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Aspirin as an Independent Risk Factor for Hypertension

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Abstract

Introduction: Hypertension is one of the most commonly occurring diseases throughout the world. Aspirin is the most recommended drug to prevent cardiovascular diseases in high-risk patients. As this may be true, Aspirin has shown to increase the risk of hypertension. The objective of our study is to see the correlation between Aspirin an NSAID and hypertension within the Anguillan population.

Methods: This was a cross-sectional study comprising of males and females in Anguilla above the age of 20 years. Our study's focus was those that took Aspirin as a self-directed medication or as physician-directed for the prevention of cardiovascular disease. The participants were given a survey to fill out. Surveys were formatted to include demographics, medical, family and social history. Consent for surveys was obtained and permission was granted by the ARB (Anguillan Review Board). Comorbidities were evaluated by self-reporting in the medical history. The goal of this study was to understand whether there was any correlation between Aspirin use and the increased risk of hypertension.

Results: Primary outcome was significant with the p-value of 0.0008; however, secondary outcome was not statistically significant (p= 0.7) because whether the Aspirin was prescribed by physician or taken as a self-directed medication does not have influence in the mechanism of action of Aspirin. There was no statistical significance in the male gender between the control and the target groups (p= 0.054). Moreover, statistical significance was noted in female gender between the control and the target group (p= 0.004).

Conclusion: The results showed that there was significance in the Blood Pressure of patients who were on Aspirin as compared to those who did not take Aspirin indicating that Aspirin plays a role in hypertension.

Keywords: Hypertension; Aspirin; Nonsteroidal Anti-Inflammatory Drug (NSAID)

Introduction

Hypertension is one of the most commonly occurring diseases throughout the world. It is essential to prevent consequent cardiovascular events in hypertensive patients. It is defined as being above or equal to 140/90 mmHg [1]. Aspirin an NSAID (Nonsteroidal Anti-Inflammatory Drug) is proven to be effective in preventing cardiovascular diseases such as stroke and heart attack, which hypertensive patients are at a greater risk for when compared to normotensive

patients. According to American Heart Association, Aspirin is one of the most widely used medical treatments worldwide. Recommended dose for long-term cardiovascular disease prevention is 75 to 100 mg daily because higher doses increase risk of having side effects such as gastrointestinal bleeding without any significant increase in its protective effects [2]. NSAIDs are also popular for their analgesic effects. Long-term use of NSAIDS has been correlated to the development of hypertension.

Aspirin's mechanism of actions differs based on the dosage. Low doses (75-81mg/day) are sufficient to irreversibly acetylate serine of cyclooxygenase (COX)-1. This action inhibits platelet's ability to generate thromboxane A2 leading to antithrombotic effect. Intermediate doses (650 mg to 4g/day) inhibit COX-1 and COX 2, leading to decreased production of prostaglandin leading to analgesic and antipyretic effects. High doses (4 – 8 g/day) are known to inhibit COX-2 leading to the anti-inflammatory effects in certain diseases such as rheumatic disorders [3]. When used for analgesic effect, the doses are between intermediate and high.

NSAID use has been associated with hypertension due to the inhibition of prostaglandins and sodium retention [4]. As known, sodium retention attracts water and increases blood volume leading to hypertension. SUN project reported 543 new cases of hypertension in Aspirin users (total number of participants = 9986) after adjusting for other confounding factors. It was concluded that daily use of Aspirin was associated with an increased risk of hypertension [4]. COX-2 is inhibited when high doses of Aspirin are taken for analgesic purpose, which leads to decreased production of COX-2 dependent endothelial synthesis of prostacyclin. Prostacyclin is cardioprotective and antithrombotic that relaxes vascular smooth muscle cells, dilates blood vessels and lower blood pressure. When it is inhibited, there is an increase in vascular resistance leading to hypertension [5]. The objective of our study is to see the correlation between Aspirin an NSAID and hypertension.

Methods

A cross sectional study design was used composed of adults above 20 years of age, both males and females from the general population. The study would include participants who took Aspirin as either a self-directed medication or physician directed as a preventive for cardiovascular diseases. Consent for surveys was obtained and permission was granted by the ARB (Anguillan Review Board). Surveys were formatted to include demographics, medical, family and social history. Comorbidities were evaluated by self-reporting in the medical history.

Study Population

The surveys were answered by 229 participants, 139 females and 90 males with ages ranging between 20 and 87 years. Participants who reported taking ASA were considered the target population while those who did not take ASA were used as a control group. 101 participants were in the target population and 128 were in the control group. The highest education attained in the target population was PhD degree and in the control population MD in process was the highest degree. About 53% of the total sample populations were employed while the rest was currently unemployed during the time of the survey.

Measurements

Assessment of Exposure; The questionnaire contained questions on the use of Aspirin, Ibuprofen and other NSAIDs. The participants were asked whether they took acetylsalicylic acid (ASA), what dosage they used (81mg or 375mg), the length of therapy and whether it was physician directed or self-directed. Assessment of Hypertension; the questionnaires asked if the participants were diagnosed with hypertension, or if they are on any hypertensive medications. The patients were also asked about family history of hypertension. Objective Blood Pressure (BP) readings were obtained by examiners during the time of the survey.

Measurement

Within the survey, the participants were asked about sociodemographic factors such as age, sex, education level, and employment status. The participants were also asked about Health-related habits (diet, smoking, alcohol consumption) and Clinical Variables (Personal and family history of Hypertension, Stroke, Diabetes and other heart diseases) in the questionnaire.

Statistical Analysis

A two tailed student T-test was used to compare means of age, gender and the various blood pressures between the two samples to generate a p-value. The data was analyzed comparing the target group with hypertension and the control group without hypertension. Other confounding variables such as BMI, diet, and family history were considered but were unable to control within our study. Any p-value discussed in this paper was generated from student T test.

Results

Table 1 below shows the baseline characteristics of the studied population along with the associated p-values. As

shown on the chart, primary outcome was significant with the p-value of 0.0008; however, secondary outcome was not statistically significant (p= 0.7) because whether the Aspirin was prescribed by physician or taken as a self-directed medication does not have influence in the mechanism of action of Aspirin. There was no statistical significance in the male gender between the control and the target groups (p= 0.054). Moreover, statistical significance was noted in female gender between the control and the target group (p= 0.004). Important significance was also seen within the gender of control group (p= 0.023). However, no important significance was seen in the gender between the target groups (p= 0.58). Other variables such as age was also found to be significant (p=0.00).

Baseline General Characteristics of Research Population			
	Control (128)	**Target Population (101)**	**P-Value**
Democraphic Data			
Mean Age	30-40	40-50	0.00*
Females (F)	30-40	40-50	
Males (M)	30-40	40-50	
Gender			
Females	74	67	
Males	55	34	
Gender Comparison			
Control (F) Vs Target (F)			0.004*
Control (M) Vs Target (M)			0.054
Control (F) Vs Control (M)			0.023*
Target (F) Vs Target (M)			0.58
Bp			0.0008*
Prescribed Vs Self-Directed			0.7
Social History			
Smoking			0.578
Yes	10	2	
No	118	99	
Alcohol			0.325
Yes	48	28	
No	80	76	
Medical History			
Myocardial Infarction	0	2	
Stroke	4	3	
Diabetes	11	8	
Cardiovascular	2	1	
Medications Reported In Both Groups			
Hctz			
Lisonopril			
Metformin			
Newly Diagnosed Htn	6	22	0.15

*Significant P<0.05

Table 1: Baseline Characteristics of the Studied Population.

Discussion

Studies have shown that NSAIDs may increase BP values, particularly in hypertensive patients [6,7]. However, while NSAIDs are reported in some studies to have reduced BP effects in normotensive individuals [8,9], some other studies reveal an increased risk of incident hypertension [10,11]. Research has shown that Aspirin could be a risk factor for hypertension and our research showed this to be true. The research that we conducted showed there is a correlation with Aspirin use and hypertension when comparing target group with the control; based on our p-value (p=.0008) which is our primary outcome. Aspirin has been used as a preventative measure for cardiovascular diseases as well as pain relievers for many years. But previous research has shown that Aspirin may increase the risk of hypertension for chronic users. A study done by Steven Novella found that Aspirin usage increased the risk of hypertension by 26% [12]. This study did not consider whether there was a correlation between the duration of Aspirin intake. Studies have also reported that compared with other NSAIDs, aspirin had a minimal BP effect after adjusting for sodium intake [13,14]. Furthermore, a systematic review and meta-analysis conducted recently by Li, *et al*. showed no significant difference in blood pressure between the aspirin and control groups in hypertensive patients, thus suggesting that aspirin has no effect on blood pressure [15]. These correlations might intrigue researchers to investigate physician-directed and self-directed use of Aspirin and its effects on hypertension. As for the study we conducted, we found no significant difference (p=0.7) between physician-directed and self-directed use of Aspirin which was our secondary outcome. BP effects of NSAIDs are supposed to correlate with the inhibition of the COX pathway. There are two isoforms of COX enzymes, i.e., COX-1 and COX-2. COX-1 is constitutively expressed in most tissues, while COX-2 is upregulated with inflammation and cell injury. While some NSAIDs may inhibit the COX-2 isoform, others may preferentially inhibit COX-1 or have a balanced effect [16].

As mentioned previously, Aspirin is the most used NSAID in the prophylactic management of cardiovascular health. An important factor to consider by clinicians before prescribing Aspirin to their patients is the benefits and risks of Aspirin. Not all patients are good candidates for ASA. Patients with history of heart attack, women older than 65 years, and those at increased risk of stroke or cardiovascular disease are all good candidates to be considered for ASA [17]. Nevertheless, this decision should be made on an individual basis. Allergies to Aspirin, asthma-induced by Aspirin, kidney disease, ulcers, and gout are all contraindication to Aspirin usage; therefore, patients with any of these contraindications would not be prescribed Aspirin even if they met the criteria to be on Aspirin [17]. Hence, patients, especially older and hypertensive individuals should be monitored for BP changes when initiating NSAID treatment [16].

Even though these are promising results, more research must be done to make a definite conclusion because we were unable to get a large sample size. We anticipated enrolling about 250 people in this study but due to decreased amount of people taking Aspirin on this island as well as restrictions from the hospital, made it difficult for us to meet our goal. Due to the limitation of the small sample size, we were unable to conclude any major clinical significance based on our study alone. The best way to approach this study is to do a double-blinded study, in which both the participants and the researcher would not know which group took ASA and which group took the placebo drug. Although this approach may take some time, this will allow us to control any confounding variables such as ethnicity, family history, lifestyle, etc. and potentially give an accurate result. Another limitation that we encountered with our research was that we lacked the serial blood pressure data necessary to fully diagnose or identify participants at increased risk of developing hypertension. This study would yield better results if the area in which the study was conducted had more prevalent use of Aspirin as well as conducting the study over a good period. The questionnaires were limiting as to how much information we could obtain from the participants. Our older participants had a hard time recalling a lot of the information which may have resulted in some false information. Further study should be conducted to fix all these limitations as well as find a different approach to collecting the data rather than solely relying on the participant's memory.

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