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ORIGINAL ARTICLE

Aspirin resistance: Prevalence and clinical outcome in Egypt

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KEYWORDS

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Abstract *Introduction:* The antiplatelet drug aspirin is considered as a cornerstone in medical treatment of patients with CV or cerebrovascular diseases. Despite its use, a significant number of patients had recurrent adverse ischemic events. Inter-individual variability of platelet aggregation in response to aspirin may be an explanation for some of these events. Multiple trials have linked aspirin resistance to these adverse events.

Objectives: The aim of this study was to estimate the prevalence of aspirin resistance among patients with coronary artery disease (CAD) in Egypt and evaluate its impact on clinical outcome.

Methods: A total of 50 patients with documented history of CAD were included; they were on aspirin 150 mg/day for more than seven days and no other antiplatelet drugs. They were evaluated for aspirin resistance using light transmission aggregometry. Aspirin resistance was defined as a mean aggregation of >20% with 0.5 mg/ml arachidonic acid. They were followed up after six months for cardiac death, unstable angina (UA), myocardial infarction (MI), and stroke.

Results: Prevalence of aspirin resistance was 48% in our study group. Aspirin resistance was significantly higher in patients with family history of CAD ($p = 0.044$), smoking ($p = 0.011$), history of MI ($p = 0.024$), history of percutaneous coronary intervention (PCI) ($p = 0.001$), and concomitant NSAIDs intake ($p = 0.047$). Moreover, aspirin resistance was more common among patients with multi-vessel CAD ($p = 0.024$). Aspirin-resistant patients had a significantly higher rate of UA ($p = 0.001$) and all major adverse cardiac events (MACE) ($p < 0.001$).

1. Introduction

Atherothrombosis has long been recognized as a key contributor to cardiovascular (CV) events such as myocardial infarction (MI), unstable angina (UA), stroke, and transient ischemic attack (TIA). Given the important role of platelets in acute thrombus formation, antiplatelet therapies have become one of the cornerstone treatments of these atherothrombotic syndromes.

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In 1897, Felix Hoffman first developed acetylsalicylic acid and registered it under the name aspirin [1]. Aspirin specifically inhibits thromboxane (TX) A2 generation by irreversibly acetylating a serine residue at position 529 of the cyclooxygenase-1 (COX-1) enzyme [2].

The Antiplatelet Trialists Collaboration has shown a 25% reduction in strokes, MI, and CV deaths with the use of aspirin. However, aspirin has been shown to have variable antiplatelet effect in individual patients [3]. Incidence of treatment failure occurs with any drug and aspirin is not an exception, raising the possibility of aspirin resistance [4,5]. Aspirin resistance has been associated with adverse clinical events, increasing both morbidity and mortality [6–11].

2. Patients and methods

The protocol of this study was reviewed and approved by the Local Institutional Ethics Committee of Critical Care Department, Faculty of Medicine, Cairo University, Egypt.

Additionally, written informed consent entailing all moral and ethical consideration was obtained from all the patients participating in the study.

2.1. Patients

Our study was conducted prospectively on patients admitted to Critical Care Department, Faculty of Medicine, Cairo University, in the period from December 2009 to December 2010. The patients included in the study had a documented history of coronary artery disease (CAD) such as UA, MI, percutaneous coronary intervention (PCI), and/or coronary artery bypass graft surgery (CABG). Patients were excluded from the study on the basis of the following reasons: (1) administration of unfractionated heparin or low-molecular-weight heparin LMWH in the last 24 h before platelet aggregation testing, (2) personal history of bleeding disorders, (3) history of myeloproliferative disorder, (4) major surgical procedure in the last one week, (5) platelet count less than $150 * 10^9$/L or more than $450 * 10^9$/L.

Based on the above criteria, 50 patients were included for the study. Of the total selected patients, 30 (60%) patients were male, 35 (70%) were hypertensive, 25 (50%) were diabetic, 19 (38%) were smokers, 23 (46%) were obese, 27 (54%) had a family history of CAD, 13 (26%) had a history of MI, and nine (18%) had a history of PCI.

All patients were maintained on aspirin (150 mg/day) for more than seven days. No other antiplatelet therapies were implemented for their treatment.

2.2. Platelet function testing

Three samples of whole blood were collected in 3.8% sodium citrate (blue capped tube). The last dose of aspirin was administered within 1–24 h before sampling.

Blood samples were processed within two hrs of blood collection. Whole-blood specimens were centrifuged for 10 min at 120 g to obtain platelet-rich plasma (PRP). Platelet aggregation was performed on CHRONO-LOG platelet aggregometer (Chrono-Log Corporation, Havertown, USA) using the agonist arachidonic acid (AA) at 0.5 mg/ml. The tube containing platelet-rich plasma (PRP) was inserted in the aggregometer between a light source and a photocell, and then the agonist was added. When the platelets started to aggregate, the light transmission increased, which was directly proportional to the percent of platelet aggregation. Aspirin resistance was defined as a mean aggregation of $>20\%$ with 0.5 mg/ml AA.

2.3. Clinical follow up and study endpoints

In-hospital and post-discharge (after six months) follow-up data were prospectively collected. Compliance to medical treatment including aspirin was addressed. The study endpoints were CV death, UA, MI, and non-hemorrhagic cerebrovascular strokes. Other clinical events in the selected patients were assessed on the basis of phone interviews, outpatient follow up, and the information gathered from the hospital readmission records.

2.4. Statistical analysis

Data were statistically analyzed and presented as descriptive statistics, such as mean ± standard deviation (SD), frequencies (number of cases), and percentages, etc.

Comparison of numerical variables was done using Student's t test for independent samples. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used when the expected frequency was less than 5. Accuracy was represented using the terms sensitivity and specificity.

For our study, p values less than 0.05 were considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

3. Results

3.1. Prevalence of aspirin resistance

On the basis of the results of light transmission aggregometry, the patients were classified into aspirin sensitive (26/50; 52%) and aspirin resistant (24/50; 48%) as shown in Fig. 1.

3.2. Predictors of aspirin resistance

As shown in Table 1, aspirin resistance was found to be significantly higher in patients with a family history of CAD (70.8% vs. 38.5%, $p = 0.044$), smoking (58.3% vs. 19.2%, $p = 0.011$), MI (41.7% vs. 11.5%, $p = 0.024$), PCI (37.5% vs. 0%, $p = 0.001$), and concomitant non-steroidal anti-inflammatory

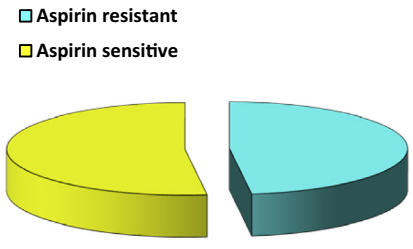

Figure 1 Prevalence of aspirin resistance.