January-March
April-June
July-September
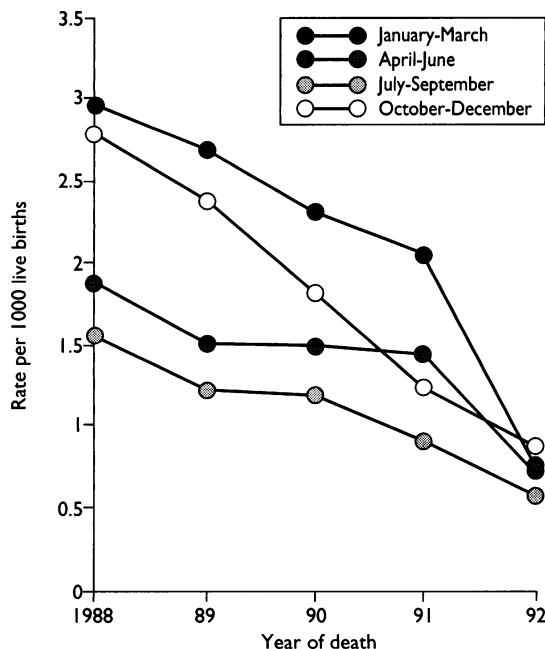October-December

Rate per 1000 live births

Year of death

Sudden infant deaths in England and Wales in each quarter from 1988 to 1992

steep slopes being seen in October-December (b = −0·52, −0·39 to −0·65) and January-March (b = −0·31, −0·24 to −0·39). Differences between slopes were significant (P < 0·001). Between 1991 and 1992 the rate in April-June fell sharply for the first time since 1989 (by half), while the decline in January-March steepened abruptly. All quarterly rates converged over the period, until in 1992 there was little difference between them.

Comment

Although sudden infant death rates were falling before the campaign, the rates fell dramatically in 1992. Large falls occurred in 1992 in the first and second quarters, those immediately after the campaign's launch, while sudden infant death rates in July-September and October-December were within the range expected on the basis of the slopes during 1988-91.

In Avon the proportion of infants laid to sleep on their backs increased from 5% in September 1991 to 23% in December 1991 and 40% in June 1992.[2] If the campaign had caused national changes in infant care practices which persisted throughout 1992, the larger drop in sudden infant death rates in the first two quarters of 1992 could indicate that the interaction between prone sleeping position and the underlying pathogenic mechanisms that it affects (overheating or respiratory obstruction, possibly exacerbated by infection) is more important in the early part of the year. Alternatively, the lack of a noticeable drop in rates in the last two quarters of 1992 could indicate a waning of the campaign's impact on infant care practices. Less likely, the observed trend might have been dependent on other factors.

Although it is satisfying to see such dramatic reductions, monitoring of the infant care practices featured in the campaign is needed to identify the effect of the campaign on the trend in sudden infant death. Continued monitoring of rates, and the seasonal distribution of sudden infant deaths will also be interesting.

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3 Mitchell EA, Brunt JM, Everard C. Reduction in mortality from sudden infant death syndrome in New Zealand: 1986-92. *Arch Dis Child* 1994;70:291-4.
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Neonatal vitamin K prophylaxis in the British Isles: current practice and trends

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In 1992 an unexpected association was reported between intramuscular vitamin K prophylaxis in the neonatal period and later childhood cancer.[1] Although unconfirmed, the report obliged paediatricians to review their prophylaxis policies and led the British Paediatric Association to recommend the routine use of oral vitamin K in all healthy neonates, reserving intramuscular prophylaxis for those at greatest risk of vitamin K deficiency bleeding.[2] We have documented changes in prophylaxis policies so that any consequences can be assessed in terms of either the incidence of vitamin K deficiency bleeding or any possible side effects.

Materials, methods, and results

In October 1993 a questionnaire was sent to every neonatal unit listed by the Neonatal Nurses' Association requesting information on annual delivery rate, details of vitamin K prophylaxis policy, and any policy changes since January 1992. Results were compared with those in a similar survey in 1988.[3] Replies were received from 253 (98%) units, representing 747 000 deliveries a year (90% of births in the British Isles). Trends in practice since 1970 include an increase in the proportion of babies given any prophylaxis (from 23% to 98%) and an increase in the proportion given vitamin K by mouth (from none to 58%). The proportion of babies routinely given intramuscular vitamin K increased from 23% in 1970 to 58% in 1982 and 1988, falling again to 38% in 1993 (table).

No consensus exists regarding the dose or frequency of administration of oral vitamin K, the total dose varying by a factor of 65. The commonest regimens recommend three doses of 0·5-1·0 mg over the first six weeks, but 37 neonatal units (15% of births) did not recommend any doses beyond 7 days of age, despite reports of late failure of single oral dose prophylaxis.[4]

Three quarters (73%) of the neonatal units surveyed had amended their vitamin K policy since January 1992, including 39 units which still recommended parenteral prophylaxis for all but offered oral prophylaxis if parental consent for injection was withheld.

Changes in routine vitamin K prophylaxis in British Isles since 1970. Figures are percentages

Year	Type of study	Intra-muscular	Oral	Route not specified	Nil
1970	Prospective cohort of 16 000 babies[5]	23	–	–	77
1982	Retrospective national survey (% of units)[3]	58	5	–	37
1988	Contemporary national survey (% of births)[3]	57	30	–	13
1993	Contemporary national survey (% of births; present report)	38	58	2	2

Note: 1982 data are expressed as percentage of neonatal units surveyed, as retrospective information on annual live birth rate for each unit was not obtained. Prospective data from 1988,[3] however, were similar whether expressed as percentage of births per year or percentage of neonatal units.

Reasons for a policy change included concern over possible adverse effects of intramuscular vitamin K (71%), reports of vitamin K deficiency bleeding (49%), and problems over the use of an unlicensed oral preparation (27%).

Comment

Almost all infants born in the British Isles now receive vitamin K prophylaxis and the trend towards oral administration continues. Nevertheless, 27% of nurseries cited concern about the unlicensed oral use of vitamin K preparations as a reason for policy changes. Professionals may feel trapped by a dilemma. Giving vitamin K by intramuscular injection is seen as undesirable and may be associated with an increased risk of cancer, yet the injection uses a licensed preparation and provides reliable protection against vitamin K deficiency bleeding. Conversely oral regimens avoid the trauma of injection and any potential risk of extremely high blood concentrations and have not been implicated in any cancer risk. However, the efficacy of multiple oral dose regimens is not well established. They are complicated to administer, and their use of unlicensed preparations may theoretically expose professionals to litigation in the event of failure of prophylaxis or of unforeseen adverse effects.

The data highlight the current confusion over the optimal dose of oral vitamin K. Formula fed infants, whose vitamin K intake is around 25 μg daily, rarely bleed from vitamin K deficiency. Hence it would be logical to suppose that a similar daily supplement given to breast fed infants would also be protective while avoiding unphysiological peak plasma concentrations.[2]

Whatever regimen is used, we suggest that parents should be given written information about vitamin K prophylaxis and deficiency bleeding early in pregnancy to allow time for deliberation. The recommendations of the maternity unit can then be stated, including endorsement of breast feeding, and signed consent requested.

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Statistics Notes

Calculating correlation coefficients with repeated observations: Part 2—correlation between subjects

J Martin Bland, Douglas G Altman

Means of repeated measurements of intramural pH and $PaCO_2$ for eight subjects[3]

Subject	pH	$PaCO_2$	Number
1	6·49	4·04	4
2	7·05	5·37	4
3	7·36	4·83	9
4	7·33	5·31	5
5	7·31	4·40	8
6	7·32	4·92	6
7	6·91	6·60	3
8	7·12	4·78	8

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In earlier *Statistics Notes*[1 2] we commented on the analysis of paired data where there is more than one observation per subject. It can be highly misleading to analyse such data by combining repeated observations from several subjects and then calculating the correlation coefficient as if the data were a simple sample.[1] The appropriate analysis depends on the question we wish to answer. If we want to know whether an increase in one variable within the individual is associated with an increase in the other we can calculate the correlation coefficient within subjects.[2] If we want to know whether subjects with high values of one variable also tend to have high values of the other we can use the correlation between the subject means, which we shall describe here.

The table shows the mean pH and $PaCO_2$ for each of eight subjects, with the number of pairs of observations for each. The 47 pairs of measurements from which these means were calculated were given previously.[2] Here we are interested in whether the average pH for a subject is related to the subject's average $PaCO_2$.

We can calculate the usual correlation coefficient for the mean pH and mean $PaCO_2$. For the data in the table this gives $r = 0.09$, $P = 0.8$.

This analysis does not take into account the different numbers of measurements on each subject. Whether this matters depends on how different the numbers of observations are and whether the measurements within subjects vary much compared with the means between subjects. We can calculate a weighted correlation coefficient, using the number of observations as weights. Many computer programs will calculate this, but it is not difficult to do by hand.

We denote the mean pH and $PaCO_2$ for subject i by $\bar{x}_i$ and $\bar{y}_i$, the number of observations for subject i by m_i, and the number of subjects by n. It is fairly obvious[4] that the weighted mean of the $\bar{x}_i$ is $\Sigma m_i \bar{x}_i / \Sigma m_i$. In the usual case, where there is one observation per subject, the m_i are all one and this formula gives the usual mean $\Sigma \bar{x}_i / n$.

An easy way to calculate the weighted correlation coefficient is to replace each individual observation by its subject mean. Thus the table would yield 47 pairs of observations, the first four of which would each be pH = 6·49 and $PaCO_2 = 4.04$, and so on. If we use the usual formula for the correlation coefficient on the expanded data we will get the weighted correlation coefficient. However, we must be careful when it comes to the P value. We have only 8 observations (n in general), not 47. We should ignore any P value printed by our computer program, and use a statistical table instead.

The actual formula for a weighted correlation coefficient is:

$$\frac{\Sigma m_i \bar{x}_i \bar{y}_i - \Sigma m_i \bar{x}_i \Sigma m_i \bar{y}_i / \Sigma m_i}{\sqrt{\left(\Sigma m_i \bar{x}_i^2 - (\Sigma m_i \bar{x}_i)^2 / \Sigma m_i\right)\left(\Sigma m_i \bar{y}_i - (\Sigma m_i \bar{y}_i)^2 / \Sigma m_i\right)}}$$

where all summations are from $i = 1$ to n. When all the m_i are equal they cancel out, giving the usual formula for a correlation coefficient.

For the data in the table the weighted correlation coefficient is $r = 0.08$, $P = 0.9$. There is no evidence that subjects with a high pH also have a high $PaCO_2$. However, as we have already shown,[2] within the subject a rise in pH was associated with a fall in $PaCO_2$.

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3 Boyd O, Mackay CJ, Lamb G, Bland JM, Grounds RM, Bennett ED. Comparison of clinical information gained from routine blood-gas analysis and from gastric tonometry for intramural pH. Lancet 1993;341:142-6.
4 Armitage P, Berry G. Statistical methods in medical research. 3rd ed. Oxford: Blackwell, 1994:215.