Clinical Evaluation of Aspirin Effects on Gastrointestinal Tract and Circulatory System

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Summary

Aspirin, also known as salicylic acid, is one of the most well-known and widely used medicines. Throughout the previous century, it has been used to treat symptoms of fever and rheumatic pain, and it remains a superior therapy to its alternatives.In Iraq, we did not find a study explaining the effects of aspirin so the current study aims to know the side effects of aspirin on digestive disorders, as well as on circulatory system in different . The current study included done diagnosis and questionnaire for 120 individuals who took aspirin based on the instructions of the specialist, and their ages ranged between 8 to 88 years. Several tests were conducted to detect digestive disorders, such as the detection of *Helicobacter pylori* (*H.pylori*) based on blood, stool and exhalation tests so endoscopic examination of stomach ulcers was used for some patients. Heart activity measurements and medical examinations were also conducted .The current study showed that most patients who use aspirin (65%) do not suffer from health problems as a result of taking it. Disorders associated with taking aspirin are digestive disorders (13%), blood thinning (10%) and heart palpitations (5%). One of the most important digestive disorders associated with taking aspirin in some patients are gastric ulcer (62.5%), colon irritation (25%) and duodenal ulcers (12.5%), so that GIT disorders mainly detected in people aged 51-55 years and this harmful effect led to patients not continuing to take aspirin when health problems associated with taking it appeared. In conclusion, aspirin is a treatment that has a major role in reducing the risk of many diseases, especially heart diseases, but it must be used as directed by the specialist doctor, in order to monitor the emergence or development of side effects that may threaten the patient's life, such as stomach ulcers, haemophilia and palpitation.

Keywords: Aspirin, side effects, gastrointestinal tract, circulatory system, peptic ulcer, bleeding

Introduction

Aspirin or salicylic acid is a nonsteroidal anti-inflammatory drug (NSAID) that acts similarly to other NSAIDs but also inhibits the normal function of platelets [1,2]. During the previous century, it was widely used to treat symptoms of clotting, fever, and lung discomfort, and it is still a superior therapy to its alternatives. The study also showed that patients who continued to take aspirin after the clinical trials that were conducted became more and more low risk of various cancerous tumors, and for pain or fever, the effects of aspirin usually start within 30 minutes [3,4,5]. More than a century ago, aspirin became the most widely produced and marketed medication in the world, and since German Bayer AG began selling acetylsalicylic acid under the brand name AspirinTM in 1899, the substance has become a generic term. Aspirin has recently gotten a lot of scientific interest. Other chemists developed the chemical synthesis and devised the most effective methods of producing today's aspirin during the following 50 years. [6,7,8].

Aspirin is on the World Health Organization's list of essential medications. Aspirin was the 42nd most often prescribed medication in the United States in 2017, with over 17 million prescriptions. Aspirin is also used long-term to help prevent an increased incidence of heart attacks, strokes and blood clots in people at high risk [9,10]. It may also reduce the risk of developing certain types of cancer, especially colorectal cancer. the authors noted a 36% reduction in cancer metastases in patients taking aspirin, which may explain the lower mortality rate. This decrease is more significant in cases of cancers arising from one gland, such as the thyroid gland, breast, or glandular tissue, such as the lungs, stomach, colon, etc moreover, taking aspirin, especially for long periods, is accompanied by side effects [11,12,13]. The most serious adverse effects include stomach ulcers, bleeding in the stomach, and worsened asthma. Because the risk of bleeding is higher in the elderly, those who consume alcohol, those who take other NSAIDs, or those who take other blood thinners, aspirin is not advised for use in the latter stages of pregnancy [14,15] and generally not recommended for children with infection because it causes a risk of developing Reye's syndrome and high doses may lead to ringing in the ears. Other research has found that low-dose aspirin and other NSAIDs are important causes of upper gastrointestinal hemorrhage across the world. Low-dose aspirin is widely utilized for cardiovascular prevention, but even at dosages as low as 75 mg daily, it doubles the risk of bleeding ulcers. [16,17]. According to epidemiologic research, the use of NSAIDs increases the incidence of ulcer complications. In people using low-dose aspirin or other NSAIDs, a history of upper gastrointestinal bleeding is a major risk factor for recurrent bleeding [18,19]. There are currently few effective methods for preventing ulcers from bleeding in patients who take aspirin or other NSAIDs and are at high risk of bleeding. Furthermore, because the risk of cardiovascular disease is higher in the elderly, the potential advantages of aspirin may be larger than in younger groups. However, the senior age group has been linked to an increased risk of bleeding. The risk–benefit balance in this age range is uncertain since only a small number of older people have been involved in prior primary prevention trials [19,20].

The reason for conducting this study is to note the emergence of disease symptoms in some people who take aspirin, despite its wide use in various countries of the world, but studies on the side effects of this treatment are few and on a narrow range, so the current study aimed to follow up on the side effects of aspirin, especially on GIT and circulatory system for people with different age groups.

Patients and Methods

Sample Collection: The current study was conducted on 120 individuals, their ages ranged between 8-88 years. 80 of these people were seen in Al-Zahraa Teaching Hospital, and 40 were from outpatient clinics. After blood, urine, and stool samples collection, laboratory and clinical tests were conducted in the care units and laboratories of Al-Al-Zahraa Teaching Hospital during the period from 3/1/2021 to 4/4/2021, and the approval was taken from all the participants, who were all of the same Arab race. The questionnaire included all the following information:

i. Name, gender and age of the participants.
ii. Reason for taking aspirin.
iii. The period of taking aspirin.
iv. Side effects resulting from taking aspirin.
v. Other notes, such as the type of aspirin and amount of the dose, were also recorded.

Medical examinations: The attending physician asks some questions related to the symptoms that appeared in the event of suspicion of peptic ulcer, palpitations or headache as a result of taking aspirin, and questions related to the general health status. Among the most important medical examinations conducted for the persons from whom the information was taken are the following:

1. Diagnosis of peptic ulcer: in this research, blood , stool and breathing tests preformed if the patient have peptic ulcer, or another disease (such as indigestion or irritation / irritation of the mucous layer of the stomach) whose symptoms are similar to those of peptic ulcers, in order to look for the presence of *H. pylori*. Blood test procedure depend on detection antibodies against *H. Pylori* in blood by using AimStep H. Pylori kit/AMAZON. The OneStep *H. pylori* Antigen Rapid Test is an in vitro qualitative immunochromatographic assay for the rapid detection of *H. pylori* antigens in human stool specimen by using Pylori Antigen Rapid Test Kit/ USA. In additional, Urea ^{13}C Breath Test kit is based on secretion of much active urease by gastric *H. pylori* that can break down urea into ammonia and carbon dioxide (CO2).
2. Endoscopic biopsy: This procedure is done in the hospital or outpatient center throughout taking biopsy from stomach lining so done to visualized ulcer in duodenum and other parts of GIT. Endoscopic test is the most accurate way to detection *H pylori* infection throughout direct examination and culture.
3. Electrocardiography (ECG): In this noninvasive (non-surgical) test, the patient's chest is placed with leads that record the electrical signals that make their heart beat. An ECG can help to detect any problems with the heart's rhythm and

structure that could lead to heart palpitations. This test is done either at rest or while exercising (stress ECG).

4. Holter monitoring: A Holter monitor is used to detect heart palpitations that cannot be detected during a normal ECG. Some personal devices, such as smart watches, are equipped with ECG monitoring. It records the electrical activity of the heart continuously over 24 hours or longer.
5. Echocardiography(echo) This noninvasive (non-surgical) test produces moving images of heart using sound waves. Usually this test show problems with blood flow and the structure of the heart.
6. Headache diagnostic tests: Sometimes taking aspirin is accompanied by a headache, in current study there are three tests that are relied upon to determine the tissues that were affected by aspirin. Among the tests that were conducted during the current study:
    i. Complete blood count analysis.
    ii. Examination of the eye and the fundus of the eye.
    iii. Sectional procedures on the brain.

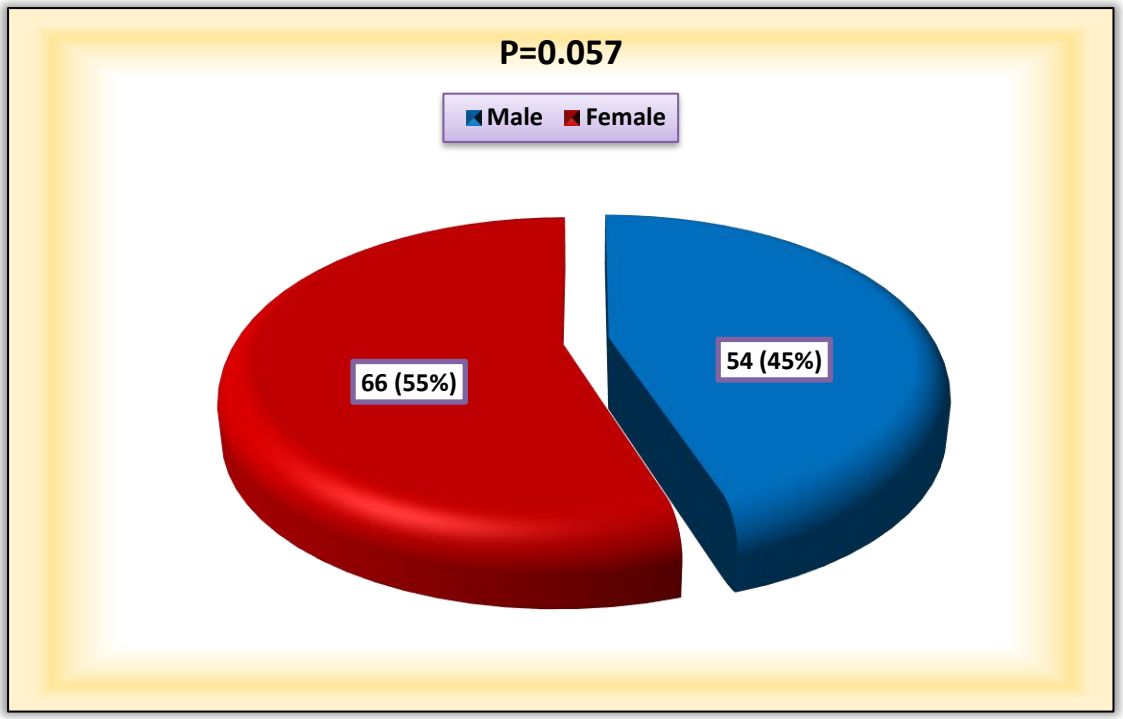
Statistical Analysis: The current study's findings were evaluated using Excel 2010 and Statistical Package for Social Analysis version 19, with a P value of less than 0.05 considered statistically significant.

Results

The current study included 120 patients whose ages ranged from 8 to 88 years, with a mean age of 48 ± 19.82 as in Table (1). The results of the current study also showed that most (55%) of the participants were females, as shown in Figure (1). All of these individuals used aspirin as directed by their physician. One of the most important reasons for taking aspirin was to treat high blood pressure (hypertension) 24 (20%), blood viscosity 20 (17%), myocardial infraction 16 (13%), stroke 14 (12%) and head pain 12 (10%) as in Figure (2).

Table(1): Age mean of aspirin taking individuals

Patients ages (year)	
Range	8 - 88
Mean ± SD	48 ± 19.82
SE	2.558
Total number of patients	120
(SD= Standard Deviation; SE= Standard Error)	



Figure(1): percentage of aspirin taking according to patient´s gender

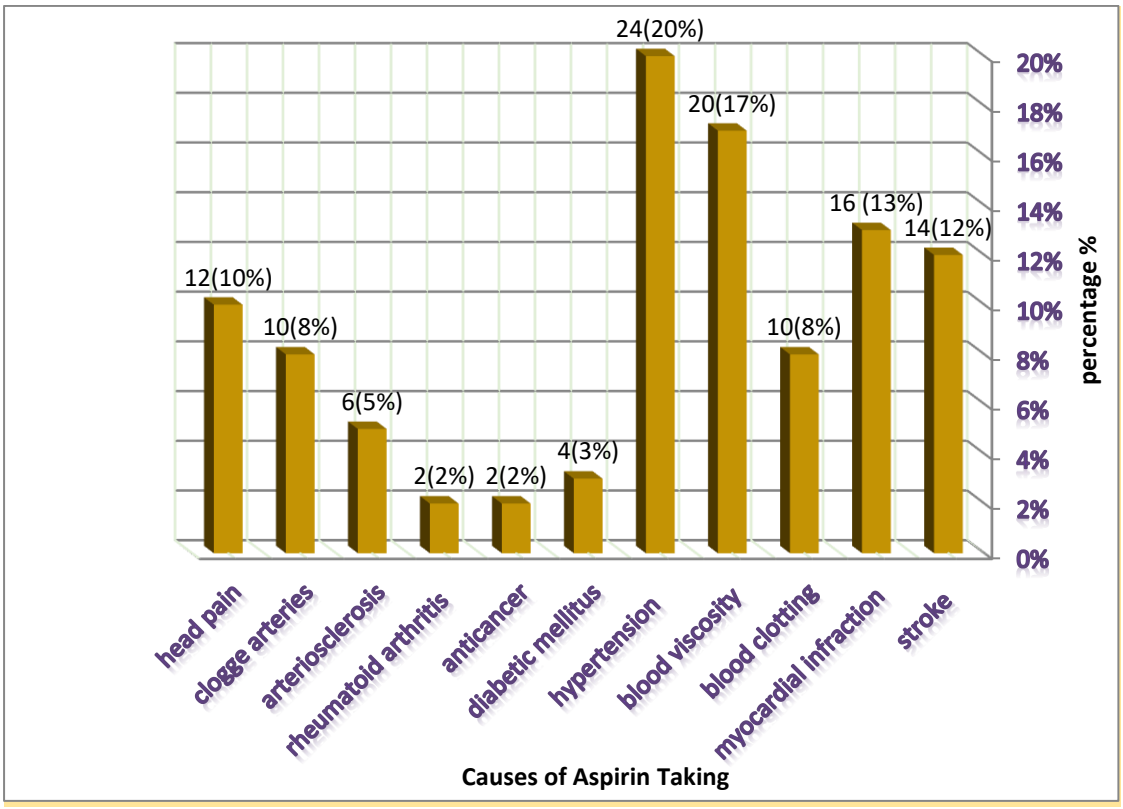


Figure (2): Causes of aspirin tanking

The results of the current study showed that 65% of the individuals who took aspirin did not suffer from any side effects as showed in Figure 3, and they were within different age groups from 8 to 88 years, and most of them (93%) continued to use

aspirin (Table 2 and 3). While 13% of the patients had digestive disorders as a result of the use of aspirin, and these patients had an age mean of 52.32 years and as a result of these disorders, they did not continue to take aspirin, as most of these patients (81%) used aspirin for a period of less than 6 months. The current study also showed that 10% of patients suffer from blood haemophilia, and most of them (50%) took aspirin for a period between 3 to 8 years and their ages were between 8-67 years and an average age of 23.89 years.

On the other hand, 5% of patients (with an age mean of 33.72 years) suffer from heart palpitations as a result of most of them taking aspirin for a period of 3 to 8 years. The results also showed in Table (3) that patients who take aspirin and do not suffer from side effects are the only ones from they continued to use aspirin as a treatment, while patients suffering from side effects as in Figure (3) used aspirin for different periods of time ranging from one month to 8 years, and these results led to significant statistical differences (P=0.000109, X^2=48.06 , DF=18).

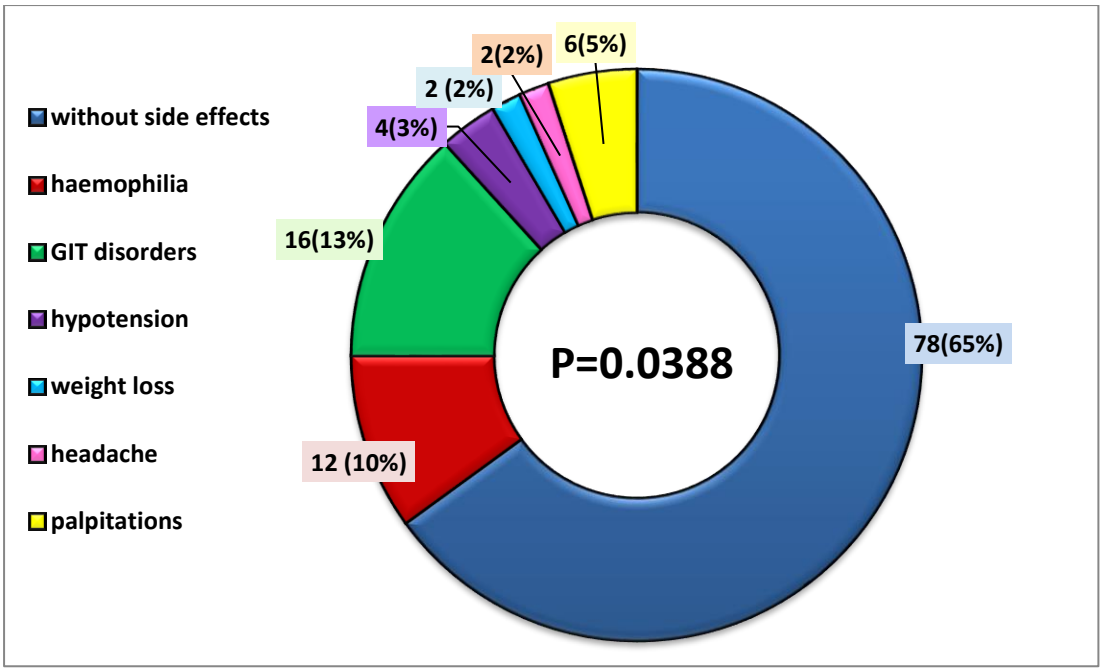


Figure (3): Effects aspirin of circulatory system and GIT

Table (2): Age range and mean of patients with side effects of aspirin taking

Effects of aspirin	Age range / year	Age mean/year
GIT disorders	**51-55**	**52.32**
Haemophilia	**8-67**	**23.89**
Palpitations	**31-35**	**33.72**
Hypotension	**45-53**	**46.35**
Weight loss	**37-42**	**39.90**
Headache	**60-65**	**62.14**
Without side effects	**8-88**	**34.77**

Table (3): Distribution of aspirin effects according to patient ages

Side effects of aspirin	Total number	> 6 month	6 month to 3 years	3 to 8 years	Continues	DF	X^2	P Value
		N (%)	N (%)	N (%)	N (%)			
GIT disorders	16	13 (81)	3 (19)	0 (0)	0 (0)	18	48.06	0.0001
Haemophilia	12	4 (33)	3 (25)	5 (42)	0 (0)			
Palpitations	6	0 (0)	2 (33)	3 (50)	1 (17)_			
Hypotension	4	3 (75)	1 (25)	0 (0)	0 (0)			
Weight loss	2	0 (0)	0 (0)	1 (50)	1(50)			
Headache	2	1 (50)	0 (0)	0 (0)	1 (50)			
Without side effects	74	0 (0)	1(1.4)	4 (5.6)	69 (93)			
DF= degree of freedom, X^2= chi square								

According to endoscopic diagnosis and *H. pylori* tests, the results of the current study (Figure 4) showed that digestive disorders resulting from taking aspirin, which are represented by gastric ulcer (62.5%), colon irritation (25%) and duodenal ulcers (12.5%), where stomach ulcers were one of the main problems associated with taking aspirin that associated with statistical differences (P=0.0162).

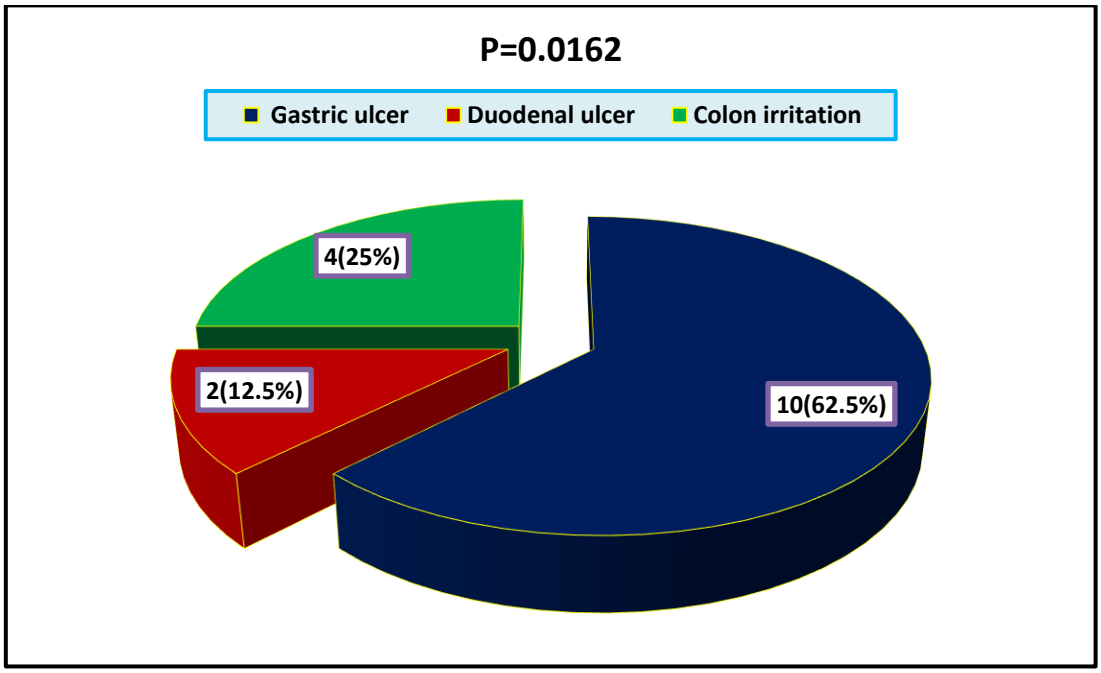


Figure (4): Side effect of aspirin on GIT

Discussion

Aspirin is a typical analgesic for mild aches and pains as well as a fever reducer. It's also an anti-inflammatory and can be taken as an anticoagulant in persons who are at risk of blood clots, strokes, or heart attacks. Studies have not established an age limit for its use [21,22]. In present research taking of aspirin mainly appeared in adult and significantly associated with emerging of negative effects as in table 2 and this finding similar to previous results which showed that age is a key factor when weighing the pros and cons of aspirin. There is a significant rise in the risk of aspirin-induced bleeding episodes when an individual reaches 60 years old, with a non-linear connection between increasing risk and subsequent age [23,24, 53].

In the current study, the ages of the patients using aspirin ranged from 8 to 88 years, and most of them were female, and they used aspirin as directed by the doctor. In the United States, it is recommended to be taken by people aged 50-59 years, who are at risk of heart disease, such as those with high cholesterol or high blood pressure (provided that it is under control), and a low dose of it (75 mg) is taken daily. In contrast, medical recommendations for aspirin in Britain are more cautious, and they only recommend its use to people who have already developed heart problems [25,26,27].

The current study showed that most patients (65%) who use aspirin do not suffer from side effects as a result of taking it. However, there were cases that included disorders of the digestive system, and this was confirmed in other studies when they mentioned that taking aspirin on a daily basis increases the possibility of forming a stomach ulcer, and if the patient previously suffered from a bleeding ulcer or from digestive bleeding anywhere in the digestive system, then taking aspirin may cause more severe bleeding and may lead to his life, and this is one of the life-threatening damages of aspirin [28,29,30,31]. Ulcer risk was considerably enhanced by *H. pylori* infection and advanced age (>70 years). *H. pylori* infection increased the incidence of simple peptic ulcer by 2–3.5 times and GI bleeding by 2–2.5 times in NSAID users, according to other research. Because *H.pylori* is a significant risk factor for ulcers and ulcer bleeding in people on LDA, it is suggested that patients with a history of ulcer disease have a thorough test for and eradication of *H.pylori* before beginning aspirin. [32,33].

The current results also showed that the use of aspirin by some patients is accompanied by hypotension. Despite the above, the effect of aspirin treatment on blood pressure control is still controversial, as more research and studies are needed, so that some recent data indicate the effectiveness of aspirin in improving blood pressure [34], the flexibility and expansion of blood vessels, but high doses of it have been associated with inhibition of the second analogue of cyclooxygenase COX-2, which reduces renal blood flow and glomerular filtration rate, and affects the kidneys negatively [34,35,36]. There are no studies confirming the effect of taking aspirin on blood pressure, and most scientific results indicate that it can be used in low doses but when notice a difference in the normal blood pressure levels after using aspirin, should consult doctor immediately [35,36].

In addition, the current study showed that 10% of patients using aspirin suffer from blood haemophilia, and showed that acetylsalicylic acid has an analgesic and anti-inflammatory effect, but at the same time it causes blood thinning, even with small doses [37,38]. The blood-thinning effect of acetylsalicylic acid begins with a daily dose of less than 100 milligrams. This effect is formed in a few minutes, but then lasts for about a week. Therefore, everyone who accepts a surgical intervention, for example at the dentist, should tell the doctor about the dose of acetylsalicylic acid he took and at what time [37,38,39].

On the other hand, a recent American study warned healthy elderly people from taking aspirin daily, despite its proven benefits for patients following heart attacks or strokes. According to the study, experiments did not confirm the benefits of aspirin for healthy people over the age of seventy, but these tablets increased the risk of fatal internal bleeding [40,41]. The findings were deemed extremely significant by experts, who recommended against self-treatment with aspirin. Aspirin is prescribed to patients following a heart attack or stroke because it thins the blood and lowers clotting, lowering the odds of recurrence. Some completely healthy people use aspirin to avoid future risks, and research into whether the medicine can be used to reduce cancer risk is underway. However, the majority of studies on aspirin's benefits is conducted in middle-aged people, and as we get older, there is more data about its hazards [42,43,54].

Another study involved 19,114 people over the age of 70 in the United States and Australia who were all healthy and had no previous heart problems, who were given half a daily dose of aspirin for five years [44]. The side effects of aspirin on the digestive system include inflammation and heartburn that occur in people who use aspirin regularly and result in some symptoms such as abdominal pain, discomfort, nausea and vomiting, and this is what was recorded in the current research [44,45]. This proves that the use of aspirin increases the risk of gastrointestinal bleeding. Although some enteric-coated formulations of aspirin are advertised as "gentle on the stomach", in one study, enteric-coated aspirin did not appear to reduce this risk.A Japanese study reported that low aspirin dose (100 mg) significantly increased the risk of lower GI bleeding, but the number of bleeding cases (n=44) was relatively small [46]. Low aspirin dose increased the incidence of lower GI bleeding (including bleeding from the small and large intestine) by 2.7 times compared to no aspirin usage in a Spanish case-control study (>1,000 bleeding observations) [47]. Moreover, various research have looked into the link between low aspirin doses and the development of diverticular bleeding and diverticulitis [48,49]. In a recent prospective study on diverticular disease in Japan, researchers evaluated the efficacy of low aspirin doses and discovered a strong link to diverticular bleeding [49]. A study of health professionals found that low aspirin doses (2–5.9 tablets of 325 mg per week; multivariate HR, 2.32; 95 percent CI, 1.34–4.02) increased the risk of diverticular bleeding when compared to no aspirin use [50].

Combining aspirin with other NSAIDs has also been proven to enhance this risk. The use of aspirin in conjunction with clopidogrel or warfarin increases the risk of upper GI hemorrhage. Aspirin-induced COX-2 overexpression appears to be part of

gastric defense, and concurrent administration of COX-2 inhibitors with aspirin enhances stomach mucosal erosion [51,52]. When taking aspirin with any "natural" substance that inhibits COX-2, such as garlic extracts, curcumin, bilberry, pine bark, ginkgo, or fish oil, caution should be exercised because of the potential for interaction. Companies have utilized "buffering" in addition to enteric coating to attempt and reduce GI bleeding [55,56]. To prevent aspirin from collecting in the stomach walls, buffering agents are used. However, the benefits of buffered aspirin are debated. For example, Magnesium oxide can be utilized as a buffering agent in almost all antacids. As an alternative to acid-blocking medications, calcium carbonate and vitamin C have been studied in combination [57,58]. In addition, combining aspirin with equal amounts of vitamin C may lessen the amount of stomach damage that happens when aspirin is taken alone. As previous studies have shown, it is preferable not to take aspirin on an empty stomach so many studies mentioned taking aspirin on an empty stomach is likely to cause irritation to the stomach, and this may affect the stomach lining, causing ulcers in addition the dose should be adjusted to not more than 6000 mg per day [59-72].

Conclusions

The current study showed that most patients who use aspirin (65%) do not suffer from health problems as a result of taking it also found that aspirin is used by different age groups from 8-88 years in Iraqi population and the most prominent disorders associated with taking aspirin were digestive disorders (13%), haemophilia (10%) and heart palpitations (5%).The current study showed that one of the most important digestive disorders associated with taking aspirin is stomach ulcers especially in older people.

Recommendation

The current study concluded that aspirin has negative effects on the circulatory system and digestive system for most patients, so there is a need for more scientific research on a larger number of patients to determine the benefits and harms of daily aspirin intake by adults under 50 and over 70 years old. It is preferable that these studies be at the genetic or immunological level, or both. On the other hand, the specialist must make sure that there are no digestive disorders, especially peptic ulcers, or sensitivity to non-steroidal treatments before giving aspirin as a treatment.

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