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Associations Between PFA-Measured Aspirin Resistance, Platelet Count, Renal Function, and Angiotensin Receptor Blockers

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Abstract

Aspirin resistance is used to describe patients who are undergoing aspirin therapy but fail for the inhibition of thromboxane biosynthesis in platelets. Although the true mechanism is unclear, drug–drug interaction remains a possible factor. The study aimed to determine whether there was association between aspirin resistance and the concomitant cardiovascular medication. Using the Platelet Function Analyzer-100 system, aspirin resistance was evaluated in aspirin-treated patients from the outpatient department. The associations between aspirin resistance and their concomitant common cardiovascular medication were analyzed. Aspirin resistance was prevalent in 147 (17.7%) of 831 patients. Concomitant angiotensin receptor blocker (ARB) treatment and low platelet count were associated with aspirin response ($P = .04$, .02, respectively). Multivariate logistic regression analysis results showed an association between aspirin response and ARB therapy (adjusted odds ratio [OR] 1.48; 95% confidence interval, CI: 1.08-2.18). And the association was blunted when platelet count was considered (adjusted OR 1.43, 95% CI: 0.92-2.23). In ARB-treated patients, increased creatinine and decreased hematocrit laboratory data increased the risk of aspirin resistance ($P = .02$, .04, respectively), and the effect of platelet count on aspirin resistance was diminished by ARB therapy. Concomitant ARB treatment in aspirin-treated patients decreased the risk of aspirin resistance, and the effect was dependent on low platelet count. In ARB-treated patients, increased creatinine and decreased hematocrit data increased the risk of aspirin resistance. In addition, the effect of platelet count on aspirin resistance was diminished by ARB treatment.

Keywords

aspirin resistance, angiotensin receptor blocker, platelet count, renal function, PFA-100

Introduction

Platelet activation is a crucial mechanism in atherothrombotic disease. Aspirin is an effective antiplatelet agent and exhibits its action by inhibiting the platelet cyclooxygensase 1 (COX-1) enzyme and by preventing thromboxane A2 (TXA2) synthesis. Aspirin is widely used for the primary and secondary prevention of cardiovascular events. Despite the strong evidence for the preventive effects of aspirin in cardiovascular events, aspirin therapy can be ineffective in some patients.[1] This phenomenon has led to the concept of "aspirin resistance" and has prompted the investigation of the possible mechanisms involved. In addition to genetic factors, poor compliance, clinical features (diabetes, congestive heart failure, acute coronary syndrome, obesity, and inflammation status), and alternative pathways other than COX-1 can be possible mechanisms in aspirin resistance. And drug–drug interaction also remains one possible factor related to aspirin resistance. Clinically, there are multiple risk factors related to vascular atherosclerosis. Many chronic diseases such as hypertension, diabetes, and hyperlipidemia are well-known cardiovascular risk factors and frequently found to be associated with cardiovascular disease. Polypharmacy is common in cardiovascular prevention, and drug–drug interaction can develop and influence the aspirin response.[2,3]

There are several clinical methods for evaluating aspirin resistance. Although the effect of aspirin on thromboembolic inhibition is complicated, each method for aspirin resistance offers clinically relevant data.[4] Despite the lack of a standard laboratory method for assessing aspirin resistance, the Platelet

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Function Analyzer (PFA)-100 system is a well-documented, convenient, and quick instrumental method for screening platelet function.[5] In this study, we aimed to use this conventional method to evaluate whether there was association between aspirin resistance and concomitant common medication for cardiovascular prevention.

Methods

Patients

Patients with and without known cardiovascular events receiving treatment of daily aspirin (100 mg; available dose in Taiwan) for $\geq$2 weeks followed up in our cardiovascular outpatient department from January 2008 to July 2009 were enrolled in the study. All the patients underwent a blood test and evaluation for aspirin resistance at our outpatient department. To avoid adverse interaction with other drugs, the initial exclusion criteria were patients who regularly consumed medications such as nonsteroidal anti-inflammatory drugs as well as anticoagulant, immunosuppressive, or cytotoxic drugs. Patients with concomitant use of other antiplatelet medication (clopidogrel, dipyridamole, cilostazol, etc) were also excluded. Other exclusion criteria were the presence of acute or chronic inflammatory disease, acute liver or kidney disease, myeloproliferative disorder, thyroid disease, or malignancy. To avoid possible influencing factors for measurement of aspirin resistance, patients' basic characteristics, past medial history, and other laboratory data were checked at the same time with aspirin resistance measurement. All the data were collected for analysis to find whether there were associations between those factors and aspirin resistance. Patients who were included in the study agreed to participate by providing written informed consent prior to giving blood sample for aspirin resistance measurement. The study was approved by Research Ethics Committee of the Taipei City Hospital. Blood samples were drawn by direct venipuncture at room temperature. All of the blood samples were collected during the daylight hours when the participants visited the outpatient department. Other laboratory data, such as biochemistry (fasting sugar, blood urea nitrogen [BUN], creatinine [Cr], aspartate transferase [GOT], alanine aminotransferase [GPT], total cholesterol [Chol], triglyceride [TG], low-density cholesterol [LDL-C], high-density cholesterol [HDL-C], and hemoglobin A_{1C} [HbA_{1C}]) and blood routine data (white blood cell count, red blood cell count, hemoglobin [Hb], hematocrit [Hct], and platelet count) were collected at the same time. After checking the laboratory data, patients with platelet counts lower than 100 000/mm^3 or higher than 450 000/mm^3 and/or hematocrit levels lower than 30% or higher than 52% were excluded from this final study finally. To find whether there were associations between aspirin resistance and concomitant medication, medication records of all the patients were carefully reviewed. We traced back their medication records and evaluated whether there were association between aspirin resistance and concomitant medication including drugs for hypertension (angiotensin receptor blocker [ARB], angiotensin-converting enzyme inhibitor [ACE I], calcium channel blocker [CCB], and β-blocker [BB]), hyperlipidemia (fibrate and statin), and diabetes (biguanide, sulfonylureas, thiazolidinedione, and so on). The included patients were divided into 2 groups with regard to aspirin resistance for analysis. Moreover, if association did exist with some drugs, we thought to find out the possible factors related to aspirin resistance in such subgroup and call attention to further prevention. Common cardiovascular medication as for hypertension, diabetes, hyperlipidemia, nitrate, and diabetes were traced back for 3 months. Finally, a total of 831 patients were included in our study.

Measurement of Aspirin Resistance

Aspirin resistance was measured by PFA-100 in patients who were undergoing aspirin therapy at the outpatient department. Immediately after blood collection, 2 mL of venous blood were collected and loaded into prefabricated proprietary cartridges containing a combination of collagen and epinephrine as platelet agonists. Platelet reactivity was measured using the PFA-100 system (Siemens, Munich, Germany), which is a convenient method for assessing platelet function for clinical evidence and has the validity correlated with clinical cardiovascular diseases.[6-8] The time to aperture occlusion (the closure time) was recorded in seconds and was inversely related to the degree of shear-induced platelet activity. Platelet Function Analyzer-100 closure time was detected, and a closure time <193 seconds was used to define aspirin resistance according to criteria established by the manufacturer.[9]

Statistical Analysis

All numerical variables with normal distribution were expressed as the mean mean $\pm$ standard deviation (SD). Differences in baseline characteristics between 2 groups were determined by the independent *t* test for continuous variables and the χ^2 test for categorical variables. Using logistic regression, concomitant cardiovascular drugs were examined to determine their relationship with aspirin resistance, and the adjusted odds ratios (ORs) with 95% confidence were calculated. Two-sided values of $P < .05$ were considered statistically significant. SPSS for Windows (version 17.0; Chicago, Illinois) was used for all statistical analysis.

Results

Demographic and Clinical Characteristics in Those With/Without Aspirin Resistance

Overall, 147 (17.7%) of the 831 patients were diagnosed with aspirin resistance. Patients with ARB treatment had a lower risk of aspirin resistance than patients without ($P = .04$). The phenomenon was not seen in other common cardiovascular medication such as antihypertension drugs (ACE I, CCB, and BB), hyperlipidemia medication (statin and fibrate), nitrate, and oral antidiabetic drugs (OAD). No significant differences

occurred between the aspirin resistance and the aspirin response groups regarding their age, gender, basic characteristics (height, weight, body mass index, and systolic/diastolic blood pressure), comorbidities (hypertension, dyslipidemia, diabetes mellitus, and gout), habits of cigarette smoking, and alcohol drinking. Comparing the laboratory data between patients with and without aspirin resistance, those with aspirin resistance had higher platelet counts than those without ($P = .02$). The basic demographics, characteristics, comorbidities, and laboratory data as well as the differences between these data of the 2 groups are shown in Table 1.

Associations Between Aspirin Resistance and Concomitant Common Cardiovascular Medications

The associations between aspirin resistance and concomitant cardiovascular medication were analyzed by logistic regression. In univariate analysis, aspirin response was associated with platelet count (OR: 0.996; 95% confidence interval [CI]: 0.99-1.00) but not any of cardiovascular medications. In multivariate analysis, platelet count remained associated with aspirin response (adjusted OR: 0.996; 95% CI: 0.99-1.00). And for concomitant cardiovascular medications, the initial results showed ARB-treated patients shared a higher aspirin response than those without ARB treatment (adjusted OR: 1.48; 95% CI: 1.08-2.18). However, the association was not kept in ARB treatment when platelet count was adjusted as a variable (adjusted OR 1.43; 95% CI: 0.92-2.23). The results were shown in Table 2.

Comparison Between Those With/Without Aspirin Resistance in ARB-Treated Patients

In ARB-treated patients, there were 54 (15.1%) of 358 patients found with aspirin resistance. Although hypertension, diabetes, smoking, and alcoholic drinking had a higher risk of aspirin resistance; however, there was no significant difference. Neither significant difference was found between aspirin resistance and other common cardiovascular prevention drugs in ARB-treated patients. In laboratory data, increased blood creatinine level and decreased hematocrit data increased the risk of aspirin resistance ($P = .02$, .04, respectively). Different from the results based on total included population, platelet count was higher in aspirin resistance group than in the aspirin response group, but they did not reach statistical significance in ARB-treated patients. The basic demographics, characteristics, comorbidities, and laboratory data as well as the differences between data of the 2 groups in ARB-treated patients are shown in Table 3.

Table 1. Demographic Data of Patients Included in the Study.

Variables	Total 831 (%)	Asprin Resistance 147 (%)	Aspirin Response 684 (%)	*p*
Gender (male)	592 (71.2%)	106 (72.1%)	468 (68.4%)	0.17
Age (years)	65 ± 11	65 ± 12	66 ± 11	0.40
Height (cm)	161 ± 10	161 ± 9	162 ± 9	0.39
Weight (kg)	70 ± 13	69 ± 13	70 ± 13	0.29
Waist (cm)	92 ± 12	91 ± 12	93 ± 11	0.11
BMI	27 ± 4	27 ± 4	27 ± 4	0.42
SSBP (mmHg)	130 ± 16	129 ± 17	131 ± 15	0.09
SDBP (mmHg)	75 ± 11	75 ± 13	76 ± 10	0.21
PFA (seconds)	265 ± 65	140 ± 31	292 ± 28	<0.001
Dyslipidemia	433 (52.1%)	69 (46.9%)	325 (47.5%)	0.45
Hypertension	605 (72.8%)	108 (73.5%)	536 (78.4%)	0.09
DM	274 (32.9%)	47 (32.0%)	227 (33.2%)	0.38
Gout	106 (12.7%)	16 (10.9%)	90 ((13.2%)	0.22
Smoke	130 (15.6%)	24 (16.3%)	106 (15.5%)	0.42
Drink	60 (7.2%)	9 (6.1%)	51 (7.5%)	0.27
Concomitant Drugs				
ARB	358 (43.1%)	54 (36.7%)	304 (44.4%)	0.04
ACE I	105 (12.6%)	17 (11.6%)	88 (12.9%)	0.33
ARB or ACE I	463 (55.7%)	71 (48.3%)	392 (57.3%)	0.03
CCB	424 (51.0%)	75 (51.0%)	349 (51.0%)	0.50
BB	395 (47.5%)	64 (43.5%)	331 (48.4%)	0.14
Statin	286 (34.4%)	53 (36.1%)	233 (34.1%)	0.32
ARB and statin	134 (16.2%)	21 (14.3%)	113 (16.5%)	0.25
Fibrate	36 (4.3%)	6 (4.1%)	30 (4.4%)	0.43
Nitrate	260 (31.3%)	47 (32.0%)	213 (31.1%)	0.42
OAD	242 (29.1%)	44 (30.0%)	198 (28.9%)	0.41
Laboratory data				
F/S (mg/dL)	111 ± 28	107 ± 26	112 ± 29	0.053
BUN (mg/dL)	20 ± 9	22 ± 9	20 ± 9	0.11
Cr (mg/dL)	1.3 ± −1.0	1.4 ± 1.0	1.2 ± 0.9	0.16
Uric acid (mg/dL)	7 ± 5	6 ± 2	7 ± 5	0.31
GOT (mg/dL)	25 ± 11	24 ± 10	26 ± 11	0.17
GPT (mg/dL)	29 ± 28	26 ± 28	30 ± 28	0.15
Chol (mg/dL)	194 ± 69	184 ± 43	196 ± 72	0.054
TG (mg/dL)	150 ± 90	145 ± 83	151 ± 92	0.28
LDL-C (mg/dL)	101 ± 31	109 ± 35	112 ± 30	0.30
HDL-C (mg/dL)	52 ± 25	50 ± 16	52 ± 26	0.36
HbA1C (%)	7 ± 1	7 ± 2	7 ± 1	0.17
WBC ($10^{\times 3}$/dL)	7 ± 2	7 ± 2	7 ± 2	0.27
RBC ($10^{\times 6}$/dL)	5 ± 2	5 ± 1	5 ± 3.	0.13
Hb (g/dL)	14 ± 2	14 ± 2	14 ± 2	0.10
Hct (%)	42 ± 17	40 ± 5	42 ± 18	0.13
Platelet ($10^{\times 3}$/uL)	228 ± 55	238 ± 59	226 ± 54	0.02

Abbreviations: ACE I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, β-blocker; BMI, body mass index; BUN, blood urea nitrogen; CCB, calcium channel blocker; Chol, total cholesterol; Cr, creatinine; DM, diabetes mellitus; F/S, fasting/sugar; GOT, aspartate transferase; GPT, alanine aminotransferase; Hb, hemoglobin; HbA_{1C}, hemoglobin A_{1C}; Hct, hematocrit; HDL-C, high-density cholesterol; LDL-C, low-density cholesterol; OAD, oral antidiabetic drugs; RBC, red blood cell count; PFA, platelet function analyzer; SSBP, systemic systolic blood pressure; SDBP, systemic diastolic blood pressure; TG, triglyceride; WBC, white blood cell count.

Discussion

In clinical practice, drug–drug interaction can influence efficacy of medical treatment. Aspirin has a widespread use in cardiovascular disease prevention. Most patients treated with aspirin concomitantly receive other medication due to their underlying comorbidities such as hypertension, diabetes, and hyperlipidemia. However, the information between aspirin resistance and concomitant medication is currently limited. We included aspirin-treated patients with regular follow-up at

Table 2. Medications Related to Laboratory Aspirin Response in 831 Included Patients.

Medications (n)	Univariate Analysis Odds Ratio (95% CI)	Multivariate Analysis Odds Ratio (95% CI) Model 1	Multivariate Analysis Odds Ratio (95% CI) Model 2
ARB (358)	1.38 (0.95-1.99)	1.48 (1.08-2.18)	1.43 (0.92-2.23)
ACE I (105)	1.13 (0.65-1.96)	1.34 (0.75-2.39)	1.03 (0.56-1.89)
CCB (424)	1.00 (0.70-1.43)	0.96 (0.66-1.38)	
BB (395)	1.22 (0.85-1.74)	1.23 (0.86-1.78)	1.14 (0.76-1.74)
Statin (286)	0.91 (0.63-1.33)	0.91 (0.67-1.38)	0.92 (0.60-1.42)
Fibrate (36)	1.08 (0.44-2.64)	1.05 (0.42-2.59)	
Nitrate (260)	0.96 (0.66-1.41)	0.96 (0.65-1.42)	
OAD (242)	0.95 (0.65-1.41)	0.92 (0.62-1.38)	0.92 (0.58-1.52)
Platelet (per $10^{\times 3}$/uL)	0.996 (0.99-1.00)		0.996 (0.99-1.00)

Abbreviations: ACE I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, β-blocker; CCB, calcium channel blocker; CI, confidence interval; OAD, oral antidiabetic drugs.

our outpatient department and tried to find whether there was association between them.

Laboratory Aspirin Resistance and Clinical Manifestations

In analyzing the associations between aspirin resistance and clinical manifestations, platelet count was the only factor related to the risk of aspirin resistance. As for concomitant cardiovascular medication, aspirin resistance was decreased in ARB-treated patients rather than other medication. The link between aspirin and ARB has been reported. Similar to our study, analyzed by PFA-100, a prior study included patients who received endovascular surgery procedure. The results showed ARB treatment was the only factor associated with decreased aspirin resistance.[10] The findings fully supported our data.

The association between aspirin resistance and statin therapy had been studied. There were prior reports about statin therapy reducing platelet TXA2 synthesis.[11,12] A prior study, using PFA-100, demonstrated high-dose statin therapy improved aspirin resistance in patients with coronary artery disease, with concomitant decrease inLDL-C.[13] However, studies in the correlations between aspirin resistance, statin therapy, and LDL level were not consistent. Another study showed statin add-on aspirin-treated patients might improve platelet sensitivity but beyond the action of lipid lowing.[14] The true mechanism between aspirin resistance and statin was not fully understood, and inflammation had been hypothesized as a mechanism.[15] The relation between statin and aspirin resistance was not found in our result. Our results showed there was higher statin therapy in patients with aspirin resistance than those without, but the data were not statistically significant. And the effect of ARB in aspirin response was diminished in patient with ARB plus statin therapy. Different from prior study, all kinds of statins were included as a group without being classified in our study. We were not sure whether our results would be influenced by different statin potential, dosage, and even therapeutic duration.[16] In addition, in our finding, aspirin response group had higher data in total cholesterol, LDL-C, and HDL-C than aspirin resistance group. We did not know whether there were interactions between statin therapy and cholesterol level in aspirin resistance. This

Table 3. Demographic Data of ARB-Treated Patients.

Variables	Total 358 (%)	Aspirin Resistance 54 (%)	Aspirin Response 304 (%)	*P*
Gender (male)	240 (71.2%)	38 (72.1%)	202 (68.4%)	0.53
Age (years)	66 ± 11	67 ± 11	65 ± 11	0.45
Height (cm)	161 ± 9	161 ± 8	161 ± 9	0.79
Weight (kg)	72 ± 13	70 ± 13	72 ± 13	0.30
Waist (cm)	95 ± 10	93 ± 10	95 ± 10	0.44
BMI	27 ± 4	27 ± 4	28 ± 4	0.27
SSBP (mmHg)	134 ± 17	130 ± 19	135 ± 17	0.11
SDBP (mmHg)	76 ± 12	75 ± 13	76 ± 11	0.68
PFA (seconds)	272 ± 58	145 ± 31	294 ± 22	<0.001
Dyslipidemia	178 (49.7%)	23 (42.6%)	155 (51.0%)	0.26
Hypertension	317 (88.5%)	50 (92.6%)	267 (87.8%)	0.31
DM	135 (37.7%)	21 (38.9%)	114 (37.5%)	0.84
Gout	58 (16.2%)	7 (13.0%)	51 (16.8%)	0.48
Smoke	55 (15.4%)	9 (16.7%)	46 (15.1%)	0.76
Drink	27 (7.5%)	5 (9.1%)	22 (7.2%)	0.60
Concomitant Drugs				
CCB	213 (51.0%)	30 (51.0%)	183 (51.0%)	0.52
BB	171 (47.5%)	25 (43.5%)	146 (48.4%)	0.82
Statin	134 (34.4%)	21 (36.1%)	113 (34.1%)	0.81
Fibrate	16 (4.3%)	3 (4.1%)	13 (4.4%)	0.68
Nitrate	119 (31.3%)	17 (32.0%)	102 (31.1%)	0.77
OAD	122 (29.1%)	18 (30.0%)	104 (28.9%)	0.90
Laboratory data				
F/S (mg/dL)	114 ± 31	105 ± 30	116 ± 31	0.052
BUN (mg/dL)	21 ± 9	25 ± 10	20 ± 9	0.051
Cr (mg/dL)	1.2 ±0.6	1.4 ± 1.0	1.2 ± 0.4	0.02
Uric acid (mg/dL)	7 ± 2	6 ± 1	7 ± 2	0.52
GOT (mg/dL)	26 ± 11	25 ± 7	27 ± 11	0.52
GPT (mg/dL)	26 ± 15	20 ± 10	27 ± 16	0.44
Chol (mg/dL)	199 ± 91	191 ± 37	200 ± 98	0.54
TG (mg/dL)	161 ± 102	161 ± 103	161 ± 102	0.98
LDL-C (mg/dL)	110 ± 30	105 ± 28	110 ± 30	0.46
HDL-C (mg/dL)	53 ± 32	53 ± 16	53 ± 34	0.99
HbA1C (%)	7 ± 1	8 ± 2	7 ± 1	0.14
WBC ($10^{\times 3}$/dL)	7 ± 2	7 ± 2	7 ± 2	0.93
RBC ($10^{\times 6}$/dL)	5 ± 2	5 ± 1	5 ± 3.	0.52
Hb (g/dL)	14 ± 2	13 ± 2	14 ± 2	0.09
Hct (%)	41 ± 6	40 ± 6	42 ± 6	0.04
Platelet($10^{\times 3}$/uL)	230 ± 58	240 ± 59	229 ± 58	0.27

Abbreviations: ARB, angiotensin receptor blocker; BB, β-blocker; BMI, body mass index; BUN, blood urea nitrogen; Cr, creatinine; CCB, calcium channel blocker; Chol, total cholesterol; DM, diabetes mellitus; F/S, fasting/sugar; GOT, aspartate transferase; GPT, alanine aminotransferase; HbA_{1C}, hemoglobin A_{1C}; Hb, hemoglobin; Hct, hematocrit; HDL-C, high-density cholesterol; LDL-C, low-density cholesterol; OAD, oral antidiabetic drugs; RBC, red blood cell count; PFA, platelet function analyzer; SDBP, systemic diastolic blood pressure; SSBP, systemic systolic blood pressure; TG, triglyceride; WBC, white blood cell count.

could obscure the relation between statin treatment and aspirin resistance in our results. It needs further experimental data to clarify.

Some prior studies documented there was a higher prevalence of aspirin resistance in patients with diabetes than those without.[17] This was not found in our results. As for the association between aspirin resistance and OAD, present data are scanty and limited.[18,19] In our study, we used OAD for all agents treated for diabetes, and the results showed no association between aspirin resistance and OAD used. Similar to hypertension, medications for diabetes control are various with different mechanisms. Because our included population were patients who took follow-up at cardiovascular outpatient department, we could not analyze the association between aspirin resistance and different types of OAD due to our limited diabetes population. Also, we could not show whether insulin therapy had different effect on platelet function from OAD therapy.

Association Between Concomitant Cardiovascular Medication, Platelet Count, and Aspirin Resistance

In multivariate analyzing the associations between aspirin resistance and concomitant cardiovascular medications, the results showed ARB treatment shared higher aspirin response in our initial results. However, the association between ARB and aspirin resistance was blunted when aspirin count was considered. Basically, angiotensin plays a role in prothrombotic activity, and microvascular thrombosis process is mediated by angiotensin II.[20,21] The ARB abolished the prothrombotic activity of angiotensin. Although the connection between ARB and thrombosis had been documented, because of included patient's various characteristics, different physiological, clinical situation, and lack of large study, the relation between platelet function and ARB in clinical data is insufficient and equivocal. Some studies demonstrated the benefit of ARB on platelet function for hypertension treatment in different populations.[22-24] Our results included 831 outpatient department patients and suggested the link between aspirin resistance and ARB. In addition, our data evidenced the association could be platelet count involved. As the detailed connections between them, it could be complex and further study is needed.

Factors Related to Aspirin Resistance in ARB-Treated Patients

To examine the possible factors influencing aspirin resistance in patients treated with ARB, we reviewed 368 patients, and the result showed increased creatinine and decreased hematocrit data shared high risk of aspirin resistance. The connection between chronic kidney disease and pharmacodynamics response to aspirin has been documented.[25] The effect of impaired renal function on aspirin resistance was not found in our initial results but was evidenced in ARB-treated patients in our study. At present time, the data of the relation between aspirin resistance, renal function, and ARB are scanty and limited. Our results hinted possible correlations between them. The other influencing factor for aspirin resistance in ARB-treated patients was hematocrit data. We think this could be explained by the connection between renal function impairment and lower hematocrit data, although we did not analyze it. Interesting, another finding in our data demonstrated platelet count was not associated with aspirin resistance under ARB treatment. This enhanced the relation between platelet function, platelet count, and ARB.

Conclusion

Our study demonstrated concomitant ARB treatment in aspirin-treated patients increased aspirin response, and the effect was dependent on platelet count. In ARB-treated patients, increased creatinine and decreased hematocrit increased the risk of aspirin resistance, and the relation between platelet count and aspirin resistance was diminished after ARB treatment.

Limitations

Our observational study suggested the relations between ARB treatment, platelet count, renal function, and aspirin resistance. The true mechanisms remain unclear, and further study is needed.

Declaration of Conflicting Interests

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