Case Report

Warfarin Toxicity

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ABSTRACT

Warfarin is an oral anticoagulant coming under coumarin derivatives. It is used to treat and prevent blood clots in veins or arteries which reduces the risk of stroke or any other serious conditions. Oral anticoagulants are used commonly these days to control IHD. A major complication of warfarin toxicity is bleeding like hematuria, vaginal bleeding, nose bleeding, gingival bleeding, etc. Warfarin has a narrow therapeutic index so there are chances that overdosing can occur leading to an increase in the risk of bleeding, along with other co-morbidities is to be considered. We are discussing about a case regarding warfarin toxicity having a history of CVT, Hypertension, and diabetes.

Keywords: Warfarin, anticoagulant, warfarin toxicity, overdosing.

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INTRODUCTION

Warfarin is an oral anticoagulant coming under coumarin derivatives. It is used to treat and prevent blood clots in veins or arteries which reduces the risk of stroke or any other serious conditions. Oral anticoagulants are used commonly these days to control IHD. Warfarin acts by inhibiting the vitamin K-dependent coagulation factors. An ideal anticoagulant should be rapid-acting, potent, safe, easy to administer, resistant to food-drug interactions, and affordable. Due to its narrow therapeutic index warfarin tends to be causing toxicity.[8] Generally, warfarin is used for conditions like heart valve disease, Coronary artery disease, Atrial Fibrillation, Pulmonary Thromboembolism, Deep vein thrombosis, Ischemic Cerebrovascular Disease, Peripheral Artery Disease, Polycythemia Vera etc. A major complication of warfarin toxicity is bleeding like hematuria, vaginal bleeding, nose bleeding, gingival bleeding, etc. We are discussing about a case regarding warfarin toxicity having a history of CVT, Hypertension, and diabetes.

Case Summary

A 53-year-old male was admitted with complaints of bleeding PR for 4 days (2-3 episodes/day). Patient was a known case of CVT with C1 spinal (paravertebral abscess); Hypertension; Diabetes Mellitus 2 and was prescribed Tab Warfarin 5 mg once a day; Tab Metformin 500mg 0-1-1; Tab Fluconazole 150 mg; Tab Atorvastatin 40 mg 1 HS; Tab Aspirin 75mg ODPC; Tab Amlodipine 5 mg 2 OD; Tab Losartan 50 1-0-1; Inj. Glargine 12 U at 10 pm, three days before the complaints started.

The patient is a chronic tobacco chewer;3-4 packs/day for 10 years. The PT was >Max on day 1, Urea - 83, S. cr.-2.50, and 2 pints of PCV transfused for 2 days and immediate treatment was Inj. Vit. K, Inj. Tranexamic acid, Inj. Hemacel 1 pint.

Drug	Dose, Route & Frequency	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day10	Day 11	Day 12
Inj. Ciprofloxacin	2 Pints I.V 12 hrly	√	√	√	√	√	√	√	√	√	√	-	-
Inj. Vitamin K	1 amp IV OD	√	√	√	√	-	-	-	-	-	-	-	-
Inj FFP	4 pint IV stat	√	√ 2 pint	√ 3 pint	-	-	-	-	-	-	-	-	-
Inj. PCV	2 pint with inj lasix cover	√	√ 1 pint	√ 1 pint	√	√	-	-	-	-	-	-	-

Inj. Tranexamic Acid	1 amp iv 8 hourly	√	√	√	√	√	√	√	√	√	√	√	√
Inj. Plain Insulin	Acc. to 5 times RBS charting	√	√	-	-	-	-	-	-	-	-	-	-
Inj. Pantop/Emset	40mg/4mg 1 pint in 100 ml NS	√	√	√	√	√	-	-	-	-	-	-	-
Inj. Optineuron	1 amp in 100 ml NS	√	√	√	√	√	√	√	√	√	√	√	√
Inj. Hemacel	1 amp iv 12 hourly	√	√	√	-	-	-	-	-	-	-	-	-
Inj. Calcium Gluconate	2 amp in 100 ml NS	-	√	-	-	-	-	-	-	-	-	-	-
Inj. Glargine	8 U SC @ 10 pm	-	√	√	√	√	√	√	√	√	√	√	√
Inj. Tramadol	1 amp in 100 ml NS 12 hrly	-	-	√	√	√	√	√	√	√	√	-	-
Inj. Avil / hydrocort	1 amp IV stat	-	-	√	-	-	-	-	-	-	-	-	-
Inj. Augmentin	1.2 gm IV 8 hrly	-	-	-	√	√	√	√	√	√	√	√	√
Inj. Iron sucrose	2 amp diluted 12 hrly	-	-	-	-	√	√	√	√	-	-	-	-
Tab folic acid	5 mg OD	-	-	-	-	√	√	√	√	√	√	√	√
Syp laxose	30 cc with ½ glass water	-	-	-	-	√	√	√	-	-	√	√	√
Tab. Vitamin c	500 mg tds	-	-	-	-	-	-	-	-	√	√	√	√
Tab warf	2 mg @ 4 pm	-	-	-	-	-	-	-	-	-	√	-	-
INJ DNS/NS	8 hrly	-	-	-	-	-	-	-	-	-	-	√	-

Date	17/2	20/2	21/2	25/2	1/3
Urea	83	93	73	73	38
Creatinine	2.5	2.8	2.46	2.46	2.41
Bile (T)	-	0.8	-	-	-
Bilirubin (D)	-	0.3	-	-	-
Bilirubin (I)	-	0.5	-	-	-
Sodium	-	132	131	131	127
Potassium	-	5.8	5.10	5.1	4.6
Hb	-	3.9	-	7.7	8.53
RBC	-	-	-	-	3.52
TC	-	6700	-	9260	8800
N/L/E/M	-	-	-	-	74/14/5/4
PC	-	2.78 L	-	2.90 L	4.52 L
MCV	-	67	-	-	77.5
MCH	-	24.80	-	-	24.2
MCHC	-	36.80	-	-	31.24
PCV	-	10.70	-	-	27.31
RDW	-	-	-	-	96.7
PT/INR	13.8/0	13.6/1.027	13.5/0.96	12.30/0.95	13.3/1.36
APTT	82.4	30.8	31.2	-	25
APTT (Control)	27.30	33.5	33.5	-	32.8

DAY	DAILY PROGRESS
DAY 1	Adv on admission pt/inr, apt. 2pint PCV and 4 pint FFP- urgently; Surgery ref; no IM Injection, w/f bleeding; RD/ADD/SRD
DAY 2	Transferred to ICU, No pedal oedema, Pallor ++, Nominal Aphasia, U R/M, Repeat PT/INR
DAY 3	BP: 106/70; PR:88 bpm; stool: passed hematochezia 4 times approx. 200 ml, sent for surgical reference for profusely bleeding PR; Adv: T. Ciplox, T. Metro, T. Paracetamol, T. MVBC/Fe/Vit. C, Lignocaine jelly,
DAY 4	BP: 130/80; PR:100 bpm CBC,PT/INR,APTT,APTT Control, MRI Venography, Surgical Reference for pus discharge in foot, RFT
DAY 5	BP: 120/80; PR:80 bpm
DAY 6	BP: 120/80; PR:89 bpm; Neuro-surgery reference for infective debris
DAY 7	BP: 110/70; PR:78 bpm
DAY 8	BP: 120/80; PR:94 bpm; CBC, PT/INR, Neurophysician reference, RFT, Na+, K+, APTT
DAY 9	BP: 120/80; PR:98 bpm; CBC, PT/INR, Neurophysician reference, RFT, Na+, K+, APTT, stool occult blood
DAY 10	BP: 120/80; PR8:78 bpm; stool occult blood; Neurosurgery opinion- ENT opinion, No active neurological intervention, neurophysician opinion for VST(sub-acute); surgical review reference
DAY 11	BP: 130/80; PR:98 bpm; colonoscopy, ENT ref for MRI changes- no abnormality in eyes, nose: NAD; Ear: right-intact, left-debris; tab amoxiclav 625 mg 1 bd x 5 days, tab PCM, Tab. CPM, Tab FMT, Betadine gargles
DAY 12	BP: 130/80; PR:89 bpm; Plan D

Diagnostic Investigations	Result
USG	Hepatomegaly, Mild Fatty changes.
MRI of Brain	Multifocal small lesion of cytotoxic edema in bilateral centrum semiovale, extending into bilateral capsulo-ganglionic regions. Possibility of embolic infarcts is likely. Abnormal debris layer in occipital horns of bilateral lateral ventricles. Possibility of infective debris is likely. Advice: contrast study for evaluation of ventriculitis. Focal abnormal marrow signal intensity lesion in marrow of clivus, anterior arch of C1 & C2 vertebrae. It is extending as abnormal anterior epidural soft tissue at the level of cranio-vertebral junction causing moderate narrowing of spinal canal and bilateral neural foramina abutting bilateral exiting nerve roots. It is extending in pre-paravertebral soft tissues. Possibility of infective etiology is likely. Complete subacute thrombus in left transverse-sigmoid sinus and left jugular bulb.
HBsAg	Negative
HCV Rapid	Negative
Culture & sensivity	sample: Pus Resistant to gentamicin, Levofloxacin, meropenem, Cefepime, ceftriaxone, Piperacillin/Tazobactam, Doxycycline Sensitive to Polymyxin B
Occult blood	Present ++

DISCUSSION

We are discussing a 53-year-old male with a history of CVT who was on T. Warf 5 mg once a day and came back afterward with complaints of PR bleeding from 4 days after starting warfarin with PT/INR 13.8/0. In a 5-year retrospective study, nearly 48.8% of ADRs were due to medication errors.[1] This case can be considered an accidental overdosing due to misjudgment in dosing for this patient, initially starting with a lower dose, should be considered instead of starting with a higher dose.

Warfarin is considered a high alert medication due to its risk of bleeding. According to from published studies, the incidence of major bleeding is around 0.4-7.2% and minor bleeding is 15%.[1]An anticoagulant is to be prescribed after checking laboratory tests, coagulation profile, a renal function which includes patient INR on 24 hourly basis. Warfarin has a narrow therapeutic index so there are chances that overdosing can occur leading to an increase in the risk of bleeding, along with other co-morbidities is to be considered.

Warfarin works by inhibiting Vit. K epoxide reductase complex I which inhibits the synthesis of clotting factors II, VII, IX & X eventually. The onset of action is within 24-72 hours with almost 100% bioavailability due to high protein binding capacity.[4] According to a study the occurrence of drug reactions after warfarin was prescribed was 16.9% of that population had rectal bleeding and 14.6% had hematuria which is quite high in a population of 89 patients. This study also resulted in concluding that 22.5% of patient had a history of warfarin overdose along with Aspirin use was 39.3%.[2] So this study implies that warfarin along with another anti-coagulants might exacerbate bleeding complications. Bleeding complications are associated with aged population, presence of previous warfarin overdose history, concomitant drug use, the intensity of

anticoagulation, level of INR, anti-platelet use and other co-morbidities [3,5,8]

Warfarin is chosen over other anti-coagulants because data is lacking for long-time studies and there are no treatment options for sudden trauma or bleeding for other anti-coagulants, along with that it is cheaper than the newer anticoagulants. In these circumstances, dosing considerations should be implemented. A clinical pharmacist should review medication to reduce drug interactions, drug duplications & many drug-related aspects. [9]Current approach to warfarin-related bleeding is discontinuation use of warfarin and IV Vit. K, FFP & Erythrocyte suspension treatment which is done in this case.[6]

CONCLUSION

In the present scenario, oral anticoagulants are widely used. Regular use of the drugs and close follow-up of the bleeding profile is of great importance. Therefore, it is crucial to enlighten patients and their relatives thoroughly about the adverse effects of these drugs. Since warfarin has a narrow therapeutic window and has been associated with many drug-drug and drug-food interactions, patient counselling is crucial. Initiation and management of warfarin therapy is commonly tough. Guidelines are developed to help the clinician to determine target ranges for therapeutic success. Additionally, methods for speedy anti-coagulation and management of supratherapeutic INR values are delineated within the literature. Daily practice according to these guidelines ought to create the management of patients easier once warfarin therapy is needed

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