One Milligram Versus Two Milligram Intramuscular Vitamin K to Prevent Late-Onset Hemorrhagic Disease in Young Infants: A Randomized Controlled Trial

Original Article

Volume 62, Pages 116-120, 2025

Amala Srilatha Natarajan,[1] Delhikumar CG ,[1] Senthil Kumar GP,[2] Nivedita Mondal,[1] Sasirekha R[3]

Departments of [1]Pediatrics, [2]Biochemistry and [3]Obstetrics and Gynecology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India.

Correspondence to: Dr. Delhi Kumar CG, Additional Professor, Department of Pediatrics, JIPMER, Puducherry-605006, India. dillikumar14@gmail.com

Received: Mar 26, 2024; Initial review: May18, 2024; Accepted: Oct 13, 2024

ABSTRACT

OBJECTIVES

To compare the efficacy of a standard dose (1 mg) with 2 mg vitamin K administered by intramuscular (IM) route in reducing subclinical late-onset vitamin K deficiency bleeding (VKDB) assessed using serum protein induced by vitamin K absence (PIVKA II) levels.

METHODS

This was an open-labeled randomized controlled trial that enrolled healthy term neonates delivered vaginally. Neonates delivered to mothers receiving antiepileptics, anti-tuberculous drugs, or warfarin, and those with a family history of bleeding disorder were excluded. Participants were randomized to receive either 1 or 2 mg of vitamin K1 (Phytomenadione) IM at birth. PIVKA II was measured in the cord blood and at 30 and 72 days after birth by ELISA method. PIVKA II level >100 ng/mL was labeled as subclinical VKDB.

RESULTS

Forty-one neonates were recruited in each arm. On the 30 days follow-up visit 9 infants (4 in 1 mg group; 5 in 2 mg group) were lost to follow-up. All babies had PIVKA II levels >100 ng/mL at birth. The median PIVKA II values (ng/mL) in the 1 mg group were 827.68 (cord blood), 678.80 (30 days), and 644.10 (72 days). The corresponding levels (ng/mL) in the 2 mg group were higher, viz., 770.55, 726.35, and 693.14 ng/mL; P > 0.05 for all comparisons. PIVKA II level in the 1 mg group reduced significantly on 72 days of life compared to that observed at birth (cord blood) (P = 0.012). However, the fall in 2 mg group was not statistically significant.

CONCLUSION

There was no difference in PIVKA II levels between neonates receiving 1 mg or 2 mg vitamin K IM suggesting a similar risk for late-onset VKDB in both groups.

Keywords: Bleeding disorder, Phytomenadione, PIVKA II, Prophylaxis, VKDB

REFERENCES

1.Majid A, Blackwell M, Broadbent R, et al. Newborn vitamin K prophylaxis: a historical perspective to understand modern barriers to uptake. Hosp Pediatr. 2019;9:55-60.

2.Sankar MJ, Chandrasekar A, Kumar P, et al. Vitamin K prophylaxis for prevention of vitamin K deficiency bleeding: a systematic review. J Perinatol. 2016;36:S29-34.

3.National Health Mission. Operational Guidelines. Injection Vitamin K Prophylaxis at Birth (in facilities). Child Health Division, Ministry of Health and Family Welfare; 2014. Accessed on Oct 13, 2024. Available from: https://tripuranrhm.gov.in/Guidlines/3006201401.pdf

4.Ng E, Loewy AD. Position Statement: Guidelines for Vitamin K Prophylaxis in Newborns: A Joint Statement of the Canadian Paediatric Society and the College of Family Physicians of Canada. Can Fam Physician. 2018;64:736-9.

5.Mihatsch WA, Braegger C, Bronsky J, et al. ESPGHAN Committee on Nutrition. Prevention of Vitamin K Deficiency Bleeding in Newborn Infants: A Position Paper by the ESPGHAN Committee on Nutrition. J Pediatr Gastroenterol Nutr. 2016;63:123-9.

6.Sachin R, Ramesh H, Chaya KA. Late haemorrhagic disease of newborn: can it be prevented by changing prophylaxis policy. Asian J Pediatr Res. 2020;3:14-9.

7.Karaci M, Toroslu E, Karsli T, et al. Intracranial haemorrhage due to late-onset vitamin K deficiency. HK J Paediatr New Ser. 2015;20:80-5.

8.Annadurai A, Delhi Kumar CG, SM Praveen, Parameswaran N. Late-onset vitamin K deficiency bleeding: a preventable yet prevailing cause of intracranial hemorrhage in young infants—an ambispective descriptive study. Intensive Care Med. Paediatr Neonatal. 2024;2:1-6.

9.Chawla D, Deorari AK, Saxena R, et al. Vitamin K1 versus vitamin K3 for prevention of subclinical vitamin deficiency: a randomized controlled trial. Indian Pediatr. 2007;44:817-22.

10.Motohara K, Endo F, Matsuda I. Effect of vitamin K administration on acarboxy prothrombin (PIVKA-II) levels in newborns. Lancet. 1985;2:242-4.

11.Hunnali CR, Devi U, Kitchanan S, et al. Three different regimens for vitamin K birth prophylaxis in infants born preterm: A randomized clinical trial. J Pediatr. 2023;255: 98-104.

12.Ardell S, Offringa M, Ovelman C, et al. Prophylactic vitamin K for the prevention of vitamin K deficiency bleeding in preterm neonates. Cochrane Database Syst Rev. 2018;2:CD008342.

13.Jullien S. Vitamin K prophylaxis in newborns. BMC Pediatr. 2021;21(Suppl 1):350.

14.Takahashi D, Egami N, Ochiai M, et al. Vitamin K prophylaxis in neonates: comparing two different oral regimens. J Perinatol. 2024;44:1491–5.

15.Autret-Leca E, Jonville-Bera AP. Vitamin K in neonates: how to administer, when and to whom. Paediatr Drugs. 2001;3:1-8.

16. Sameshima T, Ashina M, Fukuda T, et al. Range of protein induced by vitamin K absence or antagonist-II levels in neonates at birth. Sci Rep. 2024;14:921.

17.Haroon Y, Shearer MJ, Rahim S, et al. The content of phylloquinone (Vitamin KJ in human milk, cows' milk and infant formula foods determined by high-performance liquid chromatography. J Nutr. 1982;112:1105-17.