A survey of the administration of drugs to young infants

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Medication which is given to young infants during the first months of life, an important period of development, may have effects on development which would not be observed in adults receiving the same drugs. The aim of this study was to estimate the numbers of children receiving various types of medication, including both prescription and non-prescription drugs, during the first 6 months of life. Self-completion questionnaires were posted to mothers participating in the Avon Longitudinal Study of Pregnancy & Childhood (ALSPAC) when their children were 6 months of age. These questionnaires included enquiries about the administration of drugs to the study children. The study was based in the three Bristol-based health districts of Avon in the United Kingdom. The study population comprised of 6973 children born in the 12 month period between the 1st July 1991 and the 30th June 1992. The majority of mothers, 96%, reported that their children had received medication, excluding vaccines, during the first 6 months of life. 35% had been given drugs from four or more different classes. Paracetamol had been given to 84% of the children, antibiotics to 30%. In view of potential effects of drug exposure on long term development, it is important that drugs which are administered to children are carefully assessed to ensure that they are not harmful.

Keywords cohort study drug use children paracetamol pharmaco-epidemiology non-prescription drugs

Introduction

There is awareness that certain drugs ingested by the mother during pregnancy, such as anti-convulsants, may damage the foetus causing structural malformations or neurological deficit; and there is also awareness that medications, such as tetracyclines, taken by the mother can reach the susceptible infant via the breast milk with possible adverse effects. More common, however, is the direct administration of drugs to young infants, yet this is rarely studied.

It is important to study drug administration to young children as drugs may have effects on mental and physical development which are peculiar to young children. The period of most rapid brain growth for man is between 3 months prior to term and 6 months after delivery [1]. This is possibly the period of greatest susceptibility to any external influence that may affect the developing brain. The potential sensitivity of the developing nervous system to external influences is illustrated by the adverse effects of lead on infants [2]. Prenatal exposure to various medicinal

drugs, including aspirin [3], the α_2 -adrenoceptor agonist clonidine [4], glucocorticoids [5], and hydantoin anticonvulsants [6] has been suspected of potentially causing adverse effects on mental development, although, for most of these drugs there is no conclusive evidence of such effects.

Studies of drug administration to children should consider over-the-counter preparations, as these may constitute a significant fraction of total drug usage and are available without prior medical consultation. To obtain reliable information on the actual usage of drugs, including both prescription and non-prescription preparations, it is necessary to consider reported use by the child's mother. Maternal report will give information on the *actual* consumption or use of drugs from all sources. Validation of reported drug usage is extremely difficult. There is no independent source of information available for over the counter drugs, which may constitute a large proportion of the drugs used. Independent information about prescription

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drugs may be obtained from medical records; however, the issuing of a prescription does not necessarily mean that the drug has been used, and prescription drugs may be obtained, without prescription, from friends or from surpluses left over from old prescriptions.

In this paper we present data from the Avon Longitudinal Study of Pregnancy and Childhood, a longitudinal cohort study. We investigated maternal report of the administration of drugs—including dietary supplements, prescription and non-prescription drugs, but excluding vaccines—to children between birth and 6 months of age. The aim of the investigation was to estimate the numbers of children exposed to drugs, and hence at risk of possible adverse effects caused by these drugs, in the first 6 months of life.

There have been few studies investigating drug use by children in this age group. Although Rylance *et al.* [7] studied drug use by children during the period 1984 to 1985, their study included only 18 children below the age of 1 year.

Methods

Study design

The Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC) is a geographically based cohort study investigating the factors influencing the health and development of children set in the United Kingdom [8]. Women were enrolled early during pregnancy. Information about their environment and behaviour was obtained from self-completion postal questionnaires administered at specific time points. The ALSPAC survey includes over 14,000 children, with the recruitment rate of between 80–90% of the known births from the defined area. All pregnant women from the three Bristol-based health districts of Avon with an expected date of delivery between 1st April 1991 and 31st December 1992 were eligible. Due to the seasonal variation in the use of certain drugs, a 12 month cohort, consisting of births between the 1st July 1991 and the 30th June 1992 inclusive, was selected for this present investigation. The study was approved by the three Bristol based ethics Committees and by the study's own Ethics Committee.

Questionnaire design

Structured questions enquiring about the administration of drugs to infants were included in the questionnaire administered 6 months after delivery. Mothers were asked: 'Children often have accidents or illnesses that need treatment. Please indicate which of the following have been given to your child in the last 6 months.' They were then asked to tick boxes corresponding to: 'Never', 'Yes for one episode only', or 'Yes for 2 or more episodes', for each of the following categories of drugs: 'cough medicine, antibiotics/penicillin, throat medicine, vitamins, paracetamol/calpol, ointment for skin, eye ointment, diarrhoea mixture, dimotap/decongestant, ear drops, eye drops, teething gel, laxative, and other'. The

mothers were also asked for the names of the substances used. Due to the difficulty of analysing and presenting textual information, data from these questions are not currently available. Because of the limited scope of prescription data, as mentioned in the introduction, the questionnaire responses were not compared with clinical records or prescription returns.

Response rates

Of the 8342 6-month questionnaires sent to mothers of children born in the relevant 6 month period, 6973 (84%) questionnaires, corresponding to 6805 singletons and 168 twin children, were returned. The questionnaires were completed when the children were a median age of 26 weeks, with an interquartile range of 26 to 28 weeks. 90% of the questionnaires were completed when the child was between 26 and 33 weeks of age. The median maternal age at delivery was 28 years with an interquartile range of 25 to 32 years.

Results

These data are from the 6973 returned questionnaires. The number of cases where responses were absent ranged from 104 (1%) to 277 (4%) for the enquiries about specific types of drugs. There were 3695 (53%) cases with no response for the question about any 'other' medicine. If there was no response to an enquiry about a particular type of drug, it was assumed that no relevant drug had been taken. This may have caused a slight underestimate in drug usage; e.g. disregarding cases where no response was given would have increased the estimate of the proportion of children receiving paracetamol from 84% to 86%.

According to maternal report: 96% of the children had been given at least one of the preparations listed, and 35% had received preparations from four or more of the groups (Table 1). If responses to the enquiry about vitamins, which are often considered a dietary supplement, are excluded, 96% of the children had been given a least one preparation and 28% had received drugs from four or more groups (Table 1).

Table 1 The number of different types of drug, excluding vaccines, given to children during the first 6 months of life

Number of different types of drugs	Number of children (All drugs)		Number of children (Excluding vitamins)	
None	246	(4%)	286	(4%)
1	778	(11%)	937	(13%)
2	1648	(24%)	1901	(27%)
3	1881	(27%)	1898	(27%)
4	1291	(19%)	1105	(16%)
5	688	(10%)	564	(8%)
6	290	(4%)	192	(3%)
7+	151	(2%)	90	(1%)
Total	6973	(100%)	6973	(100%)

Table 2 Number of children given different types of drugs, excluding vaccines, in the first 6 months of life

Drug	'Yes'		'Once only'		'More than once'	
Paracetamol	5875	(84%)	1432	(21%)	4443	(64%)
Teething gel	3761	(54%)	817	(12%)	2944	(42%)
Skin ointment	2725	(39%)	876	(13%)	1849	(27%)
Antibiotics	2058	(30%)	1438	(21%)	620	(9%)
Vitamins	1697	(24%)	157	(2%)	1540	(22%)
Eye drops	1166	(17%)	753	(11%)	413	(6%)
Eye ointment	1023	(15%)	689	(10%)	334	(5%)
Cough medicine	993	(14%)	715	(10%)	278	(4%)
Anti-diarrhoeal	484	(7%)	362	(5%)	122	(2%)
Decongestant	356	(5%)	181	(3%)	175	(3%)
Laxative	196	(3%)	94	(1%)	102	(1%)
Ear drops	101	(1%)	73	(1%)	28	(0%)
Throat medicine	66	(1%)	49	(1%)	17	(0%)
Other	664	(10%)	191	(3%)	473	(7%)
Total	6973	(100%)	6973	(100%)	6973	(100%)

A majority of the children received paracetamol preparations (84%); a large proportion also received antibiotics (30%) and cough preparations (14%). 54% of the population had had teething gel and 39% received skin ointments (Table 2).

Discussion

The results presented probably represent an underestimate of the true usage of drugs in the first 6 months of life; mothers are unlikely to mistakenly report the use of a drug, but may forget to report a drug that was used. Bearing this in mind, the extent of drug use is even more striking. The vast majority of children receive some form of medication, excluding vaccines, in their first 6 months of life, thus it is important to consider the safety of these drugs when given to young children, particularly with respect to possible effects on development.

Drug safety is primarily established through animal studies, with additional data provided by clinical trials and case reports of adverse effects. Establishing drug safety in children is particularly problematic. There are difficulties in interpreting data from animal studies; in particular good animal models of human mental development may not be available. Clinical

trials generally do not include infants. Children may respond to drugs differently from adults due to differences in drug absorption, metabolism and elimination. Drugs may have effects on mental and physical development which are only seen in children. Case reports tend to include obvious reactions; subtle and/or delayed effects on development are unlikely to be reported.

Adverse effects of drugs on the development of young children are unlikely to be observed through either clinical trials or case reports unless major or immediate side effects occur. Epidemiological study of the safety of drugs given to young children is therefore the only feasible method of ensuring that exposure to common medications has no adverse effects on subsequent mental or physical development [9].

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