The final version of this paper was published in *Journal of Paediatric and Child Health* 2012; 48(8):665-668

Maternal and infant characteristics by mode of vitamin K prophylaxis administration.

Amina Z. Khambalia, [1] Christine Roberts, [1] Jennifer Bowen, [2] Natasha Nassar.[1]

[1] Clinical and Population Perinatal Research, Kolling Institute of Medical Research, University of Sydney at Royal North Shore Hospital, St Leonards, NSW, 2065, Australia;

[2] Department of Obstetrics and Gynaecology, University of Sydney at Royal North Shore Hospital, St Leonards, NSW, 2065, Australia

Address Correspondence and Request for Reprints to:

Amina Khambalia, PhD

Kolling Institute of Medical Research, Building 52

University of Sydney, Royal North Shore Hospital, St Leonards, NSW, 2065

Telephone: +61 2 9926 6498 **Fax**: +61 2 9906 6742

Email: amina_khambalia@sydney.edu.au

Article Type: Original article

Running Head: Maternal and infant

Abstract word count: 233

Manuscript word count: 1, 248

Number of figures: 0

Number of tables: 1

Disclosure of interest: The authors have no conflicts of interest to disclose.

Abstract

Background: Prophylaxis of vitamin K deficiency bleeding (VKDB) is achieved with administration of intramuscular (IM) injection or oral vitamin K (VK) in newborns.

Objectives: The aim of this study was to compare maternal and infant characteristics by mode of VK administration.

Methods: De-identified computerised birth files of all babies born in NSW, Australia between Jan. 2007 and Dec. 2009 (when VK prophylaxis was measured) were included in the present study. The outcome variable, mode of VK prophylaxis, was recorded by checkbox as oral, IM injection, none or not stated.

Results: We analysed population-based birth data from 2007-2009 in NSW, Australia and found IM injection was the most prevalent mode of administration (96.3%, n=263, 555), followed by oral (2.6%, n=7,023) and none (1.2%, n=3,136). Compared to neonates receiving IM VK, those with oral or none were more likely to have vaginal births without medical interventions at birth centers or planned homebirths and were less likely to receive hepatitis B vaccination. Preterm births and those breast-fed at discharge were more likely to have oral VK compared to IM injection. Neonates with no VK recorded were more likely to be admitted to neonatal intensive care, but may have received VK later in the birth admission.

Conclusions: A small proportion of the Australian neonates may be at risk of inadequate protection from VKBD due to parental safety about the safety of IM injection of VK to neonates.

Keywords: vitamin K; vitamin K deficiency disorder (VKBD); neonate; prophylaxis; population-based study

What is already known on this topic?

1. In the 1990's, UK studies reported an association between intramuscular (IM) injection but not oral vitamin K (VK) administration and childhood cancer, particularly leukaemia.
2. Countries responded in different ways, some moved towards a uniform policy of oral prophylaxis (certain European countries), some used a variety of regimens based on clinician and hospital-based practices (UK) and some made an initial change to universal oral prophylaxis and then later reverted to IM injection prophylaxis (Australia. New Zealand).
3. There is little evidence on parental characteristics and choice of various modes of VK prophylaxis administration.

What this paper adds?

1. This is the first study to examine maternal and infant characteristics by mode of VK prophylaxis.
2. Parental decision to use oral or no VK prophlaxis is aligned with attitudes and preferences for a natural birth without medical interventions, suggesting that IM prophylaxis of VK is unattractive to parents with concerns about the "medicalisation" of birth and the risks of the injection itself.
3. A small proportion of the Australian neonates may be at risk of inadequate protection from VKBD due to parental safety about the safety of IM injection of VK to neonates.

Introduction

From the 1960's to late 1980's, intramuscular (IM) injection of vitamin K (VK) prophylaxis to neonates was the route universally adopted in many industrialised countries to prevent VK deficiency bleeding (VKDB), a rare and potentially life-threatening bleeding disorder in early infancy.[1] In the 1990's, UK studies reported an association between IM but not oral VK administration and childhood cancer, particularly leukaemia.[2, 3] Countries responded in different ways; several European countries moved towards a uniform policy of oral prophylaxis.[1] In the UK, regimens became varied, with numerous permutations of preparation used, route of administration, dose, and number of doses.[1] In Australia and New Zealand, an initial change to universal oral prophylaxis was later reverted to IM injection prophylaxis after cases of late VKBD reappeared, attributed to poor efficacy and/or compliance of oral VK.[4, 5] Australia continues to exercise caution, recommending IM injection of VK as the preferred route and providing oral prophylaxis of three doses given at birth, at 3-5 days of age, and in the fourth week of life as an alternative option for parents.[4]

There is little evidence on parental characteristics and choice of various modes of VK prophylaxis administration. Only one study examining health beliefs associated with low uptake of the measles, mumps and rubella (MMR) vaccine in the UK, also examined VK prophylaxis.[6] The investigators found that non-compliance with MMR vaccination was strongly associated with the use of complementary healthcare and rejection of VK prophylaxis.[6] Therefore, the purpose of this study is to compare maternal and infant characteristics by route of VK prophylaxis (IM injection compared to oral or none).

Methods

The New South Wales (NSW) Midwives Data Collection (MDC) is a legislated population-based surveillance system, which includes information on all babies born at ≥20 weeks' gestation or weighing at least 400 g. De-identified computerised birth files of all babies born in NSW, Australia between Jan. 2007 and Dec. 2009 (when VK prophylaxis was measured) were included in the present study. The outcome variable, mode of VK prophylaxis, was recorded by checkbox as oral, IM injection, none or not stated. Data for VK prophylaxis as "none" only included babies who had VK recorded as "none." Babies for whom the data field was left blank (n=232) were excluded from the analysis.

Explanatory variables included a range of maternal (i.e. age, parity, any medical conditions, mode and place of delivery) and infant characteristics (i.e. neonatal hepatitis B vaccination, preterm birth, admission to neonatal or special care unit). Analysis was based on mothers, therefore for multiple births only the first twin or triplet was used. Infant characteristics are recorded soon after birth and do not always include subsequent management of the infant in a neonatal or special care unit.

Multinomial logit analysis was used to examine the association between explanatory factors and the odds of neonates having oral and no VK prophylaxis compared to IM injection. Analyses were conducted using SAS, version 9.2 (SAS Institute, Cary, NC, USA). The study received ethics approval from the NSW Population and Health Service Research Ethics Committee, Australia.

Results

From Jan. 2007 to Dec. 2009, 281, 678 babies were alive at birth discharge, excluding 1,811 stillbirths and 777 babies who died during the birth admission. In 2007, 2008 and 2009, the prevalence of VK prophylaxis was 95.9%, 96.3% and 96.7% for IM administration, 2.9%, 2.5% and 2.3% for oral and 1.2%, 1.2% and 1.1% for no VK, respectively. Compared to neonates administered IM injections, those with oral or no VK were more likely to have older mothers without any medical conditions, who received antenatal care from a general practitioner or from a combination of antenatal care models, had spontaneous labour, an analgesia-free delivery, a normal vaginal delivery in a birth center or a planned homebirth, and less likely to have neonatal hepatitis B vaccine (**Table 1**). Neonates who were preterm births and breast-feeding at discharge were significantly more likely to have received oral rather than IM VK. Compared to neonates who received IM injection, neonates who had 'none' recorded on the form for VK were more likely to be planned deliveries at a birth center or planned homebirth that resulted in a hospital admission and to be admitted to a neonatal or special care unit during their birth admission; however, there was no significant difference between term and preterm births.

Discussion

To our knowledge, this is the first study to examine maternal and infant characteristics by mode of VK prophylaxis. Findings reveal that in Australia, parental decision to use oral or no VK prophlaxis is aligned with attitudes and preferences for a natural birth without medical interventions. This finding supports previous research on the health beliefs of parents with low uptake of other vaccines and suggests that IM prophylaxis of VK is unattractive to parents with concerns about the "medicalisation" of birth and the risks of the injection itself.[6] The generation

of public debate and anxiety around IM prophylaxis of VK from scientific evidence is illustrated in other examples of reported associations, such as pertussis immunisation and encephalopathy of infancy, or MMR immunisation and autism, both of which have since been dismissed.[1]

Of concern, neonates who were preterm births and those who were breast-fed at discharge were significantly more likely to have been administered VK orally compared to IM injection. Limited fetal stores of VK at birth, especially in preterm infants, and the low VK content of human milk places these infants at increased risk for VKDB.[1] Multiple oral doses are prescribed because a single dose only offers protection for approximately 4 weeks and infants exclusively breast-fed receive inadequate VK from breast milk.[4] Neonates recorded as not receiving any VK represent a relatively small group (1%); however, the absolute number is not inconsequential (n=3,136). Neonates in this group over-represented extremely ill babies who were admitted to a neonatal or special care unit and may have been administered VK later in treatment during their birth admission after the midwife had already been completed the MDC form. These neonates were more likely to have natural births without medical interventions and less likely to receive a hepatitis B vaccine, thus, it is possible that some missed out on VK prophlaxis because of parental safety concerns. Of note, the hepatitis B immunisation of infants is offered universally in NSW.[7]

While VKBD is a rare disease, the consequences are severe.[1, 8] The Australian Pediatric Surveillance Unit (APSU) reported 6 confirmed cases of VKBD from 2007-2008, the majority of which were late onset VKDB.[5] Of those with a late onset, more than half had liver disease.[5] Most children with VKDB were found to have received insufficient or no VK at birth [5]. Two of three infants who died from VKDB were without liver disease and did not receive VK at birth.[5]

Implications of a change in the mode of VK administration in newborns (introduction of oral preparations) is currently being examined in Australia.[4]

Our study does not have details on infants where the VK record was missing data. Subjects with blank entries represented a small percentage of cases (0.08%) and were excluded from analyses to avoid biasing results; however it would have been interesting to know whether missing cases related to parental choices, caregiver recommendations, or recording errors. The study also has limited generalizability. VK prophylaxis practices vary by country and results from this study may not pertain to other populations with different neonatal immunisation guidelines or parental preferences and knowledge of preventative practices. Study strengths include the size and validity of the population database used.[9]

A small proportion of the Australian public remains concerned about the safety of IM injection of VK to neonates. It is impossible to give unequivocal reassurance on this point; current scientific evidence does not support an association between IM injection of VK and increased risk of cancer; however, it is not possible to exclude a small increased risk in leukaemia due to limitations of the data.[4, 8] Oral prophylaxis is easy and non-invasive; however, parents need to be informed of the disadvantages of uncertain absorption which can be adversely affected by vomiting or regurgitation and the reliance on parental compliance to administer multiple doses in early infancy to ensure neonates have full protection from developing VKDB.

Acknowledgements

We thank Dr. Lee Taylor and the NSW Department of Health for access to the HOIST data warehouse system.

Contribution to authorship

AK conceived the study, analysed the data and wrote the manuscript and revisions; NN significantly contributed to the concept of the study; interpretation of the analyses, critically revised the manuscript and gave approval of the submitted version; JB significantly contributed to interpretation of the analyses, critically revised the manuscript and gave approval of the submitted version; and CR significantly contributed to interpretation of the analyses, critically revised the manuscript and gave approval of the submitted version.

Funding

Funding for this work and Amina Khambalia is by an Australian National Health and Medical Research Council (NHMRC) Capacity Building Grant (#573122), Christine Roberts by a NHMRC Senior Research Fellowship (#457078) and Natasha Nassar by a NHMRC Career Development Award (#632955).

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Table 1. Oral and no vitamin K prophylaxis compared with intramuscular (IM) injection in NSW Australia (2007-2009).

	Proportions (%)			Oral VK	None VK
	IM (n=263,555)	**Oral** (n=7,023)	**None** (n=3,136)	**Adjusted odds ratio (95% CI)**	**Adjusted odds ratio (95% CI)**
Maternal age, years					
<24	16.8	12.6	13.5	0.63 (0.58, 0.68)	1.05 (0.93, 1.19)
25-34	59.5	58.0	56.3	Reference	Reference
≥35	23.8	29.5	30.2	1.44 (1.36, 1.52)	1.10 (1.00, 1.20)
No. of previous pregnancies					
0	41.9	47.6	41.7	Reference	Reference
1	33.7	31.6	30.5	0.74 (0.69, 0.78)	0.86 (0.78, 0.95)
2	15.2	12.4	15.7	0.59 (0.54, 0.63)	0.92 (0.81, 1.04)
≥3	9.2	8.4	12.2	0.58 (0.53, 0.64)	1.12 (0.97, 1.28)
Smoking during pregnancy	12.4	10.2	8.7	0.82 (0.76, 0.89)	0.85 (0.74, 0.98)
Maternal medical condition[1]	11.9	9.1	9.2	0.86 (0.79, 0.94)	0.95 (0.83, 1.09)
Model for antenatal care					
Midwife only	28.2	35.2	46.4	Reference	Reference
General practitioner only	8.7	16.3	7.8	2.02 (1.88, 2.18)	1.31 (1.12, 1.52)
Hospital-based medical only	15.8	12.0	16.3	0.75 (0.69, 0.81)	0.90 (0.79, 1.01)
Private obstetrician only	33.0	18.3	12.7	0.51 (0.47, 0.54)	0.52 (0.46, 0.59)
More than one combination	14.4	18.3	16.8	1.26 (1.17, 1.35)	1.14 (1.01, 1.28)
Onset of labour					
Spontaneous	56.9	67.0	73.6	Reference	Reference
Induced	25.9	20.7	14.0	0.85 (0.80, 0.91)	0.70 (0.63, 0.79)
No labour	17.2	12.3	12.4	0.85 (0.77, 0.94)	0.87 (0.74, 1.02)
No analgesia during labour	32.3	38.3	49.7	1.06 (1.00, 1.12)	1.28 (1.16, 1.41)
Type of delivery					
Normal vaginal	58.8	65.6	69.8	Reference	Reference
Instrumental[2]	11.2	9.5	6.0	0.83 (0.76, 0.91)	0.72 (0.61, 0.85)
Vaginal breech	0.2	0.4	0.8	1.21 (0.80, 1.83)	1.29 (0.80, 2.08)
Caesarean section	29.9	24.5	23.4	0.92 (0.85, 1.00)	1.08 (0.94, 1.24)
Baby's place of birth					
Hospital	95.6	88.4	73.9	Reference	Reference
Birth Centre (BC)	2.7	8.9	11.4	2.26 (2.06, 2.49)	2.02 (1.76, 2.33)
Planned homebirth (HB)	0.04	0.8	10.5	5.50 (3.88, 7.78)	23.52 (18.12, 30.53)
Hospital admission (BC/HB)	1.2	1.3	2.9	0.85 (0.69, 1.05)	1.45 (1.15, 1.84)
Born before arrival	0.5	0.6	1.4	1.12 (0.82, 1.52)	1.82 (1.30, 2.57)
Hepatitis B birth dose given	94.7	76.0	16.2	0.22 (0.21, 0.24)	0.01 (0.01, 0.02)
Neonate health status[3]					
Term birth, not admitted to NIC[3]	84.7	82.0	74.5	Reference	Reference
Preterm, admitted to NIC	4.0	6.9	12.0	1.70 (1.54, 1.89)	1.56 (1.36, 1.80)
Term birth, admitted to NIC	9.6	8.6	12.2	1.01 (0.92, 1.10)	1.52 (1.34, 1.72)
Preterm, not admitted to NIC	1.7	2.5	1.3	1.60 (1.37, 1.87)	0.93 (0.67, 1.30)
Breastfeeding on discharge	84.6	86.9	83.3	1.09 (1.01, 1.17)	0.97 (0.86, 1.09)

[1]Coded 'yes' if mother had any of the following conditions: diabetes, gestational diabetes, hypertension or preeclampsia. Coded 'no' if mother had none of the above reported conditions.
[2]Instrumental: forceps or vacuum extraction.

[3] NIC is an abbreviation for neonatal intensive care or special care unit and preterm birth was defined as gestational age <37 weeks.