Original Article

Efficacy of Intravenous Vitamin K in Correcting Deranged International Normalized Ratio in Chronic Liver Disease

Sana Muhammad Hussain[1], Tahreem Sajjad[1], Syeda Shaheera Zaidi[1*], Amanullah Abbasi[1]

ABSTRACT

OBJECTIVE: To study the efficacy of intravenous vitamin K in deranged INR in chronic liver disease.
METHODOLOGY: This observational cross-sectional study at a tertiary care hospital included CLD patients (≥18 years) with baseline INR >1.3 who received three doses of vitamin K. Exclusions were acute liver failure, missing INR data, anticoagulant use, or blood transfusion within 72 hours before or between PT-INR sampling. The mean INR change was compared by dosing frequency (single vs multiple) and Child–Pugh class. Data were analyzed using SPSS version 24.
RESULTS: 80 patients included, with 58.75% males and 41.25% females, of whom CTP A, B, and C were 5%, 15%, and 80%, respectively. The mean change in INR after the 1st and 3rd doses was 0.078±0.265; P = 0.01 and 0.1403±0.382; P = 0.002, respectively. The mean change in INR between single versus three doses was -0.056±0.33; P = 0.049. The mean change in INR after the 1st and 3rd doses in CTP A was 0.195±0.404; P=0.001 and 0.0250±0.635; P=0.005, respectively. The mean change in INR after the 1st and 3rd doses in CTP B was 0.0825±0.449; P = < 0.001 and 0.0717±0.15; P= < 0.001, respectively. The mean change in INR after the 1st and 3rd doses in CTP C was 0.077±0.299; P= < 0.001 and 0.160 ± 0.420; P= <0.001, respectively.
CONCLUSION: Overall, the majority of CLD patients showed improvement in INR after three doses of vitamin K, primarily CTP C.

KEYWORDS: Chronic liver disease, vitamin K, cirrhosis, INR, coagulopathy, Child–Pugh Classification (CTP).

INTRODUCTION

The estimated incidence of chronic liver disease (CLD) worldwide is 20.7/100,000, an increment of 13% since 2000[1]. The estimated incidence of cirrhosis in East and Southeast Asia is 16.5/100,000 and 23.6/100,000, respectively[2]. In vitamin K deficiency, procoagulant and anticoagulant factors are synthesized in the liver and in CLD, these are decreased, resulting in both bleeding and thrombotic tendencies compared with patients without CLD[3]. As a result of defective synthesis of coagulant factors by the diseased liver, patients with CLD have deranged international normalized ratio (INR) and a prolonged prothrombin time (PT)[4].

Nutritional deficiency is commonly seen in cirrhotic patients, especially with simultaneous biliary disease. This reduces bile acid production and flow, resulting in decreased concentrations of biliary salts and decreased absorption of fat-soluble vitamins, including vitamin K[5].

A Cochrane systematic review concluded that studies conducted to date have not provided sufficient evidence to recommend or refute the practice of using vitamin K to correct coagulopathy in CLD[6].

In recent American Association for the Study of Liver Diseases (AASLD) guidelines, there is no recommendation regarding vitamin K use in cirrhosis, and there is still a lack of evidence supporting this practice[2]. Thus, this study was conducted to determine the efficacy of IV vitamin K in correcting coagulopathy in CLD.

METHODOLOGY

This study was conducted at Dr Ruth KM Pfau Civil Hospital, Karachi (CHK), after getting approval from the institutional review board, Dow University of Health Sciences, Karachi (IRB), with IRB number IRB-3262/DUHS/ Approval/2023/444. This was a prospective, single-centre, cross-sectional observational study. A non-probability consecutive sampling technique was used. Online Open Epi Sample size software was used to calculate the sample size based on the proportion reported by Anwar Hussain Abbasi et al., who reported a liver cirrhosis prevalence of 23.72% in Pakistan. With a confidence level of 90% and a margin of error of 8%, the sample size was calculated to be n=77.

Inclusion criteria were all CLD-admitted patients of age greater than 18 years who had received three doses of IV vitamin K, had a baseline INR >1.3, and had at least one repeat INR value after 12 hours post-vitamin K administration. A review of the physician's notes determined the presence of cirrhosis. CLD was

[1]*Department of Internal Medicine, Dr Ruth KM Pfau Civil Hospital, Karachi, Sindh-Pakistan*
Correspondence: Shaheera.zaidi@duhs.edu.pk
doi: 10.22442/jlumhs.2025.01246
Received: 03-02-2025 *Revised: 24-07-2025*
Accepted: 24-09-2025 *Published Online: 16-10-2025*

defined on the following clinical and pathological criteria: ascites, spontaneous bacterial peritonitis, prior record or current presentation with variceal bleed, varices appeared on endoscopy, hepatic encephalopathy, biopsy-proven liver cirrhosis, or scans demonstrating cirrhosis.[2] Exclusion criteria were acute liver failure (ALF), missing INR data around the period in which a vitamin K injection was given, or being on anticoagulants around admission. Patients were also excluded if any plasma, platelets, or packed cell volume transfusion was done within 72 hours before the first PT-INR sampling and during the period of PT/INR samplings and vitamin K administration.

All patients admitted to CHK during the study period with cirrhosis who met the inclusion criteria were enrolled. The pre-designed proforma was completed after taking a detailed history from the patient/ caregiver with their verbal informed consent. Routine labs, including CBC, PT/INR, serum albumin, and Total bilirubin, were recorded. Relevant investigations, including U/S abdomen and OGD, were reviewed, and significant details were noted. INR values obtained 24 hours after vitamin K 1st and 3rd dose administrations of vitamin K were recorded. The immediate INR reading before the vitamin K injection was considered the baseline INR.

The primary outcome was the change in INR from baseline to after the 1st and 3rd doses of vitamin K. Secondary outcomes included analysis of the primary outcome by dosing frequency (single versus multiple doses) and Child-Pugh Classification (CTP Class).

The data were analyzed using SPSS version 24. Baseline characteristics were summarized by using descriptive statistics. Student's t-test was used to compare the subgroup analysis of the primary outcome by dosing frequency and CTP class. Frequency and percentages were recorded for categorical variables. The mean ± SD was calculated for numerical variables such as age, CBC, PT/INR, etc. The statistical significance level was set at $p < 0.05$.

RESULTS

Eighty patients meeting the eligibility criteria were enrolled in the analysis. Missing INR data and blood product transfusions around the time specified above were the main reasons for exclusion. There were 58.75% males and 41.25% females, of which CTP A, B and C were 5%, 15% and 80% respectively (**Figure 1**). **Table I** includes baseline characteristics of the patients.

IV vitamin K was given for three consecutive days at an average daily dose of 10mg. The average change in INR from baseline to 24 hours after 1st dose of vitamin K administration was 0.078 ± 0.265; P=0.01. The average change in INR from baseline to 24 hours after 3rd dose of vitamin K administration was 0.1403 ± 0.382; P=0.002. There was a significant change in INR between single versus multiple doses (three doses) of vitamin K –0.056 ± 0.33; P=0.049.

The mean change in INR from baseline to 24 hours after the 1st and 3rd doses of vitamin K in CTP Class A was 0.195 ± 0.404; P=0.001 and 0.0250 ± 0.635; P= 0.005, respectively. The mean change in INR from baseline to 24 hours after the 1st and 3rd doses of vitamin K in CTP Class B was 0.0825 ± 0.449; P = < 0.001 and 0.0717 ± 0.15; P = < 0.001. The mean change in INR from baseline to 24 hours after the 1st and 3rd doses of vitamin K in CTP Class C was 0.077 ± 0.299; P= < 0.001 and 0.160 ± 0.420; P= < 0.001 (**Figure 2**). No incidence of venous thromboembolism (VTE) was noted in this study. Incidence of major bleeding was 25%, mainly due to variceal bleed (**Figure 3**).

Table I: Baseline Characteristics

Characteristics	N = 80
Age — ag± SD.	50.9 ± 10.86
Male sex — n, (%).	47, (58.75)
Female sex— n, (%).	33, (41.25)
Cirrhosis etiology— n, (%).	17, (21.3)
Hepatitis B	44, (55%)
Hepatitis C	5, (6.3%)
Alcoholic	2, (2.5%)
NASH	12, (15%)
Other	
Baseline laboratory results — avg ± SD	1.4 ± 0.57
Lowest albumin (g/dl)	20.4 ± 4.2
Highest total bilirubin (mg/dl)	9.03 ± 1.12
Average Hb (g/dl)	132.18 ± 5.13
Serum sodium (mEq/l)	1.2 ± 0.89
Baseline serum creatinine (mg/dl)	94.2 ± 53.1
Platelets on admission (K/µl)	1.7 ± 0.40
Baseline INR	17.7 ± 4.04
Baseline PT (sec)	32.2 ± 8.19
Baseline APTT (sec).	50.03 ± 54.28
ALT (U/l)	136 ± 81.68
ALP (U/l)	
Major bleeding — n, (%).	20, 25%
MELD Score — avg± SD	21.66 ± 6.51
Child-Pugh Class —n, (%).	
A	4, 5%
B	12, 15%
C	64, 80%

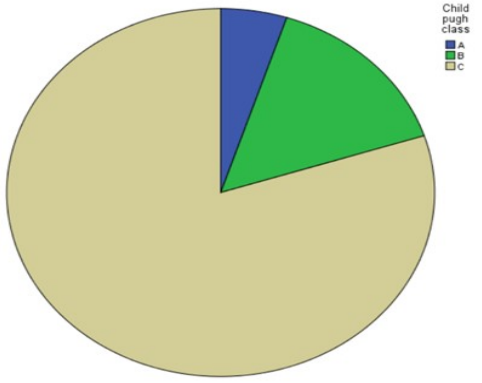

Figure 1:
Pie Chart showing percentages of CTP Class

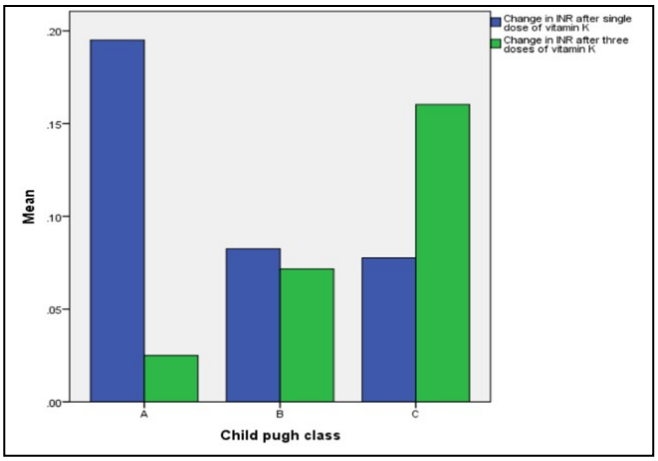

Figure 2: Change in INR after the 1st and 3rd dose of vitamin K in Child-Pugh class A, B and C

Figure 3:
Pie Chart showing percentages of major bleeding

DISCUSSION

The use of vitamin K in cirrhosis showed a statistically significant decline in INR after both single and multiple doses of vitamin K, with a relatively greater average decline after three doses of vitamin K.

If we look at the response categorically, there is a more significant decline after the 1st dose compared to the 3rd dose in Child-Pugh Class A. In Child-Pugh Class B, there is a statistically significant decline after the 1st dose, and this change remains almost static after the 3rd dose. In Child-Pugh Class C, statistically significant results are noted after both the 1st and 3rd doses of vitamin K. Still, the average improvement in INR is greater after three doses of vitamin K. No anaphylactic reaction to IV vitamin K was observed in this study. Mild to moderate incidence of in-hospital major bleed, mainly due to varices, was seen, and no incidence of VTE was noticed.

Apart from vitamin K-dependent coagulation factors, other factors are also depleted in patients with chronic liver disease, but correcting the coagulation abnormalities associated with vitamin K deficiency is easier when given intravenously, which shows significant improvement in most of cases. A few retrospective study results are consistent with our study. Zhuang Xiong's study demonstrated a decline in INR values with vitamin K in CLD. This study also showed that vitamin K reduces mortality in CLD. In the Hambley et al. study, a statistically significant decrease in INR of 0.08 was found. A small percentage of patients enrolled in this study (24/333) had an INR decrease of more than 0.4[7]. Al Sulaiman studied the efficacy and safety of vitamin K in correcting deranged INR in critically ill patients with CLD. In this study, a significant decline in INR with a median of 0.63 after the first dose was observed (P-value: <.0001). However, the decrease in INR after subsequent doses was not statistically significant[8].

Few studies showed insignificant improvement in INR after vitamin K. Saja et al.'s study showed clinically insignificant improvement in PT and APTT after vitamin K in cirrhosis[9,10] . In adults with cirrhosis, Rivosecchi and colleagues assessed the impact of IV vitamin K (81% received 10 mg) on INR and observed a mean decrease of 0.3, with 62.3% of patients failing to achieve even a 10% reduction[11]. In his study, Blanchard et al. reviewed 28 patients with liver disease, of whom 14 had cirrhosis, and seven of them had received vitamin K. These patients had abnormal prothrombin levels and increased levels of undercarboxylated prothrombin. There is no decrement in PT, and no correction in undercarboxylated prothrombin was observed[12].

The few retrospective studies mentioned above showed significant improvement in INR after vitamin K administration, but this response was not compared with the severity of CLD. In this prospective study, we categorized patients into CTP Class A, B, and C and assessed their response categorically. 10 mg of vitamin K injection given for three consecutive days is sufficient to correct vitamin K deficiency in decompensated liver cirrhosis. Oral vitamin K has no role[13,14]. There is delayed and uncertain absorption of vitamin K via the subcutaneous route compared to the intravenous (IV) route[15]. A standard dose of 10mg IV vitamin K was given to all patients, which decreases the risk of discordant results. Exclusion of patients in whom blood products were transfused and patients taking anticoagulants decreases the chances of erratic results. Studies conducted so far were retrospective, inconclusive, and performed in Western countries; our study is prospective, and our population has a greater tendency to bleed than Western populations due to genetic differences and malnutrition[15]. This is the first study in our population (Pakistan) to assess the role of vitamin K in patients with CLD and deranged INR.

Limitations included the single-centre design and small sample size, which made it difficult to generalize these results to the general population. Another limitation is the lack of a control group comparison. We have used INR for the assessment of coagulopathy, which is not the standard method in CLD; it underestimates vitamin K deficiency, evaluates the synthetic function of the liver, but does not assess

bleeding tendency.
Further studies are needed to assess the clinical outcomes of vitamin K use in the Asian population. The effect of IV vitamin K for 5 days may also be studied to further evaluate its effectiveness.

CONCLUSION

Overall, in the majority of patients with CLD, INR values declined significantly after three doses of vitamin K. No significant adverse effects of IV vitamin K were noted in the study.

Ethical permission: Dow University of Health Sciences, Karachi, Pakistan, IRB letter No. IRB-3262/ DUHS/Approval/2023/444.

Conflict of interest: There is no conflict of interest between the authors.

Financial Disclosure / Grant Approval: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors

Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

AUTHOR CONTRIBUTION

Hussain SM:Data collection, manuscript review and editing
Sajjad T: Conceived, designed and did statistical analysis and writing of the manuscript
Zaidi SS: Data collection, manuscript review and editing
Abbasi A: Final review and approval of manuscript

REFERENCES

1. Moon AM, Singal AG, Tapper EB. Contemporary Epidemiology of Chronic Liver Disease and Cirrhosis. Clinical Gastroenterology and Hepatology. 2019 Aug; 18(12).
2. Wong MCS, Huang JLW, George J, Huang J, Leung C, Eslam M, et al. The changing epidemiology of liver diseases in the Asia-Pacific region. Nat Rev Gastroenterol Hepatol. 2019; 16 (1): 57–73.
3. Smith CB, Hennessey E, Crossey CD, Crannage AJ. Impact of Vitamin K Administration on Elevated International Normalized Ratio in Chronic Liver Disease. Clinical and Applied Thrombosis-Hemostasis. 2023; 29: 10760296231 1646-107602962311646.
4. Aldrich SM, Regal RE. Routine Use of Vitamin K in the Treatment of Cirrhosis-Related Coagulopathy: Is it A-O-K? Maybe Not, We Say. P & T: a peer-reviewed journal for formulary management. 2019 Mar; 44(3): 131–136.
5. Puri P, Dhiman RK, Taneja S, Tandon P, Merli M, Anand AC, et al. Nutrition in Chronic Liver Disease: Consensus Statement of the Indian National Association for Study of the Liver. Journal of Clinical and Experimental Hepatology. 2021 Jan;11(1):97–143.
6. Martí-Carvajal AJ, Solà I. Vitamin K for upper gastrointestinal bleeding in people with acute or chronic liver diseases. The Cochrane Database of Systematic Reviews. 2015 Jun 9; 2015(6): CD004792.
7. Hambley BC, Diamond A, Connie S, Partovi S, Smith T, LoPresti C. Effect of Vitamin K on Coagulopathy of Liver Disease: A Single Center Retrospective Review. Blood. 2016 Dec 2; 128 (22): 2583–3.
8. Al Sulaiman K, Al Mutairi M, Al Harbi O, Al Duraihim A, Aldosary S, Al Khalil H et al. Appropriateness of Using Vitamin K for the Correction of INR Elevation Secondary to Hepatic Disease in Critically ill Patients: An Observational Study. Clin Appl Thrombosis/Hemostasis. 2021 Jan; 27: 107602962110509.
9. Jin S, Hong L, FakhriRavari A. The Role of Vitamin K in Cirrhosis: Do Pharmaco-K-Netics Matter? Gastrointestinal Disorders. 2022 Mar 1; 4 (1): 15–21.
10. Saja MF, Abdo AA, Sanai FM, Shaikh SA, Gader AGMA. The coagulopathy of liver disease. Blood Coagulation & Fibrinolysis. 2013 Jan; 24(1): 10–7.
11. Rivosecchi RM, Kane-Gill SL, Garavaglia J, MacLasco A, Johnson H. The effectiveness of intravenous vitamin K in correcting cirrhosis-associated coagulopathy. Int J Pharm Pract. 2017 Feb 17; 25(6): 463–465.
12. Blanchard RA, Furie BC, Jorgensen M, Kruger SF, Furie B. Acquired vitamin K-dependent carboxylation deficiency in liver disease. N Engl J Med. 1981; 305(5): 242–8.
13. Amarapurkar PD, Amarapurkar DN. Management of Coagulopathy in Patients with Decompensated Liver Cirrhosis. Int J Hepatol. 2011; 2011: 1–5.
14. Williams R. Sherlock's disease of the liver and biliary systems. Clin Med. 2011 Oct; 11(5): 506–6.
15. Liang Y. Bleeding Risk in Asian Patients: Potential for Thrombin Amplification Pathway Blockade Using Factor XI Inhibitors. JACC Asia. 2024; 4(2): 163-165.