

A snapshot on current practices and recent trends on vitamin K prophylaxis in term neonates in Flanders

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Abstract

A survey on vitamin K prophylaxis for term newborns with responses from 56/59 Flemish maternities and 17/30 midwifery units that do home deliveries unveiled relevant variability. About 50% of maternities use the intramuscular (1-2 mg), about 50% the oral (1-2 mg) route, with 5 different maintenance doses in breastfed infants. Nine/13 recently (<5 years) changed regimens were a switch from oral to intramuscular. Midwifery units only use oral vitamin K, with 6 different regimens. Both paediatricians and midwives reported personal experience with parental refusal of intramuscular (20/54 and 13/15) or any prophylaxis (11/54 and 16/16) respectively.

Introduction

Vitamin K refers to a group of fat-soluble vitamins important for blood clotting, but also of relevance in bone metabolism, endothelial functions and in regulation of blood calcium. Regarding its role in coagulation, Vitamin K is essential in the carboxylation of immature to mature coagulation factors (including factor II, VII, IX or X, but also protein C and S). In neonates, there is a natural tendency to vitamin K deficiency and low reserves because of poor placental transfer, potentially resulting in vitamin K deficient bleeding (VKDB, "haemorrhagic disease of the newborn"), typically subdivided in *early* (day 1), *classic* (day 2-7) or *late pattern* (2-12 weeks) with intracranial haemorrhage as the most feared event (1). Once the infant is beyond the age of 12 weeks, there is sufficient synthesis driven by the intestinal microflora (1).

Initiation of vitamin K prophylaxis in the 1940ies resulted in a significant decrease in VKDB, with subsequent guidelines and implementation of vitamin K prophylaxis, most commonly based on a single intramuscular dose (1 mg) (2,3). These guidelines were largely based on observational studies, further supported by a limited number of randomized controlled trials. More recently, barriers emerged to vitamin K prophylaxis, mainly related to the association of vitamin K prophylaxis and childhood cancer (including leukaemia, central nervous system, renal, hepatic or bone, soft tissue, germ cell tumour) in two consecutive case-control studies, with a higher odds ratio (1.97, range 1.3-3.0) for the intramuscular route (4). However, in subsequent meta-analyses, these findings were never confirmed (2). Another burden relates to the invasiveness and the associated procedural pain. For the Flemish Association of Paediatrics (Vlaamse Vereniging Kindergeneeskunde, VVK), this setting resulted in two equivalent options in their latest guidance (October 2008) on vitamin K of *either* a single 1 mg intramuscular at birth, *or* 2 mg oral, followed by a weekly dose of 1-2 mg vitamin K when breastfed until 12 weeks of postnatal age (with specific additional advice in the event of fat malabsorption).

More recently, additional comparative data on the efficacy of oral versus intramuscular administration emerged. Among others, Zurynski recently reported on the Australian Paediatric Surveillance program (1993-2017) (5). During the 'oral' route period (1993-1994), the VKDB rate was significantly higher when compared to the 'intramuscular' route period (1995-2017). As the VVK is preparing an update on the vitamin K guideline, we collected a snapshot on the current practices in the Flemish maternities and in midwifery units that take care of home deliveries.

Methods

Following ethical approval of the survey by KU Leuven (MP016741, 10-12-2020), and with the logistic support of the VVK secretary in the GDPR setting (General Data Protection Regulation), an online questionnaire was repeatedly circulated (February-March 2021) to all heads of the relevant departments (paediatrics, neonatology), with an additional search on midwifery units. The questionnaire was focused on the current practices on vitamin K prophylaxis in term cases and on recent changes in practices, and also collected information on experiences with parental refusal.

Results

Responses were received from 56/59 maternities (complete responses in 54), so that we attained a very high response rate (95 %), and from 17 midwife units (on about 30 contacted, response rate 57 %). Table 1 and Table 2 summarize the findings for the maternity wards involved for breastfeeding and formula feeding respectively.

The diversity in dosing regimens did not differ between hospitals with or without neonatal intensive care unit.

Interestingly, 13/54 maternities indicated that their policy has been adapted in the last 5 years. In 9/13, there was a switch from oral to the intramuscular route, while the other 4 adaptations related to changes in dosing regimen. Finally, the 17 responses from midwifery units for breastfed infants are summarized in Table 3. Related to formula fed infants, 2 mg was used in 11 units, 1 mg in 1 unit (+ 3 units, preference of the parents and 2 units not relevant, as formula feeding also never occurs). It is hereby worth to stress that none of these units uses the intramuscular route.

Reports on parental refusal were based on personal experience of the paediatrician or midwife. Experiences with refusal of intramuscular administration or any prophylaxis were reported by 20/54 and 11/54 paediatricians respectively. For midwives, this was reported by 13/15 (intramuscular) and 16/16 (any) respectively. Related to this problem, paediatricians rather focused on the efficacy of the prophylaxis and highly value an updated vitamin K guideline, while midwives focused more on the parental preference and their informed choice to select the administration route.

Discussion

In essence, this snapshot on current practices on vitamin K prophylaxis in term neonates born in Flanders provides a contemporary and reliable overview on the diversity in practices just before the VVK guideline is updated. In our personal opinion, this does provide some key findings, as summarized.

1. Irrespective of how this update will turn out, the current practices are diverse, so that the short hospital stay and the resulting multidisciplinary, multi-unit perinatal care necessitates good coordination and communication. Consequently, a uniform approach could be beneficial to avoid uncertainties or errors resulting in substandard prophylaxis.
2. There are significant differences in practices and opinions between paediatricians and midwives. Based on the Study centre Perinatal Epidemiology report, the number of home births is rather limited (0.6%), but there is still value to stimulate interaction between both groups (6). Furthermore, independent midwives are involved in postnatal follow-up at home of both mothers and infants following delivery, either or not after short hospital stay.
3. We suggest that the updated guideline should also contain some guidance, a statement or reflection on how to handle parental preferences and refusal, balancing the benefits of uniformity (within a given organization) to the value of parental preferences and shared decision making.

Conflict of interest

The authors have no conflict of interest to declare.

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Tables and table legends

Table 1: Dosing regimens used in Flemish maternity wards for breastfed term infants.

route	maternities (n=54)	dosing regimen used	maternities (n= 54)
Intramuscular	29 (54%)	1 mg IM, at birth	28 (52%)
		2 mg IM, at birth	1 (2%)
Oral	25 (46%)	2 mg oral, at birth maintenance, 1-2 mg, weekly	14 (26%)
		1 mg oral, at birth maintenance, 150 µg, daily	6 (11%)
		2 mg oral, at birth maintenance, 25 µg, daily	3 (6%)
		2 mg oral, at birth maintenance, 150 µg, daily	1 (2%)
		2 mg oral, at birth maintenance, unknown	1 (2%)
		2 mg oral, at birth 2 mg oral, day 4-6 and 4-6 weeks	0 (0%)

Table 2: Dosing regimens used in Flemish maternity wards for formula fed term infants.

route	maternities (n=54)	dosing regimen used	maternities (n= 54)
Intramuscular	30 (56%)	1 mg IM, at birth	29 (54%)
		2 mg IM, at birth	1 (2%)
Oral	24 (44%)	2 mg oral, at birth	23 (43%)
		1 mg oral, at birth	1 (2%)

Table 3: Overview of the dosing regimen used in midwifery units for breastfed infants.

	number of units (n=17)
2 mg oral, maintenance 1-2 mg weekly until 3 months	4 (24%)
3 x 2 mg oral (at birth, on day 4-7 and week 4-6)	4 (24%)
1 mg oral, maintenance 150 µg daily until 3 months	1 (6%)
5 x 2 mg oral (at birth, on day 7 and subsequently monthly)	1 (6%)
2 mg oral (at birth, once)	2 (12%)
based on the preference of the parents, following informed consent	5 (29%)

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