Patronage: Société suisse de pédiatrie (SSP) et Office fédéral de la santé publique (OFSP)

Nationwide epidemiological survey of vitamin K deficiency bleeding (VKDB) in the first 6 months of life in Switzerland

Principal investigator
Prof. B. Laubscher, Département femme-mère-enfant, CHUV, Rue du Bugnon 46, 1011 Lausanne – Tel 079 556 44 16, e-mail : bernard.laubscher@chuv.ch

Co-investigators
Prof. G. Schubiger, Rischstrasse 3, 6030 Ebikon
Dr. M. Rizzi, Département femme-mère-enfant, Unité d'onco-hématologie pédiatrique, CHUV, Rue du Bugnon 46, 1011 Lausanne

Summary
Various prophylactic regimens are recommended to prevent VKDBD (1, 2). In Switzerland, since 2003 (3), neonates can benefit (official Swiss Society of Pediatrics guideline) from 3 vitamin K dosis (Konakion® MM, hour 4, day 4, week 4) to prevent VKDB. VK prophylaxis refusal/omission and non diagnosed hepatobiliary disease are the main current risk factors for VKDB. The aim of this study is to determine the current VKDB epidemiology, risk factors, eventual increase or cluster effect to test if the 2003 recommended prevention is still adapted to current society.

Study start
01.09.2018

Study duration
Six years, 01.09.2018 – 31.08.2024 (about 500'000 births)

Aims of the study
VKDB epidemiology in Switzerland
Efficacy of the national 2003 guidelines 15 years after their implementation (including three 2 mg VK dosis (Konakion® MM) administered orally at hour 4, on day 4 and week 4) to prevent VKDB and identification of possible concurrent risk factors for VKDB and/or co-morbidities.

Background
Various prophylactic regimens are recommended to prevent VKDBD (1, 2). In Switzerland, since 2003 (3), neonates can benefit (official Swiss Society of Pediatrics guideline) from 3 vitamin K dosis (Konakion® MM, hour 4, day 4, week 4) to prevent VKDB. A previous *SPSU* survey showed that a 3 oral vitamin K prophylactic regimen offered an acceptable prophylaxis (4), as noted in 2 reviews (1, 2). All prophylactic failures were linked to non diagnosed hepatobiliary disease or vitamin K prophylaxis parental refusal. Since the last survey (4), various reports have stressed the increasing association between VKDB and parental vitamin K prophylaxis refusal (5, 6, 7). The actual societal trend off classical/academic medical care could potentially lead towards more VKDB. VKDB preventive guidelines are only effective if followed by users, namely parents, mid-wifes, obstetricians, paediatricians mainly. To date there are no current data on this potential trend in Switzerland.

To what extent are the 2003 Swiss guidelines respected and prevent VKDB in real life? Given the societal trend off official guidelines, are there VKDB clusters that should lead to new and reinforced preventive teaching measures to health care specialists?

Methodology
Observational multicenter study of all infants in Switzerland with VKDB using the *SPSU* network. Registration of all infants ≤ 6 months cared for in one of the participating hospitals because of VKDB, as defined in the case definition (see below).
Two steps approach: 1) Monthly case declaration through the *SPSU* reporting web site; 2) contact with reporting body to fill a coded questionnaire to gather information on (8):

- demographics (date of birth, sex, type of birth clinic (home, birthing center, public/private maternity/hospital)
- neonatal VK administration
- clinical course and severity
- treatment
- possible VKDB risk factors and/or underlying conditions (including type of feeds (maternal versus artificial milk), prophylaxis refusal/omission, non diagnosed hepatobiliary disease, outcome (exitus, sequelae, complete recovery).

Case definition (adapted from ref. 2, 9 and 10):
VKDB is considered in the presence of a bleeding in a neonate or infant ≤ 6 months (26 weeks) of age with:

- an international normalised ratio (INR) ≥4, prothrombine time ≥4 x control value or Quick < 20% in the presence of a normal (or increased) platelet count and normal fibrinogen (and absence of fibrin degradation product)
- rapid normalization (within 30-120 min) of these values (and/or cessation of bleeding) after VK administration is confirmative

Ethical consideration
No patients' informed consent will be required for two reasons (personal discussion with Prof P. Francioli, head of Commission cantonale d'éthique de la recherche sur l'être humain - Vaud, 29.06.2017):
VKDB is very rare (about 1 case/year in Switzerland). The risk of introducing a significant bias in the cases reporting is high, especially as parents who might refuse to participate in the survey are those who refused VK prophylaxis for their infant.
The survey is considered as a quality control of a public health recommendation.

A patient would not be included in the study if his/her parent were to refuse - orally or in writing - to let his/her child participate in the survey.
No data will be managed/kept electronically. To minimize workload of declaring physicians - and thus improve exhaustive case reporting - simple declaration sheet with date of birth, symptoms development, hospital admission or eventual exitus letalis (see annex, "declaring physician questionnaire") will be filled by declaring physicians and sent to the principal investigator who will anonymize them (see annex, "anonymized questionnaire") and destroy initial declaring physician questionnaire. All remaining data will be destroyed 10 years after the study publication.

Budget
DFME, CHUV

Questionnaires
See addendum

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Président *SPSU*: Dr. med. A. Wörner, Leitender Arzt, UKBB, Spitalstrasse 33, 4056 Basel
Secrétariat *SPSU*: Office fédéral de la santé publique, Division Maladies transmissibles, 3003 Berne
Tél. 058 463 02 97 ou 058 463 87 06 Fax 058 463 87 95
www.spsu.ch