

EVALUATION OF LOWER GASTROINTESTINAL BLEEDING RISK ASSOCIATED WITH USE OF LOW DOSE ASPIRIN

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Abstract: To evaluate risk of aspirin related lower gastrointestinal bleeding a Prospective study was performed at Department of medicine, Nishtar Hospital, Multan from July 2019 to January 2020. A total of 372 patients using low dose aspirin were selected from out-patient department of Medicine. All patients underwent diagnostic laboratory test for stool examination. A consultant pathologist confirmed the presence or absence of lower gastrointestinal bleeding. Data including age, gender, history of bleeding per rectum, blood on stools, BMI, duration of aspirin use, and reason for aspirin prescription was recorded. The study was conducted on 372 patients, 120 (32.3%) were female while 252 (67.7 %) were male. The mean age of the patients was 40 years. Mean duration of use of low dose aspirin was 22.23 ± 16.59 months. Lower gastrointestinal bleeding was noted in 81 (21.8%). Use of dose aspirin is significantly associated with lower gastrointestinal bleeding. Clinicians must anticipate adverse effects in such patients.

Keywords: Low dose aspirin, extracranial bleeding, gastrointestinal bleeding

Introduction

Low dose aspirin has been effective in preventing primary and secondary cardiovascular events (CV); however, it significantly increases the risk of bleeding events (García Rodríguez et al., 2016). Aspirin is widely used anti inflammatory, analgesic and antipyretic drug (Zhang et al., 2022). Aspirin also irreversibly inhibits eicosanoid production, thus exhibiting anti platelet activity (Knowles and Warner, 2019). Due to this property it can prevent cardiovascular events such as transient ischemic attack, myocardial infarction and stroke (Sugawara et al., 2019). However, its use is associated with various harmful effects most prominent of which is extracranial bleeding risk, particularly gastrointestinal (GI) bleeding (Wang et al., 2020). Aspirin is majorly beneficial for secondary prevention of CV events and has fewer benefits for primary prevention (Joseph et al., 2021). Thus in new clinical guidelines it is recommended that balance between risk and benefits of aspirin must be assessed on individual basis (Joseph et al., 2021). Some studies that report that lose dose of aspirin pose higher risk of GI bleeding (Chen et al., 2017; Lanas et al., 2015). A study conducted by Whitlock et al., showed that use of low dose aspirin is associated with 58% increased risk of major GI bleeding and 27% risk of hemorrhagic stroke (Whitlock et al., 2016). Another study reported prevalence of aspirin associated GI bleeding to be 41% (Hreinsson et al.,

2013). There is scarcity of research on risk of lower GI bleeding associated with use of low dose aspirin in local setup. Therefore, the aim of this study is to evaluate the risk of aspirin related lower gastrointestinal bleeding.

Methodology

The prospective study was conducted in the Department of Medicine, Nishtar Hospital from July 2019 to January 2020. The study included patients aged between 18 to 65 years who had cerebrovascular or cardiovascular disease and who used low dose aspirin regularly. Those with history of liver disease, bleeding disorder, malignant tumor of GI tract and those using anti coagulant drugs like warfarin or clopidogrel were excluded. Informed consent of the patients was recorded. The Ethical Board of hospital approved study conduction.

A total of 372 patients using low dose aspirin were selected from the outpatient department of Medicine. All patients underwent diagnostic laboratory test for stool examination. A consultant pathologist confirmed the presence or absence of lower gastrointestinal bleeding. Data including age, gender, history of bleeding per rectum, blood on stools, BMI, duration of aspirin use, and reason for aspirin prescription was recorded SPSS version 23.0 was used for data analysis. Numerical variables such as

age, BMI and duration of aspirin use were presented as standard deviation and mean. Categorical variables such as gender and presence or absence of lower gastrointestinal bleeding were presented frequency and percentage. Stratification was done to control effect modifier such as gender, age, BMI and reason and duration of aspirin use. Post stratification chi square test was used. P-value ≤ 0.05 was considered statistically significant.

Results

The study was conducted on 372 patients, 120 (32.3%) were female while 252 (67.7 %) were male.

The mean age of the patients was 40 years. Mean BMI was 26.14 ± 1.98 kg/m². 59 (15.9 %) patients were obese. 165 (44.4 %) patients were hypertensive, and 94 (25.3%) patients were diabetic.

Mean duration of use of low dose aspirin was 22.23 ± 16.59 months and 260 (69.9 %) had duration of illness up to 2 years. Of these 372 study cases, 298 (80.1%) were taking aspirin due to cardiovascular diseases and 74 (19.9%) were taking due to stroke. Lower gastrointestinal bleeding was noted in 81 (21.8%) (Table I). Stratification regarding duration and reason for aspirin use was done. (Table II,III).

Table I: Distribution of lower gastrointestinal bleeding among study cases (n=372)

Lower Gastrointestinal bleeding	Frequency	Percentage
Yes	81	21.8
No	291	78.2
Total	372	100

Table II: Stratification of Lower gastrointestinal bleeding with regards to duration of use of low dose aspirin (n=372)

Duration	Lower gastrointestinal bleeding		P – value
	Yes (n=81)	No (n=291)	
Up to 2 Years (n=260)	25	235	0.000
More than 2 Years (n=112)	56	56	
Total	372		

Table III: Stratification of Lower gastrointestinal bleeding with regards to reason for use of aspirin (n = 372)

Reasons	Lower gastrointestinal bleeding		P – value
	Yes (n=81)	No (n=291)	
Cardiovascular diseases (n=298)	81	217	0.000
Stroke (n=74)	00	74	
Total	372		

Discussion

Lower gastrointestinal bleeding is common and makes up to 30% of total cases of GI bleeding. Its prevalence is higher in elder patients and those taking multiple drugs. 9% LGIB occurs in small intestine while 85% occurs distal to ileocecal valve. Remaining cases occur in upper GI tract. Patients present with bright red blood per rectum, brisk bleeding or melena. In current study, 252 (67.7 %) patients were male and 252 (67.7 %) were female. Similar results were reported by another study which comprised of 34.2% female and 67.5% male patients (Zia et al., 2021). Another study also reported

higher percentage of male patients (Ahmed et al., 2020). Thus, it can be concluded that gender is a risk factor for LGIB in users of low dose aspirin. In current study, mean age of patients was 52.91 ± 7.46 years, it indicates that majority 201 (54.0 %) patients were aged above 50 years. In another study mean age of the subjects was 49.6±7.0 years (e Hina et al., 2021). Another study conducted by Ahmed et al., mean age of the subjects was 54.89±11.35 years (Ahmed et al., 2020). These results are closer to the findings of our study. Mean BMI in current study is 26.14 ± 1.98 kg/m² and 94 (25.3%) patients were

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diabetic. Another study reported 29.5% subjects were diabetic (Zheng and Roddick, 2019), which is closer to results of our study. In our study, 165 (44.4 %) were hypertensive. A study conducted by Chen et al., reported hypertension in 34.1% patients (Chen et al., 2017). Another study reported frequency of hypertension to be 46% (Dasa et al., 2021). Thus, it can be said that hypertension is not associated with increased risk of LGIB in low dose aspirin users. In the current study, LGIB occurred in 81 (21.8%). A study conducted by Whitlock et al., showed that use of low dose aspirin is associated with 58% increased risk of major GI bleeding and 27% risk of hemorrhagic stroke (Whitlock et al., 2016). A study conducted by Garcia et al., reported frequency of LGIB in low dose aspirin users to be 41% (Garcia Rodriguez et al., 2019)

Conclusion

Use of dose aspirin is significantly associated with lower gastrointestinal bleeding. Clinicians must anticipate adverse effects in such patients.

Conflict of interest

The authors declared absence of conflict of interest.

References

- Ahmed, J., Alam, L., Shabbir, K., Naqvi, M., Haider, E., and Farooque, A. (2020). ENDOSCOPIC FINDINGS IN PATIENTS PRESENTING WITH UPPER GI BLEED IN A TERTIARY CARE FACILITY. *Pakistan Armed Forces Medical Journal*, 112.
- Chen, W. C., Lin, K. H., Huang, Y. T., Tsai, T. J., Sun, W. C., Chuah, S. K., Wu, D. C., and Hsu, P. I. (2017). The risk of lower gastrointestinal bleeding in low-dose aspirin users. *Alimentary Pharmacology & Therapeutics* **45**, 1542-1550.
- Dasa, O., Pepine, C. J., and Pearson, T. A. (2021). Aspirin in primary prevention: what changed? A critical appraisal of current evidence. *The American journal of cardiology* **141**, 38-48.
- e Hina, R., Mansoor, H., Bilal, K., Asghar, A., Ullah, M. A. S., and Zahid, T. R. (2021). Variceal Hemorrhage as the Commonest Cause of Presentation with Acute Upper Gastrointestinal Bleeding: A Paradigm Shift. *Annals of Punjab Medical College (APMC)* **15**, 195-198.
- Garcia Rodriguez, L. A., Lanás, A., Soriano-Gabarró, M., and Cea Soriano, L. (2019). Low-dose aspirin and risk of upper/lower gastrointestinal bleeding by bleed severity: a cohort study with nested case-control analysis using primary care electronic health records from the United Kingdom. *Annals of medicine* **51**, 182-192.
- García Rodríguez, L. A., Martín-Pérez, M., Hennekens, C. H., Rothwell, P. M., and Lanás, A. (2016). Bleeding risk with long-term low-dose aspirin: a systematic review of observational studies. *PloS one* **11**, e0160046.
- Hreinsson, J. P., Gumundsson, S., Kalaitzakis, E., and Björnsson, E. S. (2013). Lower gastrointestinal bleeding: incidence, etiology, and outcomes in a population-based setting. *European journal of gastroenterology & hepatology* **25**, 37-43.
- Joseph, P., Roshandel, G., Gao, P., Pais, P., Lonn, E., Xavier, D., Avezum, A., Zhu, J., Liu, L., and Sliwa, K. (2021). Fixed-dose combination therapies with and without aspirin for primary prevention of cardiovascular disease: an individual participant data meta-analysis. *The Lancet* **398**, 1133-1146.
- Knowles, R. B., and Warner, T. D. (2019). Antiplatelet drugs and their necessary interaction with endothelial mediators and platelet cyclic nucleotides for therapeutic efficacy. *Pharmacology & therapeutics* **193**, 83-90.
- Lanás, Á., Carrera-Lasfuentes, P., Arguedas, Y., García, S., Bujanda, L., Calvet, X., Ponce, J., Perez-Aísa, Á., Castro, M., and Muñoz, M. (2015). Risk of upper and lower gastrointestinal bleeding in patients taking nonsteroidal anti-inflammatory drugs, antiplatelet agents, or anticoagulants. *Clinical Gastroenterology and Hepatology* **13**, 906-912. e2.
- Sugawara, M., Goto, Y., Yamazaki, T., Teramoto, T., Oikawa, S., Shimada, K., Uchiyama, S., Ando, K., Ishizuka, N., and Murata, M. (2019). Low-dose aspirin for primary prevention of cardiovascular events in elderly Japanese patients with atherosclerotic risk factors: subanalysis of a randomized clinical trial (JPPP-70). *American Journal of Cardiovascular Drugs* **19**, 299-311.
- Wang, Y., Wang, W., Wang, B., and Wang, Y. (2020). The risk of gastrointestinal hemorrhage in low-dose aspirin users with diabetes mellitus: systematic review and meta-analysis. *Gastroenterology research and practice* **2020**.
- Whitlock, E. P., Burda, B. U., Williams, S. B., Guirguis-Blake, J. M., and Evans, C. V. (2016). Bleeding risks with aspirin use for primary prevention in adults: a systematic review for the US Preventive Services Task Force. *Annals of internal medicine* **164**, 826-835.

- Zhang, J., Huang, J., Zhao, Y., and Zhang, W. (2022). The preventive effects of aspirin on preeclampsia based on network pharmacology and bioinformatics. *Journal of Human Hypertension* **36**, 753-759.
- Zheng, S. L., and Roddick, A. J. (2019). Association of aspirin use for primary prevention with cardiovascular events and bleeding events: a systematic review and meta-analysis. *Jama* **321**, 277-287.
- Zia, N., Alam, L., and Ashraf, N. (2021). ENDOSCOPIC FINDING IN PATIENTS PRESENTING WITH LOWER GASTROINTESTINAL BLEED-A STUDY FROM A DEVELOPING COUNTRY. *Pakistan Armed Forces Medical Journal*, 215.



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