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Drug-Induced Bleeding Of The Upper Gastrointestinal Tract

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ABSTRACI

Upper gastrointestinal bleeding (UGIB) is a significant medical disorder that can be brought on by a variety of things, including medications. An adverse event resulting in UGIB as a consequence of the use of certain medications can cause significant illness and impermanence in patients. This article sets out to offer an overview of the most commonly prescribed drugs that are associated with UGIB as well as their mechanism of action so that they can be better understood

Keywords:

Upper gastrointestinal, medications,

1. Introduction

- What is upper gastrointestinal bleeding (UGIB)?
- Cause and effects (symptoms)?
- Consequences?
- ➤ Motivation? Why this topic?
- Literature review?

2. Non Steroidal Anti Inflammatory Drugs (NSAIDs)

A non steroidal-anti inflammatory drug (NSAID) comes under a class of most popular therapeutic medicines that are widely used for reducing pain, inflammation, fever, and intercepting blood clots, such as spirin, ibrofen, naproxen, diclofenac, celecoxib (like Celebrex), and much more are the most commonly used NSAIDs. From the observations made over the last many decades, it is concluded that the use of NSAIDs has a major link to the development of UGIB conditions. NSAIDs work by inhibiting certain enzymes, specifically known as cyclooxygenase (COX) enzymes, that engender prostaglandins. A prostaglandin is a hormone-like substance that affects several organ functions, including

inflammation, pain, and contractions of the uterus. However, as part of the systemic defense against gastric ulcers, there are several mechanisms by which prostaglandin plays a crucial role, for instance, motivating the mucal discharge and bi-carbonate, increasing blood flow to the mucosa, and inhibiting acid secretion are among them. When COX enzymes are inhibited by NSAIDs, the production of prostaglandin is reduced, and the result is damage to the mucosa of the stomach, ulceration, and the condition of UGIB [1-2]. Based on a meta-analysis of randomized controlled trials (RCTs), it is concluded that the

controlled trials (RCTs), it is concluded that the use of NSAIDs nearly triples the risk of UGIB compared to placebo treatment or no treatment (odds ratio [OR] 2.78, 95% CI 2.00–3.86) [3-5]. A number of additional diseases, such as peptic ulcer disease, Helicobacter pylori infection, or concurrent use of anticoagulants and corticosteroids, enhance the risk of developing UGIB despite long-term NSAID use [4]

3. Anticoagulant And Antiplatelet Drugs

Anticoagulants. commonly called blood thinners, are chemical substances that prevent or diminish the coagulation rate of blood. Anticoagulant agents shut out swift blood curdling since they impede clotting factors, like fibrinogen, prothrombin, thromboplastin. calcium, proaccelerin, and nine more, thus. in turn prolonging the clotting duration. They are usually given to people at high risk of developing serious conditions such as strokes and heart attacks. However, it is common for anticoagulants to cause UGIB because taking anticoagulant drugs inhibits the abovementioned clotting factors in the cascade of coagulation, thereby when taken in the presence of other anticoagulants and gives birth to a medical condition called 'hemostasis' (increased bleeding risks). Note that warfarin and heparin are two of the most common anticoagulants associated with UGIB [5, 6]. Warfarin is a medication that is frequently recommended to stop the cascade of blood coagulation from growing and expanding in the blood vessels. On the other hand, heparin (or unfractionated heparin) is a medication that depends on the working of antithrombin and is specifically prescribed for the treatment of heart diseases and unstable angina. Based on many observations and studies, it is, thus, deduced that the blood clotting disorder caused anticoagulants can lead to upper gastrointestinal bleeding (UGIB) caused by impaired clotting mechanisms. Based on a systematic review and meta-analysis observational studies, anticoagulant drugs are associated with a twice increase in UGIB risk (odds ratio [OR] 2.20, 95% CI 1.80-2.70) [7]. In addition, the endoscopic history of UGIB shows that the individuals who in-take the antiplatelet drugs concomitantly also have a high chance of the condition [8-10]. Aspirin and clopidogrel are commonly used antiplatelet drugs that can cause UGIB. They inhibit platelet function, increasing bleeding risk. Aspirin prevents cyclooxygenase enzyme production in reduced thromboxane resulting production [9, 10]. Thromboxane A2, which is also known as a powerful platelet activator and comes under the thromboxane class, is released

during hemostasis and is associated with prothrombotic activities since it activates the initiation of platelets and stimulates platelet clotting. Likewise, clopidogrel activates platelets as a result of inhibiting the P2Y12 receptor. Platelet P2Y12 receptors (P2Y12Rs) for adenosine 5'diphosphate (ADP) play an important role in hemostasis, blood clotting, and thrombosis [11]. In the upper gastrointestinal tract, antiplatelet drugs impair platelet function and inhibit clot formation, increasing the risk of UGIB.

4. Selective Serotonin Reuptake Inhibitors (SSRIs)

Selective serotonin reuptake inhibitors (SSRIs) are commonly used antidepressant drugs for various physiological disorders. For instance, the two most common disorders are anxiety and depression which are treated with SSRIs. To influence the level of serotonin in the synaptic these drugs prevent reabsorption in the brain. This ultimately leads to an increase in serotonin concentration. It is important to note, however, that SSRIs can also lead to UGIB by inhibiting serotonin uptake in the gastrointestinal tract [12, 13]. Serotonin, which naturally increases the secretion of mucus and bicarbonate, is a crucial element in maintaining the health of the gastrointestinal mucosa. This is done by stimulating mucus and bicarbonate secretion and mucosal blood flow. When SSRIs inhibit serotonin uptake in the gastrointestinal tract, mucus and bicarbonate production are reduced. This results in gastric mucosal damage, ulceration, and UGIB [14, 15].

5. Conclusion

conclusion, drug-induced upper gastrointestinal bleeding is a potentially serious adverse reaction that may occur as consequence of several commonly prescribed medications. NSAIDs, anticoagulants, antiplatelet medicines are among the most often mentioned medications. The risk of UGIB with these drugs increases with age, the duration of use, and other risk factors. Strategies for preventing and controlling drug-induced UGIB include gastroprotective agents, dose reduction, drug substitution, and close monitoring of

patients. Healthcare professionals should be aware of the risk of drug-induced UGIB and take appropriate measures to prevent and manage this potentially life-threatening complication.

References

- Cook, D. J., Fuller, H. D., Guyatt, G. H., Marshall, J. C., Leasa, D., Hall, R., ... & Willan, A. (1994). Risk factors for gastrointestinal bleeding in critically ill patients. New England journal of medicine, 330(6), 377-381.
- 2. Barkun, A. N., Bardou, M., Kuipers, E. J., Sung, J., Hunt, R. H., Martel, M., ... & International Consensus Upper Gastrointestinal Bleeding Conference Group*. (2010). International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Annals of internal medicine, 152(2), 101-113.
- 3. Gutthann, S. P., GarcíaRodríguez, L. A., & Raiford, D. S. (1997). Individual nonsteroidal antiinflammatory drugs and other risk factors for upper gastrointestinal bleeding and perforation. Epidemiology, 8(1), 18-24.
- 4. Tielleman, T., Bujanda, D., & Cryer, B. (2015). Epidemiology and risk factors for upper gastrointestinal bleeding. Gastrointestinal Endoscopy Clinics, 25(3), 415-428.
- 5. Johnsen, S. P., Sørensen, H. T., Mellemkjær, L., Blot, W. J., Nielsen, G. L., McLaughlin, J. K., & Olsen, J. H. (2001). Hospitalisation for upper gastrointestinal bleeding associated with use of oral anticoagulants. *Thrombosis and haemostasis*, 86(08), 563-568.
- 6. Cerini, F., Gonzalez, J. M., Torres, F., Puente, Á., Casas, M., Vinaixa, C., ... & Garcia-Pagán, J. C. (2015). Impact of anticoagulation on uppergastrointestinal bleeding in cirrhosis. A retrospective multicenter study. *Hepatology*, 62(2), 575-583.
- 7. Lee, M. W., & Katz, P. O. (2021). Nonsteroidal antiinflammatory drugs, anticoagulation, and upper

Further research is needed to develop more effective strategies for treating and managing drug-associated UGIB and to identify new drugs that may increase UGIB risk.

- gastrointestinal bleeding. *Clinics in Geriatric Medicine*, 37(1), 31-42.
- 8. Ibanez, L., Vidal, X., Vendrell, L., Moretti, U., Laporte, J. R., & SPANISH-ITALIAN COLLABORATIVE GROUP FOR THE EPIDEMIOLOGY OF GASTROINTESTINAL BLEEDING. (2006). Upper gastrointestinal bleeding associated with antiplatelet drugs. Alimentary pharmacology & therapeutics, 23(2), 235-242.
- 9. Lanas, A., & Scheiman, J. (2007). Low-dose aspirin and upper gastrointestinal damage: epidemiology, prevention and treatment. *Current medical research and opinion*, *23*(1), 163-173.
- 10. Fletcher, E. H., Johnston, D. E., Fisher, C. R., Koerner, R. J., Newton, J. L., & Gray, C. S. (2010). Systematic review: Helicobacter pylori and the risk of upper gastrointestinal bleeding risk in patients taking aspirin. *Alimentary pharmacology & therapeutics*, 32(7), 831-839.
- 11. Liberopoulos, E. N., Elisaf, M. S., Tselepis, A. D., Archimandritis, A., Kiskinis, D., Cokkinos, D., & Mikhailidis, D. P. (2006). Upper gastrointestinal haemorrhage complicating antiplatelet treatment with aspirin and/or clopidogrel: where we are now?. *Platelets*, *17*(1), 1-6.
- 12. de Abajo, F. J., Rodríguez, L. A. G., & Montero, D. (1999). Association between selective serotonin reuptake inhibitors and upper gastrointestinal bleeding: population based case-control study. *Bmj*, 319(7217), 1106-1109.
- 13. Anglin, R., Yuan, Y., Moayyedi, P., Tse, F., Armstrong, D., & Leontiadis, G. I. (2014). Risk of upper gastrointestinal bleeding with selective serotonin reuptake inhibitors with or without concurrent nonsteroidal anti-inflammatory use: a systematic review and meta-analysis. Official journal of the American

- College of Gastroenterology | ACG, 109(6), 811-819.
- 14. Rahman, A. A., He, N., Rej, S., Platt, R. W., & Renoux, C. (2022). Concomitant use of selective serotonin reuptake inhibitors and oral anticoagulants and risk of major bleeding: a systematic review and meta-analysis. *Thrombosis and Haemostasis*.
- 15. Alam, S. M., Qasswal, M., Ahsan, M. J., Walters, R. W., & Chandra, S. (2022). Selective serotonin reuptake inhibitors increase risk of upper gastrointestinal bleeding when used with NSAIDs: a systemic review and meta-analysis. *Scientific Reports*, 12(1), 14452.