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ANALYSIS OF MANAGEMENT OF ORAL ANTICOAGULATION THERAPY AFTER GASTROINTESTINAL BLEEDING: A TRANSLATIONAL STUDY

[1]Dr. Hafsa, [2]Dr. Tayyab Mahmood Ali, [3]Dr. Mafia Akbar
[1]Woman Medical Officer at RHC Pir Mahal, Toba Tek Singh
[2]Medical officer at RHC Khudian Khas, Kasur
[3]Woman Medical Officer at RHC Khudian Khas, Kasur

Abstract:
Introduction: *Antithrombotic agents, which include antiplatelet agents and anticoagulants, are increasingly used in Asia. Management of patients on antithrombotics undergoing emergency or elective gastrointestinal (GI) endoscopy has become a common and important clinical challenge.* ***Objectives of the study:*** *The basic aim of the study is to explore and analyze the different management methods of oral anticoagulation therapy after gastrointestinal bleeding.* ***Methodology of the study:*** *This study was done basically by analyzing different management methods of oral anticoagulation therapies which were used after gastrointestinal bleeding. For this purpose, we collected the data from different hospitals of Pakistan from different age groups for analyzing different oral anticoagulation techniques. The data was collected during 2017 from both genders. For data collection we visit the different hospitals and collect both demographical data and collect the views of patients after GIT bleeding. Then we further analyze this data by using MS excel and find the different values.* ***Results:*** *In critical patients who are actively bleeding with persistent or intermittent haemodynamic instability, coagulation factors should be administered even in the case of therapeutic ranges. If the patient is haemodynamically stable and/or responds sufficiently to resuscitation, it is advisable to simply observe the patient closely and defer endoscopy.* ***Conclusion:*** *We do not recommend bridging anticoagulation therapy in patients with low thromboembolic risk. Another issue is the timing of anticoagulant resumption in patients with clinically significant GI haemorrhage and no source of bleeding identified at endoscopy.*

Corresponding author:
Dr. Hafsa,
Woman Medical Officer at RHC Pir Mahal,
Toba Tek Singh

QR code

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INTRODUCTION:

Antithrombotic agents, which include antiplatelet agents and anticoagulants, are increasingly used in Asia. Management of patients on antithrombotics undergoing emergency or elective gastrointestinal (GI) endoscopy has become a common and important clinical challenge[1]. While practice guidelines have been developed by GI and endoscopy societies in the USA, Europe and the UK, it was uncertain whether they should be fully adopted in the Asian Pacific region. In September 2015 the Asian Pacific Association of Gastroenterology (APAGE) and the Asian Pacific Society for Digestive Endoscopy (APSDE) appointed KS and FKLC to form an ad hoc working group to evaluate current practice guidelines on the management of patients on antithrombotics undergoing GI endoscopy [2].

The burden of oral anticoagulants has also been recently broadened by the introduction of new oral anticoagulants, also named direct oral anticoagulants (DOACs), which directly inhibit either thrombin or the activated coagulation factor X. DOACs have been approved in Europe as alternatives to VKAs for preventing strokes and embolic events in patients with non-valvular AF, for thrombo-prophylaxis after major orthopaedic surgery and for the prevention/treatment of deep venous thrombosis and pulmonary embolism[3]. Another direct inhibitor of the activated coagulation factor X is currently under regulatory review in Europe. These agents, who are characterized by a predictable anticoagulant effect at fixed doses, overcome some of the VKAs pitfalls such as their narrow therapeutic window, the need for frequent monitoring and dose adjustments as well as the interaction with foods and/or other drugs [4].

Acute GI bleeding in patients taking anticoagulants raises several difficulties related to the balance between thrombotic risks, associated with drug discontinuation or reversal, and haemorrhagic risks[5]. Gastroenterologists who manage such patients have largely varying attitudes and an overall scarce knowledge of this topic as recently reported in a national Italian survey. This might be related to several factors, such as the paucity of studies addressing the issue of acute GI bleeding in anticoagulated patients and the absence of RCTs comparing different management strategies. Moreover, practice guidelines by GI professional societies only marginally address this topic as they mostly focus on the management of anticoagulants in patients undergoing elective procedures [6].

Proposed management method

Objectives of the study

The basic aim of the study is to explore and analyze the different management methods of oral anticoagulation therapy after gastrointestinal bleeding.

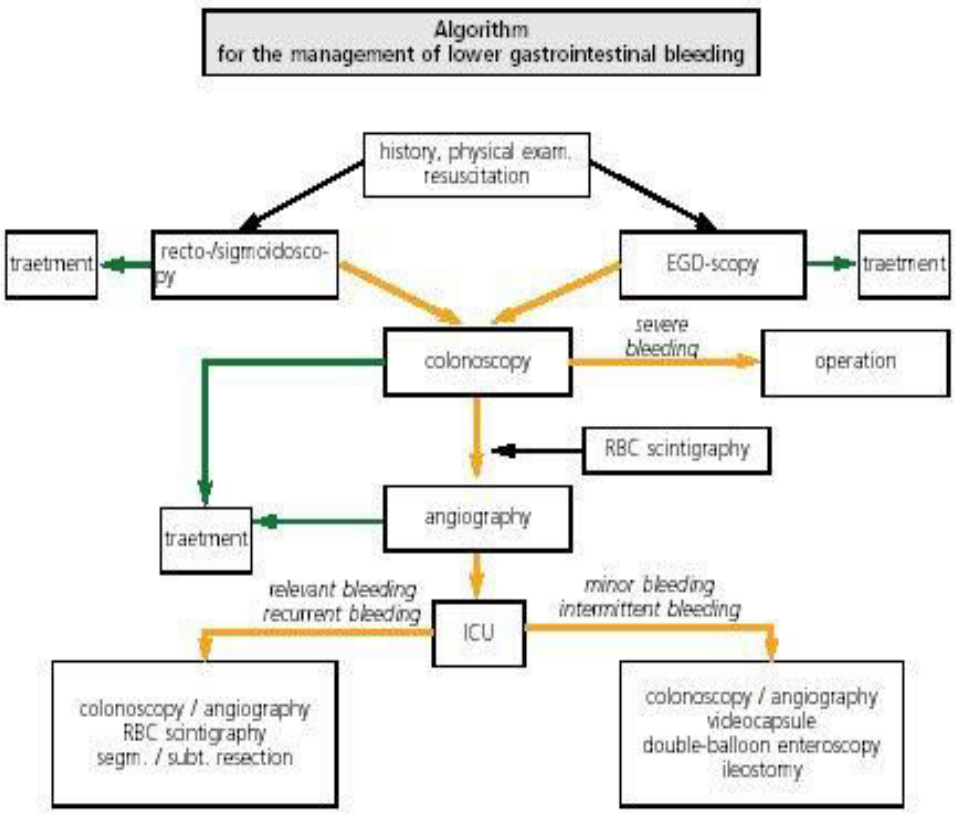
Methodology of the study

This study was done basically by analyzing different management methods of oral anticoagulation therapies which were used after gastrointestinal bleeding. For this purpose, we collected the data from different hospitals of Pakistan from different age groups for analyzing different oral anticoagulation techniques. The data was collected during 2017 from both genders. For data collection we visit the different hospitals and collect both demographical data and collect the views of patients after GIT bleeding. Then we further analyze this data by using MS excel and find the different values.

RESULTS:

Timing of endoscopy

First of all, we find the time of endoscopy because it depends either it takes less time or more time. Considering the recognized benefits of early endoscopy in acute upper GI bleeding, various authors have recommended that endoscopy should not be postponed to correct coagulopathy in patients with an international normalized ratio ≤2.5. In patients with supra-therapeutic INR values, endoscopy should preferably be postponed until the coagulopathy is partially or completely reversed[7].



In critical patients who are actively bleeding with persistent or intermittent haemodynamic instability, coagulation factors should be administered even in the case of therapeutic INR ranges and 4F-PCC rather than FFP should be used. If the patient is haemodynamically stable and/or responds sufficiently to resuscitation, it is advisable to simply observe the patient closely and defer endoscopy for 12–24 h, thus allowing for drug clearance and normal haemostatic functions to resume. The theoretical advantage of this approach is that endoscopic therapy may be easier and safer to perform in a patient who is not fully anticoagulated [8].

Conversely, for actively bleeding patients with persistent or intermittent haemodynamic instability, emergent endoscopy may be appropriate. In this case, the use of non-specific pro-haemostatic agents to accelerate anticoagulation reversal may be considered. Practice guidelines recommend the use of such reversal agents in patients with life-threatening bleeding but no reversal strategy for DOACs has yet been validated. In a recent survey among haematology specialists on current DOACs reversal practices, factor concentrates (activated PCCs and rFVIIa) were prescribed in 41% of dabigatran-associated bleedings [9].

DISCUSSION:

To date, four DOACs including dabigatran, apixaban, rivaroxaban and edoxaban have been approved by the FDA and are available in many countries in the Asia. Unlike vitamin K antagonists, DOACs are direct inhibitors of factor thrombin (dabigatran) and factor Xa (apixaban, rivaroxaban, edoxaban). This new class of anticoagulants has a rapid onset (1–4 hours) and offset of action (about 24 hours). However, drug elimination is prolonged in patients with reduced renal clearance[10]. Dabigatran is mostly eliminated by the kidneys (~80%), edoxaban has 50% of the dose undergoing renal elimination, whereas rivaroxaban (~33%) and apixaban (~25%) are less affected by renal impairment. To date, there is limited information on the management of patients with MHV and GI bleeding. With respect to anticoagulation reversal, ACC/AHA guidelines issued in 2008 raised some concerns on the safety of administering PCC due to potential thromboembolic complications, including valve thrombosis, as well as high-dose (5–10 mg) IV vitamin K due to potential "warfarin resistance". Low-dose (1–2.5 mg) IV vitamin K combined with FFP was recommended in the case of major bleeding. However, there is no evidence that bleeders with or without MHV should be treated differently; accordingly, the updated

ACC/AHA guidelines recommend PCC as a reasonable alternative to FFP when urgent reversal is required[11]. With respect to VKAs resumption, MHV patients should be considered at high risk of thromboembolic complications. In particular, prolonged anticoagulation withdrawal is a major risk factor for prosthetic valve thrombosis, a serious complication associated with significant morbidity and mortality. Hence, it might be advisable to resume VKAs early in the second week (ideally on day 7) considering heparin bridge therapy until INR reaches the therapeutic level. For MHV patients at highest thrombotic risk (mitral MHV, multiple MHVs, MHV with prior stroke or AF, and MVH implanted within 6 months) a potential role for heparin bridge therapy starting 72 h after endoscopy may be advocated, provided that the haemostasis is established and the risk of rebleeding is low [12].

CONCLUSION

We do not recommend bridging anticoagulation therapy in patients with low thromboembolic risk. Another issue is the timing of anticoagulant resumption in patients with clinically significant GI haemorrhage and no source of bleeding identified at endoscopy. In these patients, the timing should be decided based on estimates of the individual risks of rebleeding and thrombosis.

Recommendations

1. We do not recommend platelet transfusion because it does not improve the clinical outcome of patients on antiplatelet agents.
2. We recommend early resumption of aspirin, preferably within 3–5 days after endoscopic haemostasis.

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