A STUDY OF THE EFFECT OF VITAMIN K UPON NEONATAL SURVIVAL IN AFRICAN AND INDIAN PATIENTS

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The possibility that routine intrapartum administration of vitamin K may produce a reduction in the incidence of neonatal haemorrhage has been debated for many years, and opinions remain divided. This state of uncertainty served as a stimulus to the present study, in which an attempt was made to evaluate the effects of intrapartum vitamin K among African and Indian patients.

Haemorrhagic lesions in the newborn may be due to various factors, viz. (1) Vascular lesions, traumatic or anoxic; (2) low prothrombin levels, which may be the result of insufficiency of supply or inefficiency in formation, the latter consideration being particularly important in the premature baby; (3) coagulation factors other than prothrombin; and (4) factors impairing capillary resistance. The prothrombin level, therefore, is only one of several significant factors.

The average newborn baby has a birth prothrombin level of 20–50% of the normal adult value. Thereafter there is a fall till the 3rd day to approximately 10% of the adult value, and a subsequent rapid rise till the end of the 1st week.

The maximum fall in prothrombin level occurs between the 2nd and 5th days,[1, 2] and it has been shown that the intrapartum maternal administration of vitamin K prevents this fall. While the vitamin also produces a statistically significant rise in the level at birth, this rise is but slight. The 8th-day level is likewise not appreciably affected.[1, 3, 13] Consequently, it is postulated that the birth and 8th-day values are largely determined by some factor other than vitamin K, whereas vitamin K is concerned to a large degree in the fall between the 2nd and 5th days. It follows that an improvement in the stillbirth rate in patients with normal labours and deliveries cannot be expected as a result of the administration of vitamin K.

The prothrombin level falls to an even greater extent with prolonged labour, albuminuria, placental insufficiency, and the administration of barbiturates during labour. The infants in these cases also have an abnormally low prothrombin level at birth. Intrapartum vitamin K has been shown to raise the low birth level and prevent the severe fall in the large majority of these cases.[1, 4] Thus the benefit to the neonate from intrapartum maternal injection is superior to that accruing from injection of the neonate.

Vitamin K given *intra partum* by intramuscular injection is effective, after 15 minutes, in preventing the expected fall in neonatal prothrombin level, but the mother requires a repeat injection every 24 hours until delivery.[4, 5] Bohlender, however, claims to have achieved the same effect with injection of vitamin K only 5 minutes before delivery.[6]

This theoretical basis underlies the rationale of intrapartum administration of vitamin K. A large number of investigations on this basis have produced entirely contradictory results. For example, the largest reported series are those of Dam *et al.*[1] in Scandinavia, with 33,000 cases, and Potter[5] in America, with 13,000 cases. Potter found no improvement with vitamin K administration. Dam, on the other hand, who investigated prothrombin time changes in great detail, came to the conclusion that intrapartum vitamin K lowered the number of neonatal deaths from haemorrhagic lesions. It is generally accepted, however, that the improvement is too slight to warrant the routine use of vitamin K.

In view of the fact that African and Indian patients differ markedly from the average European in the degree of malnutrition, liver damage, frequency of childbearing, and traumatic factors during labour, it was decided to investigate the position in this group of patients at the King Edward VIII Hospital, Durban.

A further reason for the investigation was our observation that, as shown by the figures here reported, the incidence of fatal haemorrhagic lesions among European babies as quoted by most authorities is less than 0·5%, whereas there is a considerably greater incidence in African and Indian patients.

THE INVESTIGATION

Vitamin K (tetrasodium 2-methyl-1, 4-naphthohydroquinone diphosphoric acid ester*), given intramuscularly in the dosage of 10 mg., was used throughout the series. It was administered by the nursing staff in the admission room of the labour theatres (labour 'wards'), as far as possible to alternate patients upon arrival. The majority received the vitamin K between ½ hour and 4 hours before delivery, a slightly smaller number between 4 and 12 hours, and very few more than 24 hours before delivery.

A total of 7,802 cases was investigated between May 1957 and March 1958. Patients delivering before admission, those with stillbirths and those with babies weighing less than 1,000 g. (2 lb. 2½ oz.) were excluded from the series.

Comparison of Groups

In Table I is shown the number in each group expressed as a percentage of the total (7,802) and classified according to parity and maturity. The groups are seen to be proportionally

TABLE I. TOTAL CONSECUTIVE VIABLE LIVEBIRTHS IN HOSPITAL (7,802)

		Received Vit. K (3,312)		*No Vit. K* (4,490)	
Primiparae	Premature	1·3%	(102)	1·8%	(143)
	Mature	10·4%	(814)	12·4%	(966)
Multiparae	Premature	2·3%	(180)	4·5%	(357)
	Mature	28·4%	(2,216)	38·7%	(3,024)

comparable, with the exception of the multiparous premature group, where there is overloading of those who did not receive vitamin K. For this reason, and because maturity is shown to be an important factor in the incidence of haemorrhagic lesions, the premature and mature groups are considered separately in the final evaluation.

In assessing a series of this nature, various other factors should be comparable, such as diet, season and manner of birth.

* Synkavit (Roche).

By far the majority of patients at the King Edward VIII Hospital are drawn from the low income group of Africans and Indians, in whom the diet is invariably—and sometimes grossly—deficient.

Certain investigators have shown that there is a seasonal variation in haemorrhagic lesions—being maximal in spring.[1, 5] The generally accepted view at present is that this is due to an alteration in capillary permeability.[7] Our series includes too few cases during autumn to evaluate this factor fully but, on the figures available, comparatively few haemorrhages occurred in midsummer, while the remainder were scattered at random, with no particular peak in spring.

It is an interesting fact that artificial feeding as opposed to breast feeding has been shown to result in only a very short and slight fall in prothrombin level, of no more than 24 hours' duration.[1] The babies in this series were almost exclusively breast-fed or fed on expressed breast milk.

In Table II is shown the manner of birth expressed as a percentage for each group, viz. those receiving vitamin K

TABLE II. COMPARISON OF MANNER OF BIRTH (% OF TOTAL IN EACH GROUP)

		Received Vit. K		*No Vit. K*	
Vertex	Premature	76·9	(216)	81·9	(410)
	Mature	89·9	(2,726)	87·3	(3,484)
Breech	Premature	14·1	(40)	9·2	(46)
	Mature	1·7	(52)	2·3	(92)
Forceps	Premature	2·1	(6)	2·6	(13)
	Mature	3·0	(92)	3·6	(144)
Caesarean section	Premature	7·1	(20)	5·8	(29)
	Mature	4·2	(128)	5·7	(229)
Symphysiotomy	Premature	0·0	(0)	0·4	(2)
	Mature	1·0	(32)	1·0	(41)

and those not receiving vitamin K, with separate consideration of premature and mature babies. It is evident that these groups are comparable apart from a small disproportion among the premature breech deliveries in favour of those who did not receive the vitamin.

In the foregoing tables it is clear that the two groups—those who received vitamin K and those who did not—are comparable, with the exception of the number of multiparous premature infants.

In Table III is shown the distribution of the neonatal deaths according to the manner of delivery, grouping the

TABLE III. DISTRIBUTION OF NEONATAL DEATHS (% OF TOTAL IN EACH GROUP)

		Received Vit. K		*No Vit. K*	
Vertex	Premature	9·9	(28)	12·8	(64)
	Mature	0·5	(15)	0·85	(34)
Breech	Premature	2·5	(7)	2·4	(12)
	Mature	0·03	(1)	0·05	(2)
Forceps	Premature	0·3	(1)	0·4	(2)
	Mature	0·29	(9)	0·20	(8)
Caesarean section	Premature	0·3	(1)	1·4	(7)
	Mature	0·03	(1)	0·13	(5)
Symphysiotomy	Premature	0·0	(0)	0·2	(1)
	Mature	0·09	(3)	0·15	(6)

cases in the same manner as in Table II. There were 207 neonatal deaths, 123 premature and 84 mature. Of these, intrapartum vitamin K had been administered in 66 and no vitamin K given in 141.

Aetiology of Neonatal Deaths

Table IV shows the effects of vitamin K on neonatal deaths of varying aetiology. It will be seen from the figures

TABLE IV. COMPARISON OF THE EFFECT OF VITAMIN K UPON THE AETIOLOGY OF 207 NEONATAL DEATHS (RATE PER THOUSAND)

Aetiology		*Received Vit. K*		*No Vit. K*	
Multiple site haemorrhage	Premature	7·09	(2)	10·0	(5)
	Mature	0·0	(0)	2·3	(9)
Intracranial haemorrhage	Premature	17·7	(5)	50·0	(25)
	Mature	3·9	(12)	4·8	(19)
Other haemorrhage	Premature	10·6	(3)	12·0	(6)
	Mature	0·33	(1)	1·8	(7)
Other causes	Premature	95·7	(27)	100·0	(50)
	Mature	5·3	(16)	5·0	(20)
Total deaths	Premature	131·2	(37)	172·0	(86)
	Mature	9·6	(29)	13·8	(55)

Total neonatal deaths, 207. Postmortems performed, 86·5% (179).

that there is virtually no difference in death rate from causes other than haemorrhagic lesions. The large majority of these cases were babies dying of asphyxia neonatorum. The difference in total death rate, therefore, is due to the haemorrhagic group, both in premature and mature infants.

The expected neonatal death rate as quoted in the literature is 19–20 per thousand.[8] In the total series here reviewed it is 26·5 per thousand.

Haemorrhagic Lesions in the Premature Group

Considering the haemorrhagic lesions as a whole in premature infants, it is clearly shown that a much higher percentage died of haemorrhage than in the mature group.

Although a large number died of intracranial haemorrhage, in many cases there was no sign of tentorial tears, and haemorrhage occurred into the pons, ventricles, subarachnoid space and medulla, and in a very few extended down the cord. These cases usually had a moderate to marked degree of atelectasis. Haemorrhage was even found occurring into the pericardial sac. These findings suggest that the initial vascular lesion in a large number was anoxic rather than traumatic. In fact, in both premature and mature babies one feels that the words 'birth trauma' slip too glibly off the tongue without sufficient account being taken of other important factors.

The difference in average weights of the babies in the group which received vitamin K and that which did not is negligible, being 3 lb. 9 oz. in those who received it, and 3 lb. 11 oz. in those who did not.

As can be seen in Table V, the calculated death rate per thousand is halved in that group in which intrapartum vitamin K was given. These figures may look impressive

TABLE V. INFLUENCE OF VITAMIN K UPON THE INCIDENCE OF HAEMORRHAGIC LESIONS (PREMATURE GROUP)

	Total Haemorrhagic Lesions	*Total Cases in Group*	*Rate per Thousand*
Received vitamin K ..	10	282	35·5
No vitamin K	36	500	72·0

P=<·1

enough, but when subjected to statistical analysis, the numbers are insufficiently large to render them statistically significant. Their significance is possibly further dwarfed by the decision to administer vitamin K to a number of suspect neonates after delivery. As the intrapartum administration of vitamin K shows a resultant trend towards reduction in fatal neonatal haemorrhages, and further support stems from clinical impressions which prompted the undertaking of this investigation, it would seem unjustified to withhold its administration.

Haemorrhagic Lesions in the Mature Group

In the mature group it is again seen that the death rate is halved in those who received vitamin K (Table VI). These

TABLE VI. INFLUENCE OF VITAMIN K UPON THE INCIDENCE OF HAEMORRHAGIC LESIONS (MATURE GROUP)

	Total Haemorrhagic Lesions	*Total Cases in Group*	*Rate per Thousand*
Received vitamin K ..	13	3,030	4·3
No vitamin K	35	3,990	8·8

P=<·02

figures are statistically significant. As was seen above, the greatest disparity exists in the number of multiple-site haemorrhages—in some cases unassociated with intracranial haemorrhage—of which some were true haemorrhagic disease of the newborn.

There is a steep rise in death rate among those babies whose mothers received vitamin K more than 24 hours before delivery, presumably due to the increased hazards of prolonged labour, and perhaps also due in part to the falling efficacy of vitamin K. To achieve the optimum effect of vitamin K, patients should receive a repeat dose within 24 hours.

Complications of Vitamin-K Administration

Several investigators have reported a relationship between high doses of vitamin K and kernicterus.[9] Bound and Telfer,[10] for instance, in a series of 55 premature infants receiving 10 mg. on 3 successive days, report an average serum-bilirubin level of 15·4 mg.%; 38% of their infants had serum-bilirubin levels above their kernicterus level of 18 mg. and 2 died of kernicterus.[10] This result is borne out by Laurance,[11] and Meyer and Angus.[12]

In our series of cases, there were no deaths from kernicterus, though one baby developed the condition and subsequently recovered. Vitamin K had not been administered in this particular case. In this series, therefore, the dose administered did not have an adverse effect on the babies, though it may be higher than is necessary. It has been proved that a dosage of 2 μg. to the babies at birth is sufficient to prevent the 2nd to 5th day fall in prothrombin level.[1]

CONCLUSION

The results of this investigation permit the statement that routine intrapartum administration of vitamin K has therapeutic value in the prevention of fatal haemorrhagic lesions in newborn African and Indian babies.

SUMMARY

1. Fatal haemorrhagic lesions in the African and Indian neonate occur frequently—apparently more frequently than in Europeans.

2. In mature babies, it is clear from our figures that a significant reduction in these haemorrhagic lesions occurs when routine intrapartum vitamin K is given.

3. In premature babies, there is a similar trend—although our figures are insufficient to be statistically significant.

4. Routine intrapartum administration of vitamin K has therapeutic value in the prevention of fatal haemorrhagic lesions in newborn African and Indian babies.

OPSOMMING

Hier word 'n ondersoek beskryf wat in King Edward VIII-Hospitaal onderneem is om te probeer vasstel hoe waardevol die toediening van vitamine K is gedurende kraam om dodelike bloedings by Naturelle- en Indiër-pasgeborenes te voorkom.

Wat voltydse babas betref, toon ons syfers aan dat daar bepaald 'n betekenisvolle vermindering is van bloedende letsels wanneer vitamine K as roetine gedurende kraam toegedien word.

In die geval van vroeggebore babas is daar 'n soortgelyke strekking.

Wat Naturelle- en Indiërpasiënte betref, dui die getuienis dus aan dat die roetine-toediening van vitamine K gedurende kraam bepaalde terapeutiese waarde het by die voorkoming van dodelike bloedende letsels by pasgeborenes.

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