodine, triiodothyronine, and thyroxine concentrations in all cases where povidone-iodine has been used in a nursing mother.

There is much confusion in reports about the advisability of lactating mothers using nalidixic acid or metronidazole. Some authorities advise against their use,[3] whereas others consider nalidixic acid to be safe.[8] Metronidazole is contraindicated for use by some workers, and this advice is based on a communication from the United States Food and Drugs Administration, which states that metronidazole is both mutagenic and carcinogenic.[9] Also some preliminary work presented in a later paper on metronidazole[10] suggested that the dose of drug ingested by a suckling infant may be within the recommended therapeutic range for infants (10-20 mg/kg/day) if the mother receives 1200 mg/day; it recommends that breast feeding should be temporarily stopped. The *British National Formulary* advises that metronidazole should be avoided or used with caution during breast feeding, since it may give a bitter taste to the milk.[11] In our study 27 breast feeding mothers were taking metronidazole, and this must be a matter of concern in view of the uncertainty of its safety if ingested by the suckling infant.

It has been well established that the ingestion of occasional, small doses of mild analgesics by lactating mothers should not adversely affect the infant.[12-15] Codeine was the most common narcotic analgesic taken by mothers in this survey. Codeine, morphine, pethidine, and dextropropoxyphene have all been categorised in a "use with caution and closely monitor the infant" class.[3] Levorphanol and papaveretum, however, were taken more frequently than any of the above narcotic analgesics (excluding codeine) by the surveyed mothers. These latter two drugs have received little or no attention to date in milk excretion studies, and until their excretion pattern has been established in milk we suggest that the babies of mothers receiving these drugs should be closely monitored.

Studies on milk concentrations of psychoactive drugs reported to date have centred on those preparations that seem (so far as our study shows) to be least frequently administered to mothers. For example, amitriptyline, diazepam, and lithium have been investigated[3] but nitrazepam and temazepam, which were commonly administered in this series, have not been studied. This again is a matter for concern.

About 1% of the surveyed mothers were taking anticonvulsant drugs and, although numbers were small, based on charted nursing notes there was a greater maternal desire for breast feeding in this group; as a result of medical advice, however, breast feeding was not always carried out. This was also so for mothers receiving antihypertensive drug treatment. Fortunately, both these groups of drugs have been well researched over recent years so that the prescriber can confidently give advice on the advisability of breast feeding (see *British National Formulary*[11]).

Milk concentrations of the antiemetics cyclizine and perphenazine are presently unknown. These two drugs were taken together with narcotic analgesics in this study and they may cause synergistic side effects in the suckling infant.

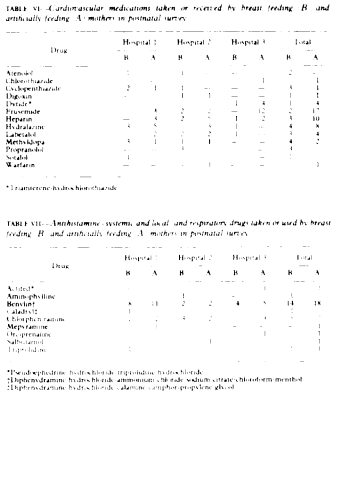
Constipation was commonly treated with anthraquinone derivatives, yet senna and its derivatives are thought to cause diarrhoea in breast fed infants.[16]

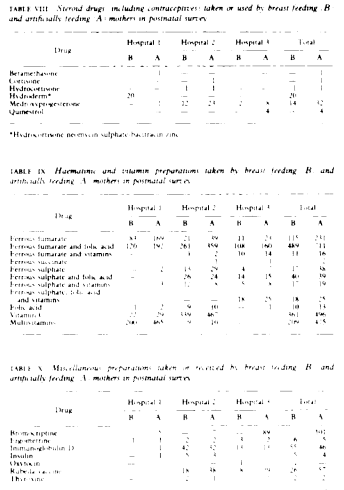
Many of the respiratory preparations used contained an antihistamine, and little is known about the excretion of antihistamines in milk. They do have sedative side effects and clearly they may cause drowsiness if ingested by the infant. A single report supporting this describes the infant as irritable, difficult to feed, and drowsy; the mother had taken an antihistamine preparation containing clemastine.[17] The incidence of usage of other respiratory preparations was low.

Oestrogen containing contraceptives are contraindicated when breast feeding, and "minipills" containing progestogens only are usually recommended.[4] Our survey showed that this advice had been well followed in the breast feeding group of mothers. Depot medroxyprogesterone acetate may, however, be used with caution by breast feeding mothers. One group of workers found a milk to plasma ratio of 1 for this preparation.[18]

Breast milk jaundice is attributed to the interference of bilirubin

MINIPRINT TABLES VI-X





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.

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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.

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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