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EC PHARMACOLOGY AND TOXICOLOGY

Review Article

Biochemical and Histological Features of Aspirin Toxicity

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Received: November 22, 2022; **Published:** December 29, 2022

Abstract

The anti-inflammatory and pain-relieving effects of aspirin have been known to science and widely used for quite some time. The list of applications for this compound continues to grow, and it now includes anti-inflammatory and anti-platelet activities. It is not necessary to place an undue amount of emphasis on the part it plays in cardiovascular diseases because of this. This study aimed to conduct a literature review on the topic of the toxicity that can be caused by the use of aspirin, with the purpose of answering the following question: The toxicity that it primarily causes over a prolonged period of time has an effect on the upper gastrointestinal system. It is also capable of causing acute toxicity if consumed in sufficient quantities to reach that threshold. When everything is taken into account, the significance of aspirin and the widespread use of the drug should not be used as an excuse to disregard the drug's potential for toxicity. Instead, treating physicians should conduct clinical evaluations of their patients in addition to any necessary blood, liver, and kidney function tests.

Keywords: *Aspirin; Toxicity; Liver Function Test; Kidney Function Test; Chronic Toxicity*

Introduction

The present study reviewed different aspects of aspirin toxicity including biochemical and histological aspects.

An overview of aspirin

At the time of Hippocrates, salicylates in the form of willow bark were used as a pain reliever, and the antipyretic effects of salicylates have been known for more than two centuries [1]. Since its first commercialization in the late 1890s, aspirin, also known as acetylsalicylic acid, has been utilized in the treatment of a wide variety of inflammatory conditions. Aspirin is most commonly known by its common

name, aspirin. The antiplatelet activity of this agent wasn't discovered until almost 70 years after it was first used, despite the fact that it was widely used [1]. As a result of recent developments in our understanding of the central role that platelets play in the pathophysiology of cardiovascular disease, in-depth investigations have been prompted into the mechanisms of action of aspirin and the clinical utility of this agent in the treatment of common cardiovascular disorders. The extent to which aspirin has been demonstrated to be effective in treating cardiovascular conditions is referred to as the drug's "clinical utility" [1].

Aspirin's primary method of exerting its therapeutic effect is by interfering with the biosynthesis of cyclic prostanoids, such as thromboxane A2 (TXA2), prostacyclin, and other prostaglandins. This is how aspirin achieves its beneficial effects. The oxidation of arachidonic acid, which is catalyzed by enzymes, is what leads to the production of these prostanoids. The arachidonic acid molecule originates from the phospholipids found in cell membranes. The metabolization of arachidonic acid is under the control of the enzyme known as prostaglandin (PG) H-synthase. The cyclooxygenase (COX) and peroxidase activities of the enzyme are responsible for the production of the products PGG2 and PGH2, respectively, during this process. The modification of PGH2 by particular synthetases results in the production of a number of different prostaglandins, including TXA2, D2, E2, and F2. Prostacyclin is also produced. These prostaglandins are responsible for mediating a variety of different cellular functions, each in their own unique way [2].

PGH-synthase, which is also known as COX, can be found in two isoforms, and the amino acid sequences that make up both of these isoforms have a significant amount of homology with one another [3]. It is possible to increase the selectivity of COX inhibitors by altering the catalytic site of the enzyme to include a single different amino acid [4]. This leads to the production of homeostatic prostaglandins, which are responsible for normal cellular functions such as the maintenance of renal blood flow, the regulation of platelet activation and aggregation, and the protection of the gastric mucosal lining. Platelets are included in the category of cells that have endoplasmic reticulums, and these endoplasmic reticulums always contain the first isoform of COX [5]. Platelets are an example of a type of cell that can express the COX-1 gene. In most mammalian cells, the second isoform of COX, which is known as COX-2, is not normally found; however, it can be rapidly induced by inflammatory stimuli and growth factors, which results in the production of prostaglandins that are involved in the inflammatory response [6].

The use of aspirin in the treatment of cardiovascular diseases

Aspirin is the primary component of action in both the primary and secondary preventive treatments for cardiovascular diseases. On the other hand, it has been linked to a number of potentially harmful effects, one of which is toxicity to the gastrointestinal system (peptic ulcer formation, bleeding). Although it is generally accepted that lower doses are safe, it is essential to keep in mind that even the smallest dose has the potential to cause bleeding in the gastrointestinal tract. This is something that should be kept in mind at all times. There is no discernible difference between the gastrointestinal toxicity profiles of regular aspirin and enteric-coated aspirin when it comes to the use of either of these medications. In patients who have cardiovascular disease and are at a high risk for gastrointestinal bleeding, the eradication of the Helicobacter pylori infection and concurrent therapy with proton pump inhibitors may help to reduce the risk of gastrointestinal toxicity [7].

Aspirin toxicity

Patients who are at risk of a secondary cardiovascular disease (CVD) event should receive antiplatelet therapy as an essential part of their preventive care. These patients really need to start the treatment as soon as they possibly can. In spite of the fact that aspirin is an exceptionally effective medication for reducing the number of cardiovascular disease (CVD)-related events, there is a significant risk of gastrointestinal (GI) toxicity associated with its use. This is the case despite the fact that aspirin can reduce the risk of cardiovascular disease (CVD)-related events. For this reason, aspirin that is taken in relatively low doses is the medication of choice for the majority of antiplatelet regimens. Patients who experience dyspeptic symptoms while taking aspirin, which can occur with or without associated ulceration

and bleeding, may be more likely to stop taking the medication, which in turn raises the risk of cardiovascular disease in those patients. Patients who do not experience dyspeptic symptoms while taking aspirin do not have an increased risk of developing cardiovascular disease. Patients who take aspirin but do not experience dyspeptic symptoms do not have an increased risk of developing cardiovascular disease even though they are taking aspirin. Patients who are already taking aspirin and who are thought to be at an increased risk of upper gastrointestinal (GI) events may be good candidates for concomitant therapy with a proton pump inhibitor. Patients who are already taking aspirin and who are thought to be at an increased risk of upper gastrointestinal (GI) events. It is strongly suggested that you go ahead and get treatment for this condition right now. These agents have been linked to increased aspirin adherence and are extremely effective in reducing the upper gastrointestinal lesions that are associated with aspirin therapy. On the other hand, widespread under-prescribing of proton pump inhibitors (PPIs) and the possibility of non-compliance with their use means that a substantial number of patients are at an unnecessary risk of upper gastrointestinal toxicity and, if aspirin therapy is discontinued, cardiovascular disease events. This puts a substantial number of patients in a precarious situation. It has been demonstrated that administering to patients a combination tablet that contains both aspirin and an immediate-release proton pump inhibitor is an effective method for reducing the risk of gastric ulcer formation and increasing patient compliance. This strategy, which may ultimately reduce the incidence of CVD outcomes because of the associated reduction in GI symptoms and the potential for greater patient adherence to aspirin, merits further investigation under both randomized controlled conditions (explanatory trials), as well as in real-world settings. This strategy may ultimately reduce the incidence of CVD outcomes because of the associated reduction in GI symptoms and the potential for greater patient adherence to aspirin. Because of the associated reduction in GI symptoms and the potential for greater patient adherence to aspirin, this strategy may ultimately reduce the incidence of CVD outcomes. This may be possible because of the potential for greater patient adherence to aspirin. This strategy may ultimately reduce the incidence of cardiovascular disease outcomes because it is associated with a reduction in gastrointestinal (GI) symptoms and has the potential for greater patient adherence to aspirin (pragmatic trials) [8].

Clinical impacts of aspirin toxicity

Patients who are treated with aspirin and report experiencing symptoms make up a relatively small portion of the population that is adversely affected by this medication. Endoscopic surveys of patients treated with 325 mg of aspirin per day have reported the presence of gastroduodenal ulcers in 11% of patients, 80% of whom were asymptomatic [9], and either gastroduodenal ulcers or erosions or both in 48% of asymptomatic patients. Endoscopic surveys of patients treated with 325 mg of aspirin per day have reported the presence of gastroduodenal ulcers in 11% of patients. 80% of these patients were asymptomatic 11% of patients who were treated with aspirin at a dosage of 325 mg per day were found to have gastroduodenal ulcers, and of those patients, 80% were women [10]. These findings imply that a sizeable percentage of asymptomatic patients are at an increased risk of developing a gastroduodenal ulcer if aspirin therapy is started or continued. This is because gastric erosions are a risk factor for gastric ulceration during aspirin therapy [11]. In the years leading up to their diagnosis, approximately one-third of individuals who would later be found to have peptic ulcers did not present any symptoms whatsoever [12]. As a result, aspirin-associated gastrointestinal toxicity may develop to the point of ulceration, with or without bleeding being associated with it, before the patient seeks treatment from a physician. In observational studies, it was found that long-term treatment with a low dose of aspirin was associated with an increased relative risk of upper and lower gastrointestinal bleeding [13]. These relative risks, which were derived from real-world settings, are in agreement with those from randomized trials [12], and the utilization of enteric-coated or buffered aspirin does not lessen the gravity of these risks in any way [14]. When determining whether or not it is reasonable to prescribe aspirin to a particular patient, it is imperative to weigh the risks of gastrointestinal events against the risks of cardiovascular disease. This is because the adverse effects of aspirin on the gastrointestinal tract occur with sufficient frequency and have the potential to be severe [14]. This is especially problematic in people who are at an increased risk of cardiovascular disease and who have had a GI bleed in the past [15]. In patients who are at an increased risk of cardiovascular disease and who have previously experienced bleeding from a peptic ulcer, discontinuing aspirin therapy is associated with a decreased risk of recurrent ulcer bleeding; however, it is also associated with an increased risk of death from any cause. This is an important finding [16].

Aspirin's potential to cause toxicity in the upper digestive tract: Risk factors

Researchers from all over the world have been trying to determine what aspects of a patient's medical history put them at increased risk for developing gastrointestinal complications as a result of taking aspirin. Previous peptic ulcer is one of the most important risk factors, and this risk is amplified if there is a history of associated bleeding in the patient's medical history [14,17]. Once an individual reaches the age of approximately 60 years, the risk begins to meaningfully increase, and the increase in risk shows a nonlinear relationship with rising age thereafter. Additionally, there is a marginal rise in danger connected to male sexual activity [14,17]. Even with this knowledge of risk factors, it is not possible to quickly quantify the risk for individual patients who have peptic ulcer disease. The most important independent risk factor for peptic ulcer disease is an infection with Helicobacter pylori. In the hope that it will be of assistance to medical professionals engaged in routine clinical practice, Lanas., *et al*. [18], developed an algorithm with the purpose of estimating the cardiovascular and gastrointestinal risks associated with the administration of low-dose aspirin in individual patients. The aim of the algorithm is to estimate the risks associated with the administration of low-dose aspirin. They focused on older age as a significant risk factor, along with being male and having a history of upper GI pain, dyspepsia, or peptic ulcers as their primary areas of investigation. These findings were based on the data that was collected from 68 different studies that had previously been published.

An overdose on salicylates is a serious situation that requires immediate medical attention. Both the deliberate ingestion of a substance and the accidental overdose of that substance can result in severe metabolic derangements, which makes treatment substantially more difficult. Consuming multiple medications at the same time can make management an already challenging task even more so [19,20].

Acute toxicity of aspirin

Medications containing salicylates are readily available for purchase over the counter. Because of their analgesic, antipyretic, and anti-thrombotic properties, they are frequently utilized in medical practice. Acute ingestion or chronic ingestion, which results in an increased serum concentration, both have the potential to cause toxicity in the body. Salicylates can be combined with medications from other categories, such as narcotics, antihistamines, and anticholinergics, to create new formulations. This can make management more difficult [8,21].

An overdose of salicylates can result in a variety of metabolic conditions. Both hyperventilation and respiratory alkalosis can be brought on by direct stimulation of the cerebral medulla in a patient. The process of oxidative phosphorylation, which takes place in the mitochondria, is caused to become uncoupled as a consequence of its metabolism. An increase in the rate of anaerobic metabolism is the direct cause of this consequence, which manifests itself as a rise in lactate levels in the blood. In addition to a negligible contribution from the salicylate metabolites, the accumulation of lactic acid is the root cause of the metabolic acidosis that has developed. As the patient works harder to compensate for the metabolic acidosis, the patient's hyperventilation becomes more severe. The patient will eventually reach a point of exhaustion where they will no longer be able to compensate for their metabolic acidosis by hyperventilating, and as a result, metabolic acidosis will take over and take control of their body. This results in instability in the patient's hemodynamic state as well as damage to the organs at the end of the chain [22].

Management of aspirin toxicity

Any patient who may be at risk for salicylate poisoning should have their blood tested to determine the level of salicylate present in their system. Taking serial levels is recommended because doing so will have an impact on treatment. Absorption is highly variable, so this is an important consideration. It is important to determine the levels of acetaminophen in the body in situations where the nature of the substance that was consumed cannot be determined with absolute certainty. It is recommended to conduct research on coagulation in addition to studies on electrolytes, such as calcium and magnesium, as well as ABG, LFTs, CBC, and lactate. It is strongly suggested that an electrocardiogram be obtained in order to screen for any irregular heart rhythms. A CT head scan should be considered for the patient

whenever there is a change in the patient's mental status. Continue to obtain serial ABGs as well as salicylate levels until it is clear that the levels are starting to decrease and the pH has stabilized. During this time, you should also continue to monitor salicylate levels. The findings of the laboratory tests could be considered normal, or they could indicate the presence of some slight electrolyte abnormalities at low salicylate concentrations. Tachypnea could be the root cause of an alkalosis in the respiratory system of a PA pure patient. At moderate levels, both metabolic acidosis and respiratory alkalosis will be present in the patient's body. There is a chance that you will experience leukocytosis and thrombocytopenia. Along with increased levels of BUN, creatinine, and lactate, hypokalemia and hypercalcemia are two of the potential adverse effects that could occur. In instances of severe toxicity, an anion gap in addition to a worsening of the metabolic acidosis will take place [22].

Patients who are suffering from salicylate toxicity typically experience volume depletion as a consequence of the hyperventilation, fever, and increased metabolic activity that occur in this condition. In order to properly administer cardiopulmonary resuscitation, the drug D5 must be combined with three ampoules of sodium bicarbonate. The dextrose can be used to treat the hypoglycemia that was present in the central nervous system (CNS). With the assistance of the sodium bicarb, the metabolic acidosis can be treated and corrected. In the event that hypokalemia is present, an additional potassium supplement may be administered. The amount of urine that should be produced each hour should be between 2 and 3 mL/kg [23,24].

Conclusion

Even though a large number of people take aspirin, and it has been shown to improve the health of millions of patients, its use in a chronic form has been linked to toxicity. This is despite the fact that aspirin is taken by a large number of people. It is also possible for it to cause acute toxicity if it is consumed in doses that are thought of as being on the higher end of the scale. As a result of the development of buffered aspirin, the toxicity of aspirin has been significantly decreased. Blood tests, kidney function tests, and liver function tests are some of the clinical evaluations that are recommended for treating physicians to perform on their patients on a regular basis in order to screen for any potential adverse effects that may be caused by the use of aspirin. Other clinical evaluations include urinalysis, which measures the amount of urine produced by the kidneys, and liver function testing, which measures how well the liver processes fatty substances.

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Volume 11 Issue 1 January 2023