International Journal of Medical Science in Clinical Research and Review
Online ISSN: 2581-8945
Available Online at http://www.ijmscrr.in Volume 6|Issue 06 (November-December)|2023 Page: 1021-1024
Original Research Paper

Effect of Vitamin K on Coagulation Profile in Patients with Chronic Liver Disease

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Article Received: 22-August-2023, Revised: 22-October-2023, Accepted: 13-November-2023

ABSTRACT:
Background: Chronic liver disease (CLD) is very common in our patient population. CLD is defined as symptomatic liver disease documented to exist for at least 6 months. Vitamin K is a fat-soluble vitamin and has the potential to cause hypervitaminosis, therefore, the practice of giving vitamin K empirically, is not without side effects. This study aimed to assess the effect of the administration of vitamin K to adult patients of stable CLD, on the coagulation profile, as estimated by PT-INR. **Material & Methods**: This prospective, observational study recruited 100 patients with stable CLD attending the medical outpatient department or wards of Yenepoya Medical College Hospital, Mangalore, over a period of 18 months, after obtaining informed consent. Vitamin K was administered subcutaneously, in a dose of 10 mg per day for 3 consecutive days. PT INR was monitored. **Result**: The age range was 21-92 years. Males and females constituted 86% and 14% respectively. Correlation between severity of coagulopathy of CLD patients and administration of vitamin K was significant. **Conclusion**: The administration of vitamin K was found to alter the PT-INR. However, the difference between those who improved and those who did not is not significant. Therefore, giving vitamin K routinely to CLD patients does not have a scientific rationale.

Keywords: Coagulopathy, Vitamin K, Cirrhosis, Prothrombin Time, INR, Chronic Liver Disease.

INTRODUCTION:

Chronic liver disease (CLD) is defined as symptomatic liver disease documented to exist for at least 6 months[1], and common among our patients. Coagulation disorders are a predictable feature of acute and chronic liver disease and an important factor in overall morbidity and mortality in these patients.[2] Prothrombin time (PT) measurement is a liver function that is extensively utilised due to its ubiquitous availability and studies have indicated its link with the liver's overall function.[3] The role of vitamin K insufficiency in the coagulopathy of liver disease is debatable and has not been scientifically investigated. Although liver damage may not produce vitamin K deficiency (VKD), such shortage is commonly observed in CLD.[4] Vitamin K insufficiency is caused by a variety of reasons, including intra and extrahepatic cholestasis, prolonged oral antibiotic medications, malnutrition and malabsorption.[5] Although vitamin K administration can achieve full correction of coagulation parameters in cases of biliary tract disease and gut sterilisation by broad-spectrum antibiotics where vitamin K deficiency is the primary cause of the coagulopathy, the benefit of administering vitamin K to these patients in cases of cirrhosis where there is extensive damage to hepatocytes is questionable, and evidence to support this practise is vastly lacking. Nonetheless, vitamin K is widely used in individuals with CLD (whether or not they are preparing for an invasive test).[4] vitamin K insufficiency is often diagnosed in clinical settings by measuring the prothrombin time (PT), which is extended in a wide range of liver illnesses. PT is also insensitive (it is only extended when the quantity of coagulation factors drops by 30-40%) and nonspecific, being prolonged even when non-VKD factors are deficient. Though studies have shown that prothrombin induced by vitamin K absence (PIVKA)[6,7] levels are a more sensitive and specific means of assessing vitamin K deficiency, we chose to correlate coagulation function with the routine prothrombin time due to its widespread use and availability, as well as the ease

with which it is routinely advised in CLD patients.[4,8–10] We aimed to assess the effect of vitamin K in terms of improving coagulation profile (surrogate measured by PT-INR) in CLD patients.

MATERIAL & METHODS:

This prospective, observational study (IEC approved) was conducted among 100 patients with stable CLD attending the medical OPD or wards of Yenepoya Medical College Hospital over a period of 18 months after obtaining the informed consent. The diagnosis of liver disease was evidenced by symptoms, signs, radiological imaging and biochemical tests. Patients with bleeding or thrombotic disorders, renal disease, transfusion of blood products in the past 7 days, recurrent use of anticoagulants, vitamin K, episodes of cholangitis, obstructive liver disease, prolonged use of antibiotic therapy, malnutrition and malabsorption were excluded from study.

All the demographic details of the patients were collected from the hospital records and the results of relevant investigations routinely ordered were also recorded. PT-INR baseline and response after 3 doses of vitamin k injection not later than 24 hours after the third dose, were estimated. These injections were part of a routine treatment that is currently in vogue in our hospital. The injections were administered subcutaneously in a dose of 10 mg. This was done under aseptic precautions by trained and qualified nurses. There was no additional risk to the patient on account of our research work.

Statistical Analysis: All data were collected and analysed using SPSS v20.0 operating on windows 10. Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation for quantitative variables, frequency and proportions for qualitative variables. Chi square was applied to test the statistical association between qualitative variables. Paired t test was used to test the mean difference of PT – INR with respect to before and after vitamin K administration in the same subject among improved and unimproved groups. Unpaired t test was applied to test the mean difference of PT – INR among improved and unimproved groups. A p-value of <0.05 was considered statistically significant for all statistical purposes.

RESULTS:

Present study included a total of 100 patients fulfilling inclusion and exclusion criteria. The majority were in the age group of 31-60yrs, had a mean age of 48.84±12.42yrs, with male preponderance (86.0%).Sixty-five percent of the patients were chronic alcoholics and 21% were alcoholic and cigarette smokers.

Table 1: Demographic and other details of the patients

		Frequency	Percent
Age group	21-30	3	3.0
	31-40	28	28.0
	41-50	32	32.0
	51-60	20	20.0
	61-70	11	11.0
	71-80	4	4.0
	More than 80	2	2.0
Gender	Female	14	14.0
	Male	86	86.0
Personal habits	Alcohol	65	65.0
	Smoking + alcohol	21	21.0
	Nil	14	14.0
Outcome	Improved	53	53.0
	Not-improved	47	47.0
Presenting complaints	Altered sensorium	22	22.0
	Bilateral swelling of lower limb	34	34.0
	Malena	12	12.0
	Hematemesis	13	13.0
	Abdominal pain and distension	76	76.0
	Yellowish discolouration	19	19.0
Physical examination	Testicular atrophy	8	8.0
	Gynaecomastia	50	50.0

	Flapping tremor	69	69.0
	Spider naevi	83	83.0
	Palmar erythema	23	23.0
	Cyanosis	16	16.0
	Clubbing	18	18.0
	Icterus	79	79.0
	Pedal edema	80	80.0
	Pallor	83	83.0
Per-abdomen	Splenomegaly	18	18.0
	Ascites	74	74.0
	Hepatomegaly	26	26.0
	Hepatosplenomegaly	19	19.0

Among the presenting complaints, 76% had abdominal pain and distension, 34% had bilateral swelling of lower limb, 22% altered sensorium, 19% yellowish discoloration, 13% haematemesis and 12% had malena. Examination findings showed the presence of pallor, pedal edema, icterus, spider naevi and flapping tremor in more than 80%. Per abdomen examination revealed that 74% had ascites, 26% had hepatomegaly, 19% had hepatosplenomegaly and 18% splenomegaly alone. Fifty-three percent improved and 47% did not improve.

Table 2: Comparison of the PT-INR of patients with administration of vitamin K

PT-INR of patients	Vitamin K administration	Mean ± SD	Mean difference	p-value
Not improved	Before administration	1.82 ± 0.72	-0.36	0.01
	After administration	2.177 ± 1.30		
Improved	Before administration	2.69 ± 1.43	0.81	0.01
	After administration	1.89 ± 0.72		
Overall	Before administration	2.3 ± 1.2	0.26	0.01
	After administration	2.03 ± 1.04		

DISCUSSION:

The purpose of this study was to see if there was any improvement in coagulation markers in individuals with CLD after receiving vitamin K injections. The most prevalent risk factor was alcohol. In our study, the most common presenting symptom was abdominal discomfort (76%), followed by bilateral lower limb edema (34%). In the case of a general physical examination, pallor and spider naevi (83%) were the most prevalent, followed by pedal oedema (80%).Hepatomegaly (26%) and ascites (74%), as determined by abdominal examination. The study conducted by Arturo and Sola (4) to assess effects of vitamin K administration in CLD patients with upper gastrointestinal bleeding showed no proven benefits of administering vitamin K rather preferred use of Fresh frozen plasma .[11] The PT-INR values in CLD patients who received vitamin K injections but did not improve in coagulation parameters had a mean difference of -0.356 and a p value of 0.001 compared to the other group who improved in PT-INR levels had a mean difference of 0.8028 and a p value of 0.01 which was statistically significant. The results were compared using the paired t test, and comparable findings were discovered using the unpaired t test before vitamin k administration (mean 0.875 and p value 0.001) and the PT-INR levels after vitamin k administration (mean -0.28 and p value 0.175). In study by Kaul et al.,(2000) vitamin K had no role to play in CLD patients and giving blood products like fresh frozen plasma will be beneficial, but has been studied only in cholestatic liver disease patients and whether these findings can be extrapolated to other CLD needs elucidation.[13]

CONCLUSION:

There is minimal improvement in the PT-INR level among the patients administered with vitamin K in CLD. The administration of vitamin K was found to alter the PT-INR (a surrogate marker for coagulopathy). However, the difference between those who improved and those who did not is not significant (p=0.175). Therefore, giving vitamin K routinely to CLD patients does not have a scientific rationale. The larger population-based studies for a long period of time is required to concrete the findings with statistical significance.

Vitamin K is routinely used in the treatment of CLD patients, with or without estimation of coagulation parameters. In cases of cirrhosis with significant hepatocyte destruction, the value of providing vitamin K to these patients is dubious, and our study found no evidence to support this practice. As a result, we urge that vitamin K not be routinely provided to CLD patients in the hope that coagulopathy may improve.

Funding*: Nil*
Conflict of interest*: Nil*

REFERENCES:

1. Cheemerla S, Balakrishnan M. Global epidemiology of chronic liver disease. Clin liver Dis. 2021;17(5):365–72.

2. Sarin SK, Choudhury A, Sharma MK, Maiwall R, Al Mahtab M, Rahman S, et al. Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific association for the study of the liver (APASL): an update. Hepatol Int. 2019;13:353–90.

3. Latona A, Hill K, Connelly A, Stuart K, Wood P. Prothrombinex®-VF in chronic liver disease: Friend or foe? Emerg Med Australas. 2023;35(1):89–96.

4. Jin S, Hong L, FakhriRavari A. The Role of Vitamin K in Cirrhosis: Do Pharmaco-K-Netics Matter? Gastrointest Disord. 2022;4(1):15–21.

5. Kini G, Yadav A, Reddy R, Mala M, Golla NKL, Manaswini GYA. Efficacy of Sodium Fluoride as an Anticoagulant in the Estimation of Glycated Haemoglobin in Diabetic Patients: An Alternative to EDTA. J Clin DIAGNOSTIC Res. 2022;16(7):1–3.

6. Wang X, Zhang W, Liu Y, Gong W, Sun P, Kong X, et al. Diagnostic value of prothrombin induced by the absence of vitamin K or antagonist-II (PIVKA-II) for early stage HBV related hepatocellular carcinoma. Infect Agent Cancer. 2017;12(1):1–8.

7. Yoon YJ, Han K-H, Kim DY. Role of serum prothrombin induced by vitamin K absence or antagonist-II in the early detection of hepatocellular carcinoma in patients with chronic hepatitis B virus infection. Scand J Gastroenterol. 2009;44(7):861–6.

8. Yang R, Moosavi L. Prothrombin time. In: StatPearls [Internet]. StatPearls Publishing; 2022. p. 1–11.

9. Saja MF, Abdo AA, Sanai FM, Shaikh SA, Gader AGMA. The coagulopathy of liver disease: does vitamin K help? Blood Coagul Fibrinolysis. 2013;24(1):10–7.

10. Dahlberg S, Schött U, Kander T. The effect of vitamin K on prothrombin time in critically ill patients: an observational registry study. J Intensive Care. 2021;9(1):11–5.

11. Martí-Carvajal AJ, Sola I. Vitamin K for upper gastrointestinal bleeding in patients with acute or chronic liver diseases. Cochrane Database Syst Rev. 2012;(9):1–10.

12. Aldrich SM, Regal RE. Routine use of vitamin K in the treatment of cirrhosis-related coagulopathy: is it AOK? Maybe not, we say. Pharm Ther. 2019;44(3):131–5.

13. Kaul V V, Munoz SJ. Coagulopathy of Liver Disease. Curr Treat Options Gastroenterol. 2000;3(6):433–8.