Safety profile and adverse effects of low dose aspirin

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ABSTRACT

Adult patients (30-50 yr.) given prescription of low dose aspirin (75mg/day) constituted the sample (n=334). The aim was to find out how far the low dose aspirin as antiplatelet agent would be safe as far as gastric, renal, immunological and otther adverse effects. The work planned to study over 6 months (data analytical study). The mechanism of action of low dose aspirin is well documented as anti-thromboxane A2, hence used as antiplatele drug in various thrombotic events. Additional mechanism reported being inhibition of platelet cyclooxygenase 1 enzyme. Adverse effects (total 12%) observed were: 1) Dermal (4.2%) - fixed drug eruption, pruritus, rash, subungual splinter bleeding. The mechanism reported is immunogenic 2) Gastric adverse effects (7.8%): - Hyperacidity, reflux esophagitis and nausea. The probable mechanism being-1) gastric irritation, 2) lack of gastric mucosal cytoprotection due to due to inhibition of PGE-2, I-2. To conclude, low dose aspirin is not free of dermal and gastric adverse effects, however these were well tolerated; none required discontinuing any drug. Keywords - Low dose aspirin, Mechanism of action, Dynamics of adverse effects. Key Messages - Adverse effects of drug in low dose (aspirin) may be qualitatively dose specific; however the magnitude and prevalence may be low. The mechanism of dynamic adverse events of low dose may differ from that of upper dose, but the therapeutic action is specifically unique.

Introduction

Aspirin (acetylsalicylic acid), a non-steroidal, anti-inflammatory - analgesic - antipyretic drug, also called as non - narcotic analgesic, has versatile therapeutic indications as per classification title. The mechanism of action (MOA) is irreversible inhibition of cyclooxygenase enzyme (COX)1 and 2, thereby inhibit synthesis of prostaglandin (PG) (which is responsible for fever, pain and inflammation). The MOA of aspirin in low dose is inhibition of enzyme thromboxane synthetase in platelets, thereby prevents availability of biogenic amine thromboxane A2 (TXA2), ultimately denying platelet aggregation. Low dose aspirin (LDAsp) is recommended as antiplatelet drug for prophylaxis and therapeutic use in the thrombotic events, e.g. Ischaemic heart diseases, stroke, peripheral vascular disorders etc. For cardio protection (20-25%), the dose 75-81 mg/days effective; for therapeutic use 40-80 mg/day is suggested1. Aspirin in dose < 100 mg/day is said to be selective for COX 1 enzyme of platelets with lower risk of gastrointestinal bleeding; however this dose is reported not risk free of gastric haemorrhage, as gastric PG E-2 and PGI-2 (gastro-protective) are also inhibited (via COX 1 blockade)'. The adverse effects (AE) include immunogenic, dose dependent / independent, gastric irritation and systemic: Immunogenic AE occur due to augmented availability of leukotriene (via unaffected lipooxygenase pathway)3 and other: 1) Dermal - a) Fixed drug eruptions, Pruritus, Steven Johnson syndrome, Toxic epidermal necrosis, Vasculitis, urticaria, rash. - b) Gastric - Anorexia, Nausea, Dyspepsia, Abdominal pain, diarrhoea, - Peptic ulcer (15-30%), Gastric haemorrhage - c) Platelets - Bruising, increased risk of gastric / cutaneous haemorrhage - d) Renal-Salt & water retention, oedema, worsen renal function in renal, cardiac and hepatic cirrhosis patients. It is an issue of consideration that whether LDAsp also induces similar AE, Apart from TXA2 inhibition, the platelet COX 1 is selectively inhibited by aspirin in dose <100mg/day1. Moreover aspirin is gastric irritant and highly unionised in acidic pH of gastric juice, may lead to ion trapping, thereby causes mucosal damage, so may augment acid secretion3. The gastric irritant effect is independent of dose2; hence LDAspis available as surface coated preparation. With this background of immunogenic, gastric irritant and unsupported gastro-protection, we thought it

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