Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/15129
DOI URL: http://dx.doi.org/10.21474/IJAR01/15129

RESEARCH ARTICLE

ANTICOAGULANT DRUG INDUCED SUPRA THERAPEUTIC INR AND ITS MANAGEMENT

Dr. Abhishek Sharma MBBS MRCEM (UK), Dr. Chiragkumar Thummar MBBS and Dr. Smiti Navin Panchal BsChB MBChB MPH

Manuscript Info

Manuscript History
Received: 31 May 2022
Final Accepted: 30 June 2022
Published: July 2022

Abstract

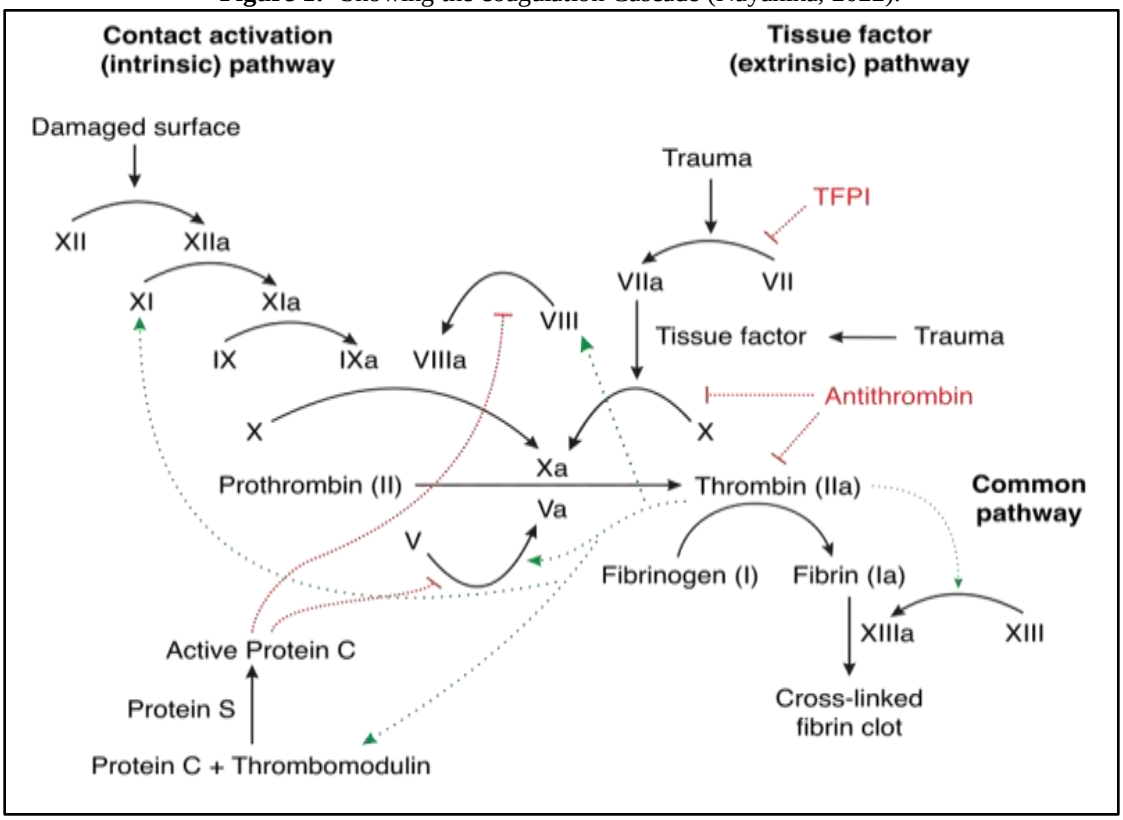
This paper has the management of Drug Induced Supra therapeutic INR and a case presentation of 33-year-old Male patient who was on oral anticoagulant (Vitamin K antagonist-VKA) and antiplatelet therapy presented with supra-therapeutic international normalized ratio (INR) with history of Single episode of blood stained Sputum. The patient is known case of posterior circulation stroke with left ventricular clot, Cortical venous sinus thrombosis with left parietal hematoma and secondary seizure, ischemic heart disease (IHD) status post Percutaneous Transluminal Coronary Angioplasty (PTCA) to LAD with left ventricular ejection fraction (LVEF) - 30% and hyper-homocysteinemia. The patient presented with history of single episode of blood stain sputum and with no other complaints. His routine blood investigation revealed INR of 9.50 hence the patient was admitted and treated accordingly. Patient's INR returned to normal after appropriate medical management. Patient was discharged with a titrated dose, advised on treatment, education and adherence counselling.

Introduction:-

Supra-therapeutic INR values are commonly seen in patients who are taking VKA hence INR is frequently monitored in such patients. Patients treated with VKA require frequent titration of the dose. If the dose is too low, clots may form which may lead to deep vein thrombosis (DVT), cerebral or myocardial infarction, systemic or pulmonary embolism and if the dose is too high, the risk of life threatening bleeding is increased. For this reason, INR must be frequently monitored to adjust the dose if necessary. (David A. Garcia; Mark A. Crowther, 2012). An INR is a standardized measure of the patient's prothrombin time to a reference value.

Corresponding Author:- Dr. Abhishek Sharma

Figure 1:- Showing the coagulation Cascade (Nayanika, 2022).



Supra therapeutic INR is defined as an INR value above the therapeutic range which is seen in patients who are taking VKA such as anti-coagulant, acenocoumarol, phenindione.

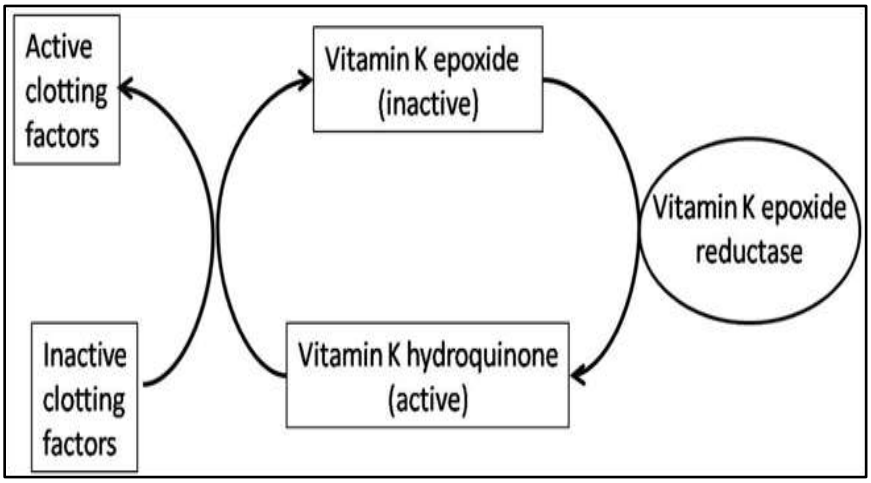


Figure 2:- Showing the Vitamin K Cycle (J, 2013).

VKA are mostly used for long-term anticoagulation for prevention of stroke in patients with atrial fibrillation and various other conditions such as venous thromboembolism, systemic or pulmonary embolism, and myocardial infarction. (Claire, Hilary, Cindy, & Doson, 2017)

VKA inhibit the Vitamin-K dependent synthesis of clotting factor II, VII, IX, X along with protein C & S. VKA specifically inhibit Vitamin-K epoxide reductase preventing regeneration of reduced Vitamin-K. As reduced

Vitamin-K is needed for gamma-carboxylation of glutamic acid resides on coagulation factor II, VII, IX, X hence the formation of functional coagulation factor is blocked. (Neill L; Weygandt L, 2018)

In this report, we described a case of supra-therapeutic INR with a single episode of blood stained sputum in a 33-year-old male patient who was managed medically and complications were prevented by early identification and management.

Case Presentation:
A 33-year-old male patient, who has history of posterior circulation stroke with left ventricular clot (26 April 2022), cortical venous sinus thrombosis with left parietal hematoma and secondary seizure (2016), IHD status post PTCA to LAD with LVEF – 30% (2013) and hyper-homocysteinemia, came for follow-up with one episode of blood in sputum. Patient was on VKA (Acenocoumarol 3 mg OD) since 4 May 2022. Patient has also been taking an antiplatelet, Antiepileptic, and diuretic drug since 2013.

On examination, the patient had stable vitals with blood pressure of 138/74 mmhg, heart rate of 98, respiratory rate of 20, temperature of 98.1 degree Fahrenheit, oxygen saturation of 100% at room air. Patient does not have any signs and symptoms of bleeding such as bruising, rashes, bleeding gums, nose bleed, blood in urine or stool, abdominal pain, dizziness, drowsiness, chest pain or shortness of breath.

The patient was investigated in the form of CBC, PT/INR, RFT, LFT, Chest X-ray, 2D ECHO, ECG and urine routine examination.

2D ECHO revealed moderate left ventricular (LV) dysfunction with LVEF – 35%, reduced LV compliance, mild mitral regurgitation (MR), mild tricuspid regurgitation (TR), no clots/vegetation/effusion was noted. CBC was indicative of anisocytosis, leucocytosis and thrombocytosis with haemoglobin of 18.7 (13-17), total WBC count of 14876 (4000-11000), platelet count of 484300 (150000-450000).

Chest x-ray and ECG were normal.

Table 1:- The Table Shows the Serial Reports of the Patient.

Date	**16/5**	**17/5**	**18/5**	**19/5**
PT	104.1 (11-16 sec)	21. (11-16 sec)	18.6(11-16 sec)	17.2 (11-16 sec)
CONTROL	12.2 sec	12.2 sec	12.2 sec	12.2 sec
INR	9.50	1.82	1.56	1.43
S. SODIUM	129	-	-	136(135-145)
S. POTASSIUM	3.3	-	2.8	3.2(3.5-5.5)
S. CHLORIDE	-	-	-	96 (96-110)
S. CREATININE	1.01	-	-	0.74(0.6-1.3)
S. UREA	-	-	-	24(15-50)

Treatment:
The patient was explained about the condition and its course of treatment. The VKA was with-held, one dose of Injection Vitamin-K 10mg IV slowly given and syrup POTKLOR 15ml TDS was started.

The patient's PT/INR was monitored every 24 hours which showed significant improvement after initial treatment. Patient's INR decreased to 1.82 after 24 hours which was further decreased to 1.56 on the 3rd day. The patient's VKA (acenocoumarol) was titrated to 2 mg OD and was started from the second day of admission. The patient was discharged with the INR of 1.43.

Outcome:
The patient had an uneventful stay during hospitalization and was stable vitals. Proper patient education was advised at the time of discharge. The patient and relatives were counselled about the need of anticoagulation with risk and benefit with frequent monitoring of PT/INR. They were also educated on the signs to watch out and when to seek medical attention.

Discussion:-

The Patient was managed accordingly to the NICE guidelines and as the guidelines follows

As per NICE guidelines

- **Measurement of INR**

i) Generally, the INR should be measured daily or on alternate days, until it is within the therapeutic range on two consecutive occasions. A meaningful INR can only be obtained 3–4 days after starting treatment. Then, twice weekly for 1-2 weeks, followed by weekly measurements until at least two INR measurements are within the therapeutic range.

ii) Thereafter, depending on the stability of the INR it should be measured at longer intervals for example up to every 12 weeks. More frequent routine monitoring (for example every 1–2 weeks) of the INR is recommended for peoples who are at increased risk of over-coagulation, for example people with severe hypertension, liver disease or renal failure. (NICE Guidelines, 2022)

- **Target INR**

i) A target INR of 2.5 is recommended for treatment of deep vein thrombosis (DVT), pulmonary embolism (PE), atrial fibrillation, mitral stenosis or regurgitation with atrial fibrillation, history of systemic embolism, left atrial thrombus or enlarged left atrium, acute arterial embolism leading to embolectomy, and post myocardial infarction.

ii) A target INR of 3.5 is recommended for recurrent DVT or PE in people currently receiving anticoagulation and with an INR above 2. (NICE Guidelines, 2022)

- **If the INR is outside the therapeutic range, ask the person about any changes in order to find a cause of the out-of-range result. For example, ask about:**

i) Adherence to anti-coagulant treatment, for example if they have missed any doses or taken too much.
ii) Use of other medications, including over-the-counter products, vitamins, and herbal or homeopathic remedies.
iii) Use of alcohol or illicit drugs.
iv) Food and drink intake (for example green vegetables and cranberry juice).
v) Weight loss, acute illness (such as gastroenteritis), and smoking cessation can increase the effect of anti-coagulant.
vi) Weight gain, diarrhoea, and vomiting can reduce the effect of anti-coagulant. (NICE Guidelines, 2022)

- **Management of INR If the INR is high**

i) **Greater than 8 with minor bleeding -** stop anti-coagulant and give vitamin K by slow intravenous injection. The dose of vitamin K may be repeated after 24 hours if the INR is still too high. Restart anti-coagulant when the INR is less than 5.

ii) **Greater than 8 with no bleeding -** stop anti-coagulant and give Vitamin K by mouth using the intravenous preparation orally (off-label use). The dose of Vitamin K may be repeated after 24 hours if the INR is still too high. Restart anti-coagulant when the INR is less than 5.

iii) **Between 5-8 with minor bleeding -** stop anti-coagulant and give Vitamin K by slow intravenous injection. Restart anti-coagulant when the INR is less than 5.

iv) **Between 5-8 with no bleeding -** withhold 1 or 2 doses of anti-coagulant and reduce subsequent maintenance dose. (NICE Guidelines, 2022)

- **Advice to a person receiving anti-coagulant**

i) It is very important to have their blood tested regularly to check their INR, at intervals agreed with the anticoagulant clinic staff.
ii) They should always take their anticoagulant treatment booklet ('Yellow book') when they go to the anti-coagulant clinic to have their INR checked. The 'Yellow book' includes advice for people taking anticoagulants, an alert card (which the person should carry at all times), and a section for recording the INR readings.
iii) They should take their anti-coagulant at the same time each day.
iv) They should not miss doses or take additional doses, without advice from a healthcare professional.
v) They must inform anticoagulant clinic staff if they think they have taken too much anti-coagulant or have missed any doses.
vi) If a dose is accidentally missed, they should continue with the regimen as prescribed, and never take a double dose.

vii) Anti-coagulant levels can be affected by diet, alcohol, acute illness, and other medications, including over-the-counter drugs, vitamins, food supplements, and herbal and homeopathic remedies. They should seek medical advice before undertaking any major changes in diet, especially if their diet is rich in vitamin K (such as broccoli, kale, or spinach) — this can potentially affect control of anticoagulation.
viii) Limit alcohol intake to a maximum of one or two drinks a day, and never binge drink.
ix) They may have to stop anti-coagulant treatment temporarily for certain surgical and dental treatments.
x) They should expect to bruise more easily.
xi) Take extra care when brushing teeth or shaving and consider using a soft toothbrush and an electric razor.
xii) Seek immediate medical advice if:
(1) Spontaneous bleeding occurs whilst on anti-coagulant and the bleeding does not stop, or recurs. This includes bruising, bleeding gums, nosebleeds, prolonged bleeding from cuts, blood in the urine or stools, coughing up blood, a sub conjunctival haemorrhage, and vaginal bleeding in a postmenopausal woman.
(2) They get sudden severe back pain (which may indicate spontaneous retroperitoneal bleeding).
(3) They experience difficulty breathing, increased breathing rate, or chest pain (which could be symptoms of pulmonary embolism).
xiii) For women of childbearing potential, advise that:
(1) They should use effective contraception during treatment because anti-coagulant is a known teratogen.
(2) If she becomes pregnant (or is planning a pregnancy), she needs to stop taking anti-coagulant and start using low molecular weight heparin. (NICE Guidelines, 2022)

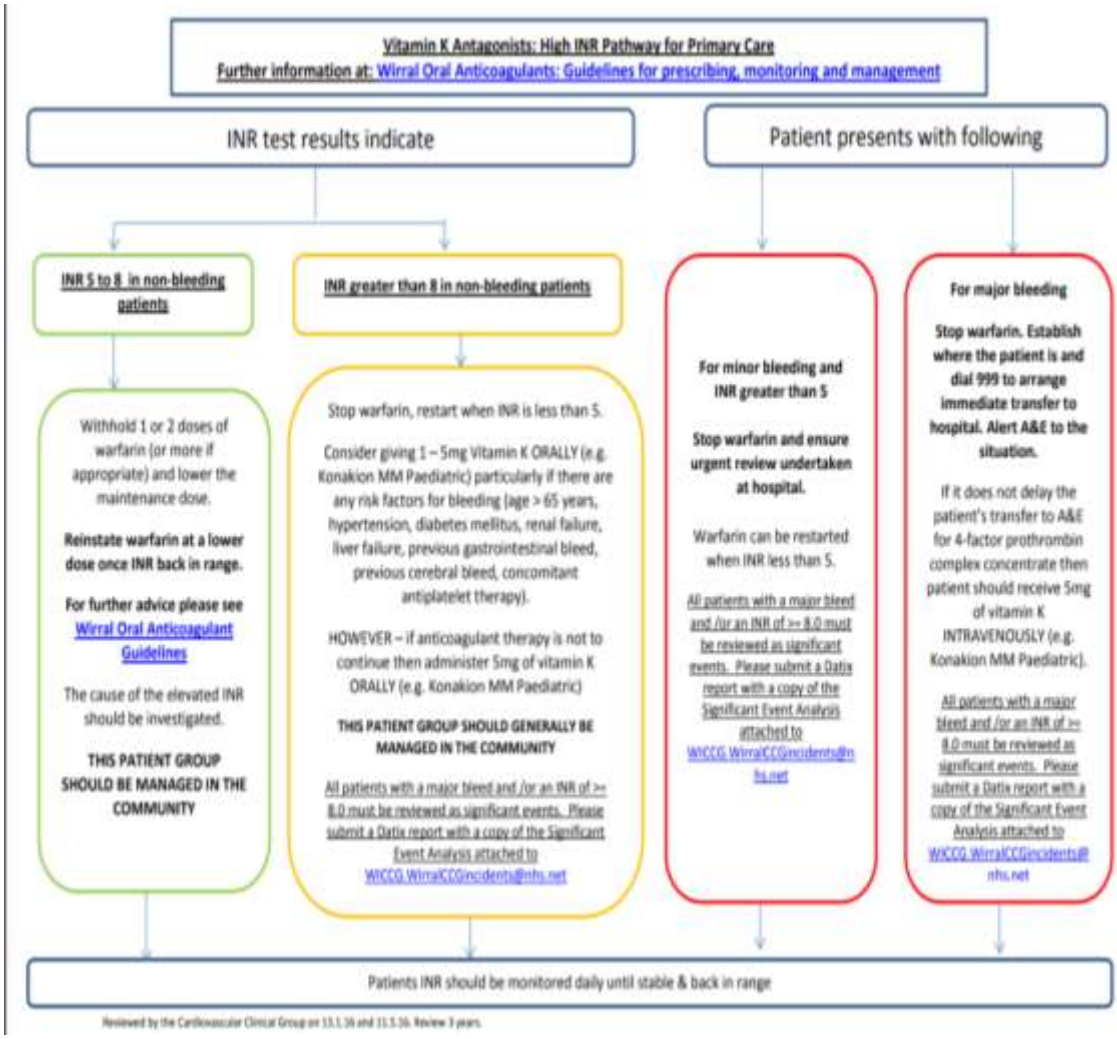


Figure 3:- High INR Treatment Pathway adapted (Mulholland & Lomas, 2018)

References:-

1. Neill L; Weygandt L. (2018). Supratherapeutic INR. Retrieved June 2022, from https://www.nuemblog.com/blog/supratherapeutic-inr
2. Claire, T., Hilary, W., Cindy, S., & Doson, C. (2017, june). Management of Supratherapeutic International Normalized Ratio without Bleeding after Warfarin Use: An Evaluation of Vitamin K Administration (SUPRA-WAR-K Study). Retrieved July 15th, 2022, from Management of Supratherapeutic International Normalized Ratio without Bleeding after Warfarin Use: An Evaluation of Vitamin K Administration (SUPRA-WAR-K Study): https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5491196/
3. David A. Garcia; Mark A. Crowther. (2012). Reversal of warfarin. Retrieved June 2022, from https://www.ahajournals.org/doi/10.1161/circulationaha.111.081489
4. Farinde, A. (2019, April). Warfarin Overanticoagulation. Retrieved from Medscape: https://emedicine.medscape.com/article/2172018-overview#a1
5. J, N. E. (2013, December). Explanation of Vitamin K cycle . Retrieved July 15th, 2022
6. Mulholland, S., & Lomas, P. (2018, october). Oral Anticoagulants (VKA and NOAC) Guidelines for prescribing, monitoring and management. Retrieved July 2022, from NHS Foundation Trust - Wirral University Teaching Hospital: http://mm.wirral.nhs.uk/document_uploads/guidelines/Anticoagulant(oral)Therapy-Prescribingguidelinesv2.pdf
7. Nayanika, S. (2022, April). Coagulation Cascade. Retrieved July 15th, 2022, from TeachmePhysiology.com: http://www.teachmephysiology.com/immune-system/haematology/coagulation
8. NICE Guidelines. (2022, May). NICE> CKS> Anticoagulation - oral> Scenario: Warfarin. Retrieved July 15th, 2022, from NICE GUIDELINES: https://cks.nice.org.uk/topics/anticoagulation-oral/management/warfarin/
a)