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A clinically suspected case of Anaphylactoid reaction to vitamin K injection in a child – a case report and review of literature

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Abstract

Vitamin K is commonly indicated in pediatric patients with coagulopathies. Its commercial preparations are available in the market since long. Minor complications are very well-known, but life-threatening events are rarely reported in children. We present a case of 8-year-old child who developed life-threatening event following intravenous Vitamin K injection. She was survived after cardiopulmonary resuscitation. The reaction was most probably due to anaphylactoid reaction to Vitamin K.

Keywords: Adverse reaction, anaphylactoid reaction, children, Vitamin K

Vitamin K is one of the first-line agents, which is used to prevent bleeding in children due to underlying acquired coagulation abnormalities for instance in hepatic failure, sepsis-induced disseminated intravascular coagulation, and warfarin overdose. It is an essential fat-soluble vitamin which is required for the maintenance of coagulation system by carboxylation of factors II, VII, IX, and X, protein C, and protein S (the natural inhibitors of coagulation) in liver.[1] It naturally occurs in two forms phytonadione (plant source) and menaquinones (intestinal source). The common indications for administration of Vitamin K are prophylactic administration at birth, prolonged antibiotic use, underlying liver disorders, malabsorption syndromes, and reversal of warfarin overdose. Here, we report a life-threatening event in a child probably due to Vitamin K injection.

Case Report

An 8-year-old female child presented in the pediatrics outpatient department with a history of fever since 7 days, headache, vomiting, and irritability. On examination, she was irritable. Her vital parameters revealed a pulse rate of 96 beats per min, respiratory rate 28/min, blood pressure (BP) 82/53 mmHg, and SpO₂ 98% on room air. Systemic examination revealed positive meningeal signs without any focal deficit. Other systemic examinations were normal. She did not have any history of allergies in the past. A diagnosis of acute bacterial meningitis was made and child was admitted. She was started on injection ceftriaxone and injection vancomycin. Cerebrospinal fluid examination including cartridge-based nucleic acid amplification test (CBNAAT) confirmed diagnosis of tubercular meningitis after 12 days. Hence, antibiotics were continued till then, and following which she was started on category 1 antitubercular therapy (ATT) as per revised national tuberculosis program (rifampicin, isoniazid, pyrazinamide, and ethambutol along with oral prednisolone). As child received 12 days of antibiotics, it was planned to give Vitamin K in view of presumed antibiotic-induced hypoprothrombinemia.

She was apparently well before giving Vitamin K. A slow intravenous Vitamin K (2 mg diluted in 2 ml normal saline) injection was given, immediately following which, she screamed, developed respiratory arrest, central cyanosis and became unresponsive. Cardiopulmonary resuscitation (CPR) was started as per the protocol and she was revived within 2 min. Pulse volume became normal, saturation with 40% O₂ was 100%, and BP was 80/56 mmHg. She also received 20 ml/kg of normal saline bolus and vitals were monitored for 24 h postevent. ECG was done which was within normal limits. Complete blood count showed hemoglobin 10.6 mg/dl, total leukocyte count 10,500/mm³, neutrophils 70%, lymphocytes 26%, eosinophils 2%, and platelet count 2.55 lacs/mm³. Renal function test showed urea 30 mg/dl, creatinine 0.3 mg/dl, sodium 135 mmol/l, potassium 4.2 mmol/l, calcium 8.8 mg/dl, and magnesium 3.8 mmol/l. Injection Vitamin K was not repeated further. She remained asymptomatic thereafter and was discharged on the 14th day of admission. She is under follow-up on maintenance phase ATT and doing well. This reaction was reported to adverse drug reaction (ADR) monitoring center of our hospital (having worldwide Vigiflow number 2015-29603).

Discussion

Antibiotic-induced hypoprothrombinemia is a known phenomenon, especially in patients receiving prolonged N-methylthiotetrazole (NMTT) group of antibiotics such as cefoperazone, cefmetazole, cefamandole, moxalactam, cefotetan, and cefmenoxime. Its incidence has been varied from 3% to 64%. Two Indian studies in children had mentioned incidence of 15% and 33% in two different settings and normalization of coagulation profile with Vitamin K administration.[2,3] The determinants for such phenomena are mostly related to nutritional status of the child and NMTT group of antibiotics. In our case, we have to give antibiotics initially because CBNAAT report was available on the 12th day of treatment.

Commercial preparations of Vitamin K for medicinal purpose are available from 1953. Since then, there have been many reports of adverse effects. Serious reactions are rare, although the exact incidence of serious side effects such as anaphylactic, anaphylactoid reactions are not known and especially in pediatric age group they are less reported. In their 5-year retrospective study, Riegert-Johnson and Volcheck reported the incidence of adverse reaction due to Vitamin K to be 3 per 10,000 doses (0.04–11 per 10,000 doses).[4]

The common reported symptoms range from facial flushing, cyanosis, dyspnea, chest pain, loss of consciousness, hypotension to cardiorespiratory arrest. Some of the reactions got reversal with supportive treatments such as saline bolus, intravenous (IV) adrenaline, steroid, and oxygen whereas few were fatal. In the index case causality assessment was done by institutional ADR monitoring center and was attributed to anaphylactoid reaction to vitamin K. This was because as there was no previous exposure of vitamin K to patient and the reaction happened immediately after injection, as well as reaction could not be explained by disease or other drugs in the stable patient. Assessment as per Naranjo's scale had score of six which comes under category of probable ADR.[5] Moreover, it required only supportive measure oxygen and CPR for treatment and there was no further recurrence. The preventability analysis for above case was done by ADR center as per the Schumock and Thornton criteria and was determined to be "not preventable." [6]

Many efforts were made to find out the reason behind such reactions. It was thought that dispersant used, i.e. polyethoxylated castor oil, might be responsible for the same because there were reports of similar anaphylactic reactions from other anesthetic and antineoplastic agents which used the same solvents for preparations and later withdrawn. Therefore, a new formulation of Vitamin K₁ in mixed micelles of lecithin and glycocholic acid (MM form) was introduced to decrease these adverse events. Havel *et al.* in their study compared both older and newer preparation and found no advantage of newer preparations as they reported one anaphylactoid reaction with MM form.[7] However, Pereira and Williams in their postmarketing surveillance of Vitamin K reported MM form to be safer than castor oil preparation.[8]

These reactions have also been linked to the route and the rate of administration, more common with IV route although reported with intramuscular (IM) and oral route as well. Rapid IV bolus injections are more commonly associated with such reactions but the slow infusions are also not completely safe. Rich and Drage have reported incidents of anaphylactoid reaction following slow bolus of Vitamin K and recommended bolus rate slower than 1 mg/min whereas Songy and Layon reported hypotension and collapse in two adult patients in midway of slow Vitamin K infusion.[9,10] Koklu *et al.* reported

anaphylactic shock in a newborn secondary to IM injection of Vitamin K.[11] These support that no single route is completely safe.

Conclusion

Vitamin K is an important factor for maintaining coagulation, commonly indicated for bleeding secondary to coumadin agents, underlying liver disorders, sepsis-induced coagulopathy, and also used as prophylaxis for prevention of hemorrhagic disease of newborn. Adverse reactions are common but fatal ones are rare. No route and preparations are completely safe though using mixed micelles formulation through IM route or slow IV infusion is comparatively safer if administered under monitoring.

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Conflicts of Interest

There are no conflicts of interest.

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