Prophylactic Vitamin K and Its Relation to Development of Neonatal Jaundice

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Abstract: Background and objectives: Neonatal jaundice is yellowish discoloration of the skin, mucous membranes, and sclera. Hyperbilirubinemia is common in the first week of life, affecting 50%- 70% of term babies and 80% of preterm babies. Since the introduction of synthetic vitamin K injection as a prophylaxis within an hour or soon after birth to prevent hemorrhagic disease of newborns, cases of neonatal hyperbilirubinemia were reported in full-term healthy newborns. So, the aim of this work is to evaluate the correlation between vitamin K administration and the development of neonatal jaundice and its severity. **Methods:** In this a cross-section comparative study we measure the total serum bilirubin in 200 full term neonates in Al-Azhar University Hospital in New Damietta at the third day of life to demonstrate the relationship between it and vitamin K injection. **Results:** We found in this study that the newborns injected with synthetic vitamin K injection soon after birth had a higher TSB level than those who did not receive it. **Conclusion:** The synthetic vitamin K injection seems to be one of the risk factors for development of neonatal jaundice even if used with appropriate dose.
[Magdy Mohammed Ashmawy Sakr, Mohammed Ibrahim Abdel-Aal, Hisham Samir Abdel-Samie, Mohammed El-Sayed Soliman. **Prophylactic Vitamin K and Its Relation to Development of Neonatal Jaundice.** *Nat Sci* 2018;16(2):62-65]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 10. doi:10.7537/marsnsj160218.10.

Key words: Neonatal jaundice, Vitamin K, Total serum bilirubin (TSB).

1. Introduction

Neonatal hyperbilirubinemia is the most common condition that requires medical attention in newborn[1]. It is defined as a total serum bilirubin level exceeding 5mg/dl. It is presented with yellow coloration of the skin and sclera as a result of accumulation of bilirubin[2]. Although up to 60% of term and 80% of preterm newborns have clinical jaundice in the first week of life, few have a significant underlying disease such as hemolytic disease, metabolic disorders, endocrine disorders, anatomic disorders of the liver and infection[3].

In some babies, serum bilirubin levels may rise excessively, which can be a cause for concern because unconjugated bilirubin is neurotoxic and can cause lifelong neurologic sequelae in infants who survive (Kernicterus) and even death. For these reasons, the presence of neonatal jaundice frequently needs diagnostic evaluation[4].

Vitamin K is a fat soluble vitamin. It is either (K1) or (K2). Vitamin K1 is derived from plant sources and contributes around 90% of our overall vitamin K need. While, vitamin K2 is derived from intestinal bacteria and contributes only about 10% of our overall vitamin K intake[5]. Vitamin K is essential for the functions of several proteins involved in blood clotting i.e.: coagulation proteins (factors II, VII, IX and X) and coagulation inhibitor proteins (proteins C, S and Z) [6]. Since the introduction of vitamin K as a prophylaxis within an hour or soon after birth, cases of hyperbilirubinemia were reported in full-term healthy newborns[7]. The synthetic form of vitamin K1 injection as phytonadione is combined with other toxic ingredients in the shot which impairs the baby's liver capacity to process bilirubin causing neonataljaundice[8].

2. Patients and method

This study was a cross-section comparative study which was carried out at NICU of Al- Azhar University Hospital in New Damietta. It was conducted on 200 neonates in the period from March 2016 to March 2017. They were classified into two groups. Group I included 100 full-term newborns who received vitamin K1 injection immediately after birth (1mg IM) and group II included 100 full-term newborns who did not receive vitamin K1 injection after birth. The cases in this study were healthy full-term babies, of both sex and at third day of life.

Exclusion Criteria:

- Preterm.
- Respiratory distress (RD).
- Neonatal sepsis.
- Infant of diabetic mother.
- ABO or RH incompatility.
- History suggesting prenatal asphyxia.
- Major congenital anomalies as

cardiovascular, pulmonary, central nervous system anomaliesetc.,

Each neonate in this study was subjected to the following:

1- Comprehensive history taking including baby data and maternal history.

2- Clinical examination of newborns.

3- Investigations.

a) Complete blood picture.

b) Serum bilirubin level (Total and Direct) at the 3rd day of life by diazomethod.

c) SGPT.

d) Alkaline phosphatase level.

e) Serum albumin level.

3. Results:

Table (1): General characteristics of the studied cases

Variables	Patient with vitamin K injection (n=100)	Patient with no vitamin K injection (n=100)	Test	P value
Gestational age (weeks) Mean± SD Range	 38.43±0.81 37-40 w	 38.13±0.77 37-41 w	 t= 1.863	 0.064
Sex Male Female	 62 (62%) 38 (38%)	 55 (55%) 45 (45%)	 X^2=5.808	 0.211
Type of feeding Breastfed Formula fed	 87 (87%) 13 (13%)	 85 (85%) 15 (15%)	 X^2=0.166	 0.684
Birth order 1st 2nd 3rd 4th 5th	 42 (42%) 31 (31%) 22 (22%) 4 (4%) 1 (1%)	 38 (38%) 37 (37%) 20 (20%) 4 (4%) 1(1%)	 X^2=0.825	 0.935
Onset of jaundice No 2nd day 3rd day	 0(0%) 23 (23%) 77 (77%)	 14 (14%) 18 (18%) 68 (68%)	 X^2=6.259	 **0.044 ***

Table (2): Maternal characteristics among studied cases

Variables	Patient with vitamin K injection (n=100)	Patient with no vitamin K injection (n=100)	Test	P value
Maternal age (years) Mean ± SD Range	 24.28±3.31 19 – 32	 24.41±3.27 19 – 33	t= - 0.287	0.774
Mode of delivery CS NVD	 76 (76%) 24 (24%)	 80 (80%) 20 (20 %)	X^2=0.466	0.495
Parity Primipara Multipara	 42 (42%) 58 (58%)	 38 (38%) 62 (62%)	X^2=0.333	0.564
Jaundice in previous sibling Yes No	 40 (40%) 60 (60%)	 38 (38%) 62 (62 %)	X^2=0.084	0.772
Maternal diseases No disease Anemia Hypertension DM Asthma	 75 (75%) 19 (19%) 4 (4%) 5 (5%) 2 (2%)	 72 (72%) 18 (18%) 5 (5%) 4 (4%) 1(1%)	X^2=0.522	0.971

Table (3): Vital data and anthropometric measurements of studied cases

Variables	Patient with vitamin K injection (n=100)	Patient with no vitamin K injection (n=100)	Test	P value
Weight (kgs)	3.47±0.33	3.50±0.38	t= -0.625	0.533
Length (cm)	50.58±0.46	50.64±0.67	t= -0.646	0.519
HC (cm)	34.27±0.56	34.21±0.57	t= 0.724	0.470
HR (b/min)	117.07±14.22	116.15±14.28	t= 0.457	0.649
RR (cy/min)	45.37±4.30	45.73±4.56	t= -0.574	0.566
Temperature (^{0}c)	36.31±0.50	36.30±0.64	t= 0.148	0.883

Table (4): CBC findings among studied cases

Variables	Patient with vitamin K injection (n=100)	Patient with no vitamin Kinjection (n=100)	t test	P value
RBCs count 6(10)	4.70±0.53	4.84±0.59	1.765	0.079
Hb (g/dl)	14.85±1.38	14.83±1.04	0.087	0.931
Hct (%)	44.89±5.50	45.74±3.55	1.298	0.195
3 TLC (10)	7530±2285.90	7830±2204.36	-0.954	0.341
3 Platelets (10)	216.48±64158.5	223.220±59122.98	-0.773	0.441

Table (5): Serum bilirubin among studied cases

Variables	Patient with vitamin K injection (n=100)	Patient with no vitamin K injection (n=100)	t	P value
Total serum bilirubin (mg/dl) Mean ± SD Range	 9.84±1.10 7.8-12.7	 5.57±1.39 2.3-8.1	24.127	**>0.001***
Direct serum bilirubin (mg/dl) Mean ± SD Range	 1.1±0.42 0.3-2.0	 0.95±0.73 0.3-1.9	-0.646	0.076

Table (6): Liver profile among the studied cases

Variables	Patient with vitamin K injection (n=100)	Patient with no vitamin K injection (n=100)	t	P value
SGPT (u/l)	18.51±7.24	12.78±4.04	6.909	**>0.001***
Alkaline phosphatase (u/l)	200.78±64.26	217.57±70.97	1.754	0.081
Serum albumin (g/dl)	4.35±0.54	4.49±0.73	-1.474	0.142

4. Discussion

Unconjugated hyperbilirubinemia is one of side effects of synthetic vitamin K injection given to newborns after birth due to presence of other toxic ingredients in the shot which impairs the baby's liver capacity to process bilirubin causing neonataljaundice [8].

Regarding to general characteristics, the post natal age was 3 days. This finding similar to many studies; for example, an Egyptian study, the mean age of jaundice was 2.89 days Abdel Fattah et al., 2010[9]. Also, Nickavar et al. 2015[10] in Iran reported the mean age of jaundice was 3.82±3.06 days.

Regarding total serum bilirubin among the studied cases, the present study showed significant increase in mean TSB in group I who received 1 mg of vitamin K injection after birth as a prophylaxis was 9.84±1.10 mg/dl which was higher than that in group II who did not receive vitamin K after birth which was 5.57±1.39 mg/dl.

Many studies investigated the role of vitamin K shots to newborns as prophylaxis on development of physiological neonatal jaundice.

A recent study examined two groups of 166 full-term healthy breast-fed newborns and reported that mean TSB in babies who received vitamin K injection was 9.21±1.01mg/dl while babies who did not receive vitamin K injection was 4.76±1.98mg/dl. This result was similar to our study results[11].

Romagnoli et al. 2012[12] was an Italian study which conducted on 1708 healthy full term infants were studied to assess the normal neonatal trend of TSB with the aim to elaborate the percentile-based hour specific nomogram. It was found that mean TSB babies received 1mg of vitamin K injection after birth was 9.9 mg/dl while who did not receive vitamin K had lower bilirubin level. Also, De Carolis et al. 2014[13] reported the mean TSB at 3rd day was 9.9± 2.4

mg/dl in healthy full-term babies received 1 mg of vitamin K injection within first six hours afterbirth.

We found an old study that reported the relation of vitamin K to hyperbilirubinemia among 119 preterm and full-term babies divided into seven groups. Two groups of full-term babies, one group received 1 mg of vitamin K injection while the second group did not injected with vitamin K then TSB level was determined at 3rd day of life in full-term babies which was (5.34± 1.12 mg/dl and 2.73±1.29mg/dl respectively). This result was much lower than our study result [14].

In contrary to our study, an old study reported effect of large doses of vitamin K in newborns among 106 full-term and 93 preterm babies. It showed that there was an increase in the serum bilirubin level due to effect of large doses of vitamin K injection in the first week of life while the usual prophylactic dose is sufficient in prophylaxis and treatment of vitamin K deficiency bleeding without any hyperbilirubinimic effect[15].

Regarding to liver profile among the studied cases, we found no significant statistical difference regards serum albumin and alkaline phosphatase but there was significant increase at SGPT level in group I (18.51±7.24 u/l) regards group II (12.78±4.04 u/l). It is evident that the presence of other toxic ingredients in the synthetic vitamin K shot may have a hepatotoxic effect rather than hemolysis as it impairs the liver capacity to conjugate bilirubin causing jaundice[8].

Conclusion

The newborns injected with synthetic vitamin K injection soon after birth had a higher TSB level than those who did not receive it. So, the synthetic vitamin K injection seems to be one of the risk factors for development of neonatal jaundice even if used with appropriatedose.

Recommendations

- Prophylactic vitamin K administration at birth to prevent hemorrhagic disease of newborns must be re-evaluated because it may lead to development of neonatal jaundice or at least aggravatesit.
- Regular follow up of newborns with physiological jaundice especially who receive synthetic forms of vitamin Kinjection.
- Additional research should be conducted on the efficacy, safety, and bioavailability of oral formulations and optimal dosing regimens of vitamin K.

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1/3/2018