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Vitamin K Deficiency Bleeding and Early Infant Male Circumcision in Africa

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Abstract

BACKGROUND—Early infant (1–60 days of life) male circumcision is being trialed in Africa as a human immuno-deficiency virus prevention strategy. Postcircumcision bleeding is particularly concerning where most infants are breastfed, and thus these infants are at increased risk of vitamin K deficiency bleeding.

CASE—During a circumcision trial, one infant bled for 90 minutes postprocedure. After discovering he had not received standard prophylactic vitamin K, we gave 2 mg phytomenadione (vitamin K1) intramuscularly; bleeding stopped within 30 minutes.

CONCLUSION—Vitamin K's extremely rapid action is not commonly appreciated. Neonatal vitamin K has been shown to be cost-effective. To increase availability and promote awareness of its importance, especially in low-resource settings where blood products and transfusions are limited, vitamin K should be included in the World Health Organization's Model List of Essential Medicines for Children.

Male circumcision has been shown to reduce the risk of heterosexually-acquired human immunodeficiency virus (HIV) infection in men, and male circumcision in early infancy (defined as 1–60 days of life by the World Health Organization [WHO]) is recommended by the WHO as part of HIV prevention strategies because of its relative ease and safety (http://libdoc.who.int/publications/2007/9789241595988_eng.pdf) compared with the procedure in older ages. Given the potential scale-up of early infant male circumcision in resource-limited settings, more attention must be paid to the prevention and treatment of potential postcircumcision bleeding associated with vitamin K deficiency. Those who perform circumcision for religious or traditional reasons should also be aware of this potential cause of postcircumcision bleeding.

Vitamin K deficiency bleeding can occur in infants up to 6 months of age, although it most commonly occurs either in the first week of life (classical) or at 3–8 weeks (late). Infants are at risk of vitamin K deficiency because they are born with low liver stores of vitamin K and

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subsequently may not be able to obtain sufficient amounts from breast milk. Before neonatal vitamin K prophylaxis became the standard of care in the United States, vitamin K deficiency bleeding had been reported after circumcisions done within the first week of life at Cincinnati General Hospital, and bleeding in this population was most common among the breastfed neonates.[1] Postcircumcision bleeding is of particular concern in the developing world where the majority of infants are breastfed and thus at increased risk of vitamin K deficiency bleeding.

In a recent report from Kenya, one of the reasons given by parents for not wanting to circumcise an infant was fear of bleeding[2] and in a recent trial of circumcision in Zambia, most of the adverse events were excessive bleeding with one case requiring a transfusion.[3] Therefore, the use of vitamin K to prevent or treat postcircumcision bleeding deserves urgent attention as countries in sub-Saharan Africa are poised to scale-up early infant male circumcision as part of HIV-prevention interventions.

CASE

We report a case of probable vitamin K deficiency bleeding that occurred during a clinical trial of infant circumcision in Botswana (registered at www.clinical-trials.gov as NCT00971958), a country in which postpartum vitamin K prophylaxis is routine. All circumcisions were performed by a medical doctor using the AccuCirc device either within the maternity ward or in a clinic adjacent to the main hospital. Among 150 newborns circumcised between 1 and 10 days of life, five instances of minor localized bleeding occurred and were successfully managed by up to 20 minutes of local pressure. A sixth newborn (estimated gestational age 39 weeks, birth weight 4.1 kilos, day two of life), however, began to bleed approximately 2 hours after circumcision and continued to bleed for more than 90 minutes despite application of local pressure. No localized, single source for the bleeding could be identified. After discovering that this newborn had not received standard vitamin K prophylaxis, we administered 2 mg phytomenadione (vitamin K1) intra-muscularly and bleeding stopped within 30 minutes.

COMMENTS

The extremely rapid action of vitamin K seen in this case is not commonly appreciated but is consistent with a report of four vitamin K deficiency bleeding cases in which intravenous vitamin K substantially corrected grossly prolonged prothrombin times and reduced bleeding as early as 20 minutes after injection.[4] This is important information in low-resource settings where blood products and transfusions may not be readily available.

The evidence for the administration of prophylactic vitamin K immediately after birth to prevent bleeding is well established and it is routinely provided to infants in developed countries.[5] Although the administration of vitamin K in low-resource settings is less well established and many health care providers are not aware of its importance, a study from Vietnam of intracranial hemorrhage and its sequelae suggests that vitamin K prophylaxis is a highly cost-effective intervention.[6]

Without vitamin K prophylaxis, the incidence of vitamin K deficiency bleeding may range from 0.25% to 1.7%. Manifestations can include intracranial hemorrhage[6] and bleeding from the gastrointestinal tract, nose, and after circumcision.[4] High mortality among hospitalized cases has been noted[4] with lack of resources and treatment delay being contributing factors. Importantly, a recent Ugandan study showed that 65% of newborns had an elevated PIVKA-II, a marker of vitamin K insufficiency,[4] with 22% of values predictive of abnormal hemostasis (S. Data et al, personal communication).

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We are not aware of any systematic review of the use of vitamin K in Africa, so we gathered information from colleagues in 10 of the 14 WHO priority countries for scale-up of male circumcision: Botswana, Kenya, Malawi, Mozambique, Rwanda, South Africa, Tanzania, Uganda, Zambia, and Zimbabwe. Despite the known efficacy of vitamin K, we found that policies and implementation of vitamin K administration to newborns vary significantly. Colleagues in 6 of 10 countries reported that there was a policy for routine administration at birth, and some specified that intramuscular administration was used. In the countries where a policy is in place, vitamin K is usually only available for hospital births, and stockouts may occur; actual coverage is generally not known and gathering this information is not part of an established evaluation scheme. In three of the four countries where a policy for routine use is not in place or is not well publicized, colleagues reported that vitamin K is only given to premature neonates, neonates admitted to neonatal high-risk wards or intensive care nurseries, or both.

Although a recent health facilities survey in Uganda included vitamin K in its list of essential medicines, and vitamin K is recommended in the WHO 2005 Pocket Book of Hospital Care for Children as standard of care for all newborns (http://whqlibdoc.who.int/publications/2005/9241546700.pdf), vitamin K is not included in the WHO 2011 Model List of Essential Medicines for Children (http://whqlibdoc.who.int/hq/2011/a95054_eng.pdf) nor in the United Nations Children's Fund supply catalog (https://supply.unicef.org/, retrieved October 3, 2012).

Health care providers in resource-limited settings should be aware of the dangers of vitamin K deficiency bleeding, the known efficacy of vitamin K prophylaxis, and, as demonstrated in our case, the rapid action of vitamin K for treating incident cases. For prophylaxis in Africa, researchers could consider the feasibility of adding an oral vitamin K formulation to safe birthing kits for out-of-hospital births, similar to the use of oral prostaglandins to prevent postpartum hemorrhage,[7] or to evaluating single-dose, prefilled, disposable devices such as the ones being considered for administration of vaccines.[8]

As early infant male circumcision is scaled-up in Africa as part of HIV prevention programs, increased vigilance will be essential to prevent deaths from vitamin K deficiency bleeding. If postcircumcision bleeding is not prevented and addressed, it may negatively affect programmatic scale-up of infant circumcision for HIV prevention.[2,3] Ideally, the WHO, the United Nations Children's Fund, and donor agencies should collaborate to promote broader awareness of the importance of vitamin K and facilitate its availability.

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