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Effect of low-dose acetylsalicylic acid on perioperative platelet reactivity in patients undergoing off-pump coronary artery bypass grafting

Reaktywność płytek krwi we wczesnym okresie po pomostowaniu tętnic wieńcowych bez użycia krążenia pozaustrojowego u pacjentów stosujących małą dawkę kwasu acetylosalicylowego

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Abstract

Introduction. Acetylsalicylic acid (ASA) is the antiplatelet drug most used in the perioperative period in patients undergoing coronary artery bypass grafting (CABG). Off-pump coronary artery bypass grafting (OPCAB) is likely to alter platelet (PLT) function to a lesser extent than CABG with the use of cardiopulmonary bypass and may potentially result in high on-aspirin platelet reactivity (HAPR) in the postoperative period.

Materials and methods. The aim of this prospective study was to characterise serum thromboxane B_2 (TXB_2) variability and ASA-dependent platelet reactivity in patients with stable coronary artery disease undergoing OPCAB treated with a single daily dose of 75 mg of ASA. Blood sampling was performed 2 hours and 24 hours after ASA intake on the day before surgery, and on the 2nd and 7th days after the operation.

Results. A PLT counts reduction and a mean platelet volume increase were observed on the 2nd day after OPCAB. A PLT counts increase was found on the 7th postoperative day. A significant increase ($p = 0.03$) in the percentage of patients with insufficient laboratory ASA efficacy (defined by serum $TXB_2 \geq 7.2$ ng/mL) was observed on the 7th postoperative day compared to preoperative values (52% vs 20% respectively, $p = 0.02$). A significant increase in median platelet reactivity and in the percentage of patients with HAPR (defined by VerifyNow® Aspirin test result ≥ 550 ARU) was observed on the 7th postoperative day in comparison with the values before OPCAB (48% vs 12%, $p = 0.007$).

Conclusions. In the group of patients taking a standard daily dose of 75 mg of ASA, a substantial number of patients failed to attain optimal inhibition of serum TXB_2 or had HAPR before surgery and on the 7th day after OPCAB. A significant decrease in serum TXB_2 levels on the 2nd day after OPCAB did not correlate with PLT reactivity. The optimal dose of ASA is of interest for further studies of efficacy and clinical outcomes after OPCAB.

Key words: acetylsalicylic acid, coronary artery bypass grafting, thromboxane, platelet reactivity

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Introduction

Acetylsalicylic acid (ASA) is the most commonly used antiplatelet drug in the perioperative period in patients undergoing coronary artery bypass grafting (CABG). ASA induces platelet dysfunction by irreversible inhibition of the cyclooxygenase 1 (COX-1) enzyme in platelets [1]. Damage to the vascular endothelium during CABG leads to platelet (PLT) activation and many other factors may increase the risk of early thrombotic occlusion of vein grafts. Perioperative use of ASA decreases vein graft failure, the rate of perioperative cardiovascular complications and, consequently, morbidity and mortality [2–4].

The use of cardiopulmonary bypass during CABG interferes with platelet reactivity [5]. Off-pump coronary artery bypass grafting (OPCAB) is likely to alter platelet function to a lesser extent and may potentially result in high on-aspirin platelet reactivity (HAPR) in the postoperative period [6, 7]. HAPR is known to be related to graft failure [8]. The effect of low-dose acetylsalicylic acid on perioperative platelet reactivity in patients who are undergoing OPCAB has rarely been studied.

The aim of this study was to characterise serum thromboxane B_2 (TXB_2) variability and ASA-dependent platelet reactivity (VerifyNow® Aspirin test) in patients with stable coronary artery disease undergoing OPCAB, treated with a standard single dose of 75 mg of ASA in the perioperative period.

Materials and methods

Patients

In this prospective study, patients with stable coronary artery disease scheduled to undergo elective CABG at the Department of Cardiac Surgery at the First Department of Cardiology of the Medical University of Warsaw were screened. All patients were chronically on 75 mg of ASA in a single daily dose before the operation. After receiving institutional review board approval (KB/154/2012) on 12 June 2012, and obtaining informed written consent from all the patients, we enrolled 25 elective OPCAB patients who started the ASA study (EC, enteric-coated tablets; Acard®, Warszawskie Zakłady Farmaceutyczne Polfa S.A.) regimen one day before surgery and continued until the seventh postoperative day. Exclusion criteria were unstable angina, acute coronary syndrome or myocardial infarction or percutaneous coronary intervention or thrombolysis at least six weeks before the operation, the intake of any platelet inhibitor other than enteric-coated form of ASA (75 mg) during the four weeks prior to surgery, co-medication of non-steroidal anti-inflammatory drugs, known bleeding disorder or kidney failure, preoperative platelet count outside of the range 100,000–450,000/ /μL or a haemoglobin level below 8 g/dL, major combined operations such as aortic and/or mitral valve replacement, the preoperative use of a mechanical heart assist device, and an emergency operation. Patients with a haematocrit under 25% were also excluded. All operations were performed without the use of extracorporeal circulation.

Blood collection

The effectiveness of acetylsalicylic acid was analysed by determining the concentration of thromboxane B_2 in blood serum as a measure of COX activity in the blood. Laboratory evaluation of platelet reactivity was performed using the VerifyNow® Aspirin test. Blood samples for analysis were collected two hours and 24 hours after taking the morning dose of ASA on the day before surgery, and again on the second and seventh days after the operation. Blood was obtained from an antecubital vein using vacutainer tubes containing EDTA for haematological analyses, no additive for serum TXB_2 measurements and 3.2% sodium citrate for whole blood platelet aggregometry (VerifyNow® Aspirin test). Complete blood cell counts and mean platelet volume were assessed in samples anticoagulated with K3EDTA within 20 minutes of sampling to minimise platelet swelling, using a Pentra DX 120 (Horiba Medical, Kyoto, Japan).

Anaesthesia and surgical technique

All anaesthetic procedures were performed using the same anaesthetic protocol. All surgical procedures were performed by four surgeons using the same surgical technique. After a median sternotomy, the left internal thoracic artery was harvested as a bypass conduit. The saphenous vein or left radial artery was used to make jump-grafts, Y-grafts or T-grafts, as necessary. The conduits were immersed in warm diluted papaverine saline solution (1 mg/mL). Systemic heparinisation was achieved with an initial dose of 1.5 mg/kg heparin, and this was maintained with additional heparin doses to reach an activated clotting time above 300 s. To facilitate anastomosis, the heart was stabilised with a suction-type mechanical stabiliser (Octopus; Medtronic, Minneapolis, MN, USA). After the completion of anastomosis, the effect of heparin was reversed with protamine.

Assays for effectiveness of ASA and platelet reactivity

Serum TXB_2 levels were assessed to measure the inhibition of the cyclooxygenase pathway as the primary efficacy variable for ASA, as recommended by the European Medicines Agency [9]. Five millilitres of venous blood without anticoagulant was sampled in a glass tube, allowed to clot at 37 °C for 60 min, and centrifuged at 1,200 g for 10 min. The serum was stored at −80 °C until assayed for TXB_2 using a commercial enzyme immunoassay (Cayman Chemicals, Ann Arbor, MI, USA).

Assays for platelet function were performed using the VerifyNow® Aspirin Assay (Accumetrics Inc., San Diego, CA, USA). The VerifyNow® Aspirin Assay is a turbidimetric-based optical detection system which measures platelet aggregation. It contains a lyophilised preparation of human fibrinogen-coated microparticles of arachidonic acid. The instrument measures the change of light transmission caused by platelet aggregation and reports this value in aspirin reaction units (ARU). High on-aspirin platelet reactivity was defined as an ARU value ≥ 550 according to the manufacturer's reference values.

Statistics

Statistical analysis was conducted using SPSS 12.0 for Windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used for all baseline variables, with means and standard deviations for normally distributed continuous variables, medians and interquartile ranges for non-normally distributed continuous variables, and rates and proportions for categorical variables. Categorical data was compared with the chi-square test or Fisher's exact test. Continuous data between the groups was compared by unpaired Student's t-tests for the normally distributed variables and the Mann-Whitney rank sum test for the non-normally distributed variables. Repeated measurements analysis of variance (ANOVA) was used to analyse time-dependent data and, if a significant result was obtained, statistical comparisons in order to test the within-group change between baseline and second day as well as between baseline and seventh day were made using the Wilcoxon test for correlated means. Contingency tables were used for time-dependent change of patient proportions with specified variables. Differences were considered significant at p values < 0.05.

Results

Patient characteristics

A total of 25 patients with a mean age of 67.9 years (± 10.4 years) were enrolled consecutively in the study. Baseline patient characteristics and perioperative clinical and biochemical results are presented in Table 1 and in Table 2.

Table 1. Baseline characteristics at recruitment

Patient characteristics	Study group ASA 1 × 75 N = 25
Age, [years], mean ± SD	67.99 ± 10.41
Male, N [%]	16 (64)
BMI [kg/m^2], mean ± SD	28.63 ± 4.11
CCS 2, N [%]	18 (72)
CCS 3, N [%]	7 (28)
Previous MI, N [%]	12 (48)
Previous PCI, N [%]	5 (20)
LVEF > 50%, N [%]	16 (64)
LVEF 30–50%, N [%]	9 (36)
LVEF < 30%, N [%]	0 (0)
Diabetes mellitus type 2, N [%]	9 (36)
Hypertension, N [%]	22 (88)
Peripheral arterial disease, N [%]	11 (44)
Neurological deficits, N [%]	0 (0)
Chronic obstructive pulmonary disease, N [%]	1 (4)
Chronic kidney disease, N [%]	5 (20)
Creatinine > 2.2 mg/dL, N [%]	2 (8)
Hyperlipidaemia, N [%]	9 (36)
EuroSCORE (logistic), mean ± SD	5.55 ± 5.4
Beta-blockers, N [%]	25 (100)
ACEI, N [%]	22 (88)
Calcium channel blockers, N (%)	5 (20)
Statin, N [%]	24 (96)

ASA — acetylsalicylic acid; N — number of patients; SD — standard deviation; [%] — percentage of patients; BMI — body mass index; CCS — Canadian Cardiovascular Society Angina Grading Scale; MI — myocardial infarction; PCI — percutaneous coronary intervention; LVEF — left ventricular ejection fraction; ACEI — angiotensin-converting enzyme inhibitors

Haematological analyses

We observed a significant platelet counts reduction, and a mean platelet volumes increase, on the 2nd day after OPCAB compared to the preoperative results. A significant platelet counts increase without any major change of mean platelet volumes was observed on the 7th postoperative day (Table 3).

Serum thromboxane B_2

Serum TXB_2 results are presented in Table 4 and in Figure 1. A serum TXB_2 decrease on the 2nd day after OPCAB and an increase on the 7th day after surgery were observed in relation to the corresponding preoperative values. A significant median serum TXB_2 increase was observed between measurements at two and 24 hours after taking ASA before surgery ($p < 0.001$).

There was a significant increase ($p = 0.01$) in the percentage of patients with insufficient laboratory ASA efficacy (defined by serum $TXB_2 \geq 7.2$ ng/mL) between the measurements obtained at two and 24 hours after ASA administration before surgery (20% and 44%, respectively). There were marked drops in rates of patients with serum $TXB_2 \geq 7.2$ ng/ml (at 24 hours after ASA intake) on the 2nd day after OPCAB in relation to preoperative values (8% and 44% respectively, $p = 0.003$). In contrast, the percentage of patients with serum $TXB_2 \geq 7.2$ ng/mL on the 7th day after OPCAB (at two hours after ASA administration)

Table 2. Perioperative biochemical and clinical characteristics

Biochemical and clinical characteristics	Study group ASA 1 × 75 N = 25
Number of anastomoses, mean ± SD	2.68 ± 1.07
Intensive care unit stay [hours], mean ± SD	56.44 ± 42.01
Mechanical respiratory therapy [hours], mean ± SD	8.44 ± 6.25
Troponin I [ng/mL], mean ± SD:	
• 6 hours after OPCAB	1.88 ± 3.03
• 18 hours after OPCAB	3.39 ± 8.62
• 42 hours after OPCAB	3.12 ± 8.32
CK-MB mass [ng/mL], mean ± SD:	
• 6 hours after OPCAB	7.30 ± 8.57
• 18 hours after OPCAB	12.03 ± 15.55
• 42 hours after OPCAB	8.99 ± 11.66
Chest drainage [mL], mean ± SD:	
• 6 hours after OPCAB	537.4 ± 553.47
• 12 hours after OPCAB	754.4 ± 714.4
Haemoglobin [g/dL], mean ± SD:	
• day 0	13.34 ± 1.56
• day 2	9.95 ± 0.91
• day 7	10.15 ± 1.07

Table 3. Postoperative platelet (PLT) counts and mean platelet volumes (MPV) compared to preoperative levels

Study day	PLT [10^3/μL] N = 25	MPV [fL] N = 25
Day 0		
Min; Max	124; 324	8.3; 12.5
Median	195	10.4
Q1; Q3	168; 247	9.9; 11
Day 2		
Min; max	53; 239	8.3; 13.3
Median	142	11.2
Q1; Q3	122; 169	10.5; 12.6
Day 2 vs day 0, p-value	< 0.001	0.004
Day 7		
Min; max	111; 397	8.2; 12.2
Median	256	10.4
Q1; Q3	219; 313	9.5; 11.3
Day 7 vs day 0, p-value	0.01	0.5

min. — minimum; max. — maximum; Q1 — quartile 1; Q3 — quartile 3; p-value — probability value

significantly increased (20% and 52% respectively, p = = 0.02) (Table 5, Figure 2).

VerifyNow® Aspirin test

The results of arachidonate-induced platelet reactivity from turbidimetric aggregometry in whole blood using the VerifyNow® Aspirin test are shown in Table 4 and in Figure 1.

Despite a significant serum TXB_2 decrease in the whole study population on the 2nd postoperative day, platelet reactivity did not change significantly compared to preoperative results. A significant increase in median platelet reactivity and in the percentage of patients with HAPR (defined by VerifyNow® Aspirin test result ≥ 550 ARU) were observed on the 7th postoperative day (24 hours after taking ASA) in comparison with the values before OPCAB (48% and 12% respectively, p = 0.007) (Table 5, Figure 2).

Relationship between platelet counts, mean platelet volumes, serum thromboxane B_2 and arachidonic acid-induced platelet aggregation

There was a significant, positive correlation before operation between serum TXB_2 and platelet reactivity both two and 24 hours after ASA intake (rho = 0.4, p = 0.03; rho = 0.5, p = 0.01; respectively). On the 2nd postoperative day there was a significant, positive correlation between serum TXB_2 and platelet count two hours after ASA administration (rho = 0.5, p = 0.02). On the 7th postoperative day, two hours after ASA intake, there was a significant, negative correlation between platelet count and mean platelet volume (rho = 0.5, p = 0.005) and a significant, positive correlation between serum TXB_2 and platelet reactivity (rho = 0.7, p < 0.001).

The proportion of patients with both serum $TXB_2 \geq 7.2$ ng/mL and platelet reactivity ≥ 550 ARU on the 7th postoperative day was significantly higher (24 hours after ASA administration) in relation to preoperative values (32% and 4% respectively, p = 0.008) (Table 5, Figure 2).

Discussion

We used serum thromboxane as the primary outcome measure in our study because it is a sensitive and specific measure of the antiplatelet effects of ASA. At least 95% suppression of serum TXB_2 is required to achieve an optimal antiplatelet effect [10]. In patients chronically treated with ASA, a maximum level of serum TXB_2 of 10 ng/mL corresponds to ≥ 98% inhibition of COX-1 [11]. We used in our study an even more rigorous target serum TXB_2 concentration of ≥ 7.2 ng/mL in accordance with other authors [12, 13]. Platelet aggregation studies are also widely used to measure the antiplatelet effects of ASA, but are less sensitive and specific than serum TXB_2. Consistent with this, some patients had complete suppression of platelet aggregation despite a postoperative rise in serum thromboxane level, and vice versa.

Table 4. Serum thromboxane B_2 (TXB_2) levels and arachidonate-induced platelet aggregation results in whole blood measured by VerifyNow® Aspirin Assay

Study day	TXB_2 [g/mL] N = 25	VerifyNow® Aspirin (ARU) N = 25
Day 0, 2 h		
Min; max	0.16; 74.37	384; 645
Median	3.25	514
Q1; Q3	1.33; 6.68	424; 534
Day 0, 24 h		
Min; max	0.32; 83.01	383; 650
Median	6.14	445
Q1; Q3	3.53; 9.88	424; 477
Day 0, 24 h vs 2 h, p-value	< 0.001	0.06
Day 2, 2 h		
Min; max	0.09; 10.8	378; 605
Median	0,4	517
Q1; Q3	0.23; 0.98	484; 544
Day 2, 24 h		
Min; max	0.05; 13.01	377; 583
Median	0.5	495
Q1: Q3	0.29; 0.66	423; 513
Day 2, 24 h vs 2 h, p-value	0.3	0.02
Day 2 vs day 0, 2 h, p-value	< 0.001	0.2
Day 2 vs day 0, 24 h, p-value	< 0.001	0.2
Day 7, 2 h		
Min; max	0.25; 55.35	367; 643
Median	8.57	540
Q1; Q3	1.91; 18.08	453; 594
Day 7, 24 h		
Min; max	0.51; 64	403; 644
Median	13.09	544
Q1; Q3	3.18; 24.74	465; 604
Day 7, 24 h vs 2 h, p-value	0.8	0.6
Day 7 vs day 0, 2 h, p-value	0.04	0.1
Day 7 vs day 0, 24 h, p-value	0.06	0.003

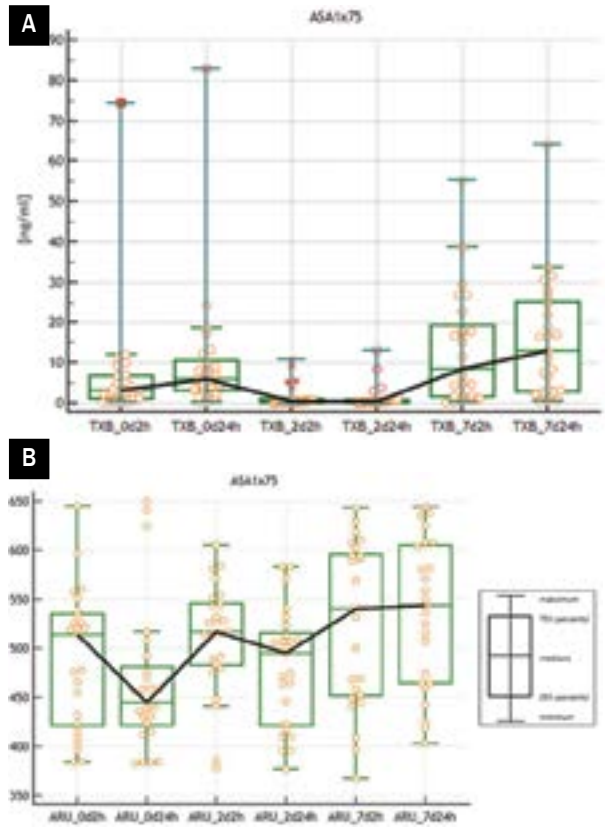

Figure 1. Serum thromboxane B_2 (TXB_2) levels (**A**) and arachidonate-induced platelet reactivity results measured by VerifyNow® Aspirin test (**B**). Box and whisker plots of daily perioperative serum TXB_2 levels in the treatment group (ASA 1 × 75 — acetylsalicylic acid [ASA] 75 mg once-daily). The horizontal line contained within the box represents the median, the upper and lower ends of the box represent the 25th and 75th centiles, the upper and lower horizontal lines at the end of the whiskers represent the maximum and minimum levels and the small open circles outside the whiskers represent outliers; 0d2h — day 0 before surgery, 2 hours after ASA intake; 2d24 — day 2, 24 hours after ASA intake *etc*.

We observed a decline in platelet counts following OPCAB surgery on day 2 and this was followed by a rise in platelet counts to levels higher than baseline. Although almost all patients had nearly complete suppression of serum TXB_2 on the second postoperative day, there was a subsequent rise in serum TXB_2 levels that occurred in parallel with the postoperative increase in platelet counts.

The drop in haemoglobin levels and platelet counts with mean platelet volume increase on the 2nd day after OPCAB reflects blood loss and haemodilution during the early postoperative period. A significant increase in platelet counts on the 7th postoperative day may be associated with high platelet turnover and can result in reduced antiplatelet activity of ASA [14]. Enhanced platelet turnover, which corresponds with platelet hyperactivity, causes the release of young platelets still able to form thromboxane via uninhibited COX-1 and possibly through up-regulated COX-2 generating critical amounts of thromboxane despite antiplatelet treatment.

The important finding of our study is that nearly half of all the patients taking 75 mg of enteric-coated ASA preparations daily failed to attain optimal inhibition of serum TXB_2 or had HAPR on the 7th day after OPCAB. Reasons for the failure to respond to ASA may be pharmacokinetic (failure to achieve an adequate level of drug)

Table 5. Rates of patients stratified by results of serum thromboxane B_2 (TXB_2) ≥ 7.2 ng/mL, arachidonate-induced platelet reactivity ≥ 550 ARU and both serum TXB_2 ≥ 7.2 ng/mL and arachidonate-induced platelet reactivity ≥ 550 ARU

Study day	Patients, N [%], stratified by TXB_2 < 7.2 ng/mL vs ≥ 7.2 ng/mL	Patients, N (%), stratified by VerifyNow® Aspirin < 550 ARU vs ≥ 550 ARU	Patients, N (%), stratified by TXB_2 < 7.2 ng/mL and VN < 550 ARU vs ≠ (TXB_2 ≥ 7.2 ng/mL and VN ≥ 550 ARU)
Day 0, 2 h	20 (80%) vs 5 (20%)	20 (80%) vs 5 (20%)	24 (96%) vs 1 (4%)
Day 0, 24 h	14 (56%) vs 11 (44%)	22 (88%) vs 3 (12%)	22 (88%) vs 3 (12%)
Day 0, 24 h vs 2 h, p-value	0.01	0.4	0.2
Day 2, 2 h	23 (92%) vs 2 (8%)	19 (76%) vs 6 (24%)	23 (92%) vs 2 (8%)
Day 2, 24 h	23 (92%) vs 2 (8%)	22 (88%) vs 3 (12%)	24 (96%) vs 1 (4%)
Day 2, 24 h vs 2 h, p-value	1.0	0.3	0.3
Day 2 vs day 0, 2 h, p-value	0.08	0.7	0.3
Day 2 vs day 0, 24 h, p-value	0.003	1.0	0.3
Day 7, 2 h	12 (48%) vs 13 (52%)	14 (56%) vs 11 (44%)	17 (68%) vs 8 (32%)
Day 7, 24 h	9 (36%) vs 16 (64%)	13 (52%) vs 12 (48%)	17 (68%) vs 8 (32%)
Day 7, 24 h vs 2 h, p-value	0.2	0.7	1.0
Day 7 vs day 0, 2h, p-value	0.02	0.1	0.008
Day 7 vs day 0, 24 h, p-value	0.2	0.007	0.1

or pharmacodynamic (failure to inhibit platelet function). Poor patient compliance, interindividual pharmacodynamic variability, inadequate dosing, and drug interaction must also be considered. We went to considerable lengths to ensure patient compliance (every ASA intake was made in the presence of hospital staff) and prevent drug interaction (every ASA ingestion was made three hours before any other drug intake). The administration of NSAIDs can prevent COX acetylation by ASA, and we did not use NSAIDs in the postoperative period [15].

These days, many patients who take ASA as antiplatelet therapy for the secondary prevention of cardiovascular events receive low-dose EC preparations. Dose-finding studies, on which current regimens are based, used plain ASA which differs significantly in its pharmacokinetic profile from EC preparations. With plain ASA preparations, peak plasma levels occur 30 to 40 minutes after ingestion and platelet inhibition is apparent after one hour. It takes 3–4 hours to achieve peak plasma levels with EC ASA [16]. Bioavailability of EC ASA may be lower than plain ASA due to slower absorption and a more alkaline environment in the upper small intestine. If immediately before ingestion of the daily ASA dose a significant amount of circulating platelets are competent for thromboxane formation, circadian inhibition of platelet function may be incomplete. Reduced suppression of thromboxane has been linked with an increased risk of premature graft failure following CABG surgery [17].

Even though most studies have shown the potential of platelet function testing to predict atherothrombotic events after CABG, the evidence is still insufficient to recommend routine platelet function testing to guide treatment in CABG patients for this purpose [18–20]. The results of our study suggest that the dose of ASA delivered by 75 mg of EC tablets is insufficient to prevent platelet activity in many patients after OPCAB.

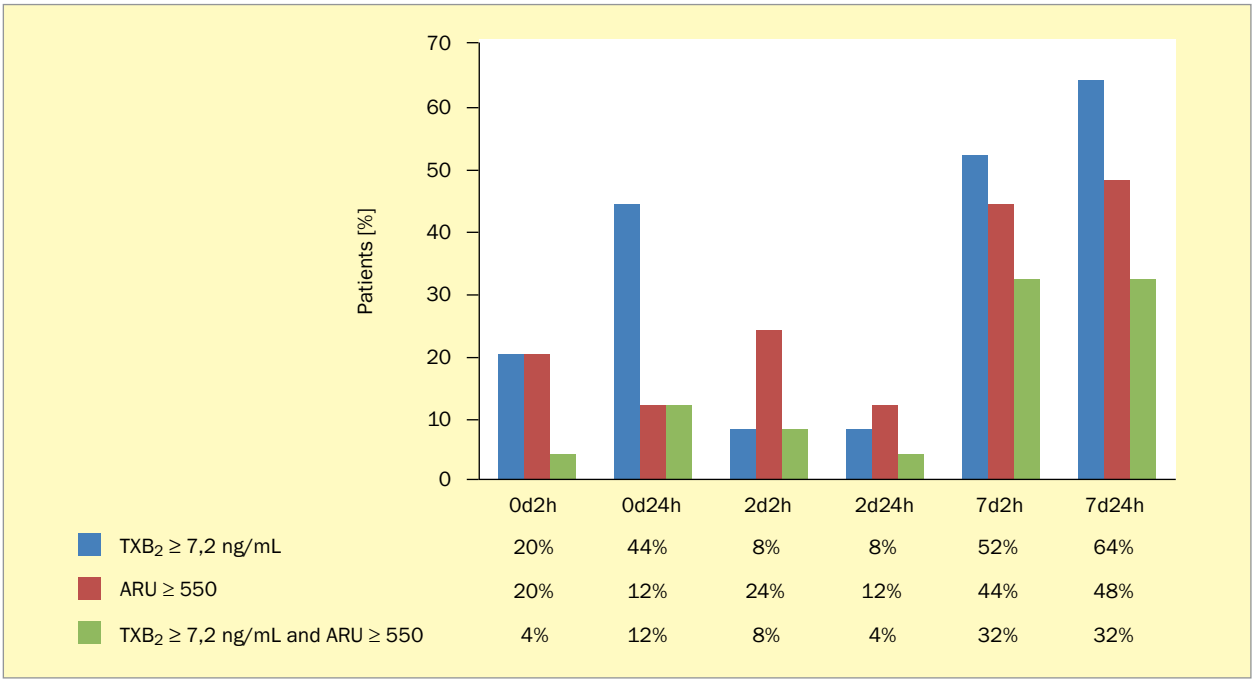

Figure 2. Analysis of patients % stratified by levels of serum thromboxane B_2 (TXB_2) ≥ 7,2 ng/mL or/and results of VerifyNow® Aspirin ≥ 550 ARU

Limitations of the study

Our study was underpowered for clinical events, but our results nonetheless provide clear-cut clues to more efficient perioperative ASA dosages than 75 mg enteric-coated formulation.

Conclusions

In the group of patients taking a standard daily dose of 75 mg of ASA, a substantial number of patients failed to attain optimal inhibition of serum TXB_2 or had HAPR before surgery and on the 7th day after OPCAB. A significant decrease in serum TXB_2 levels on the 2nd day after OPCAB did not correlate with platelet reactivity. The optimal dose of ASA is of interest for further studies of efficacy and clinical outcomes after OPCAB.

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Conflicts of interest(s)

None of the authors have any conflict of interest to report in relation to this work.

Streszczenie

Wstęp. Kwas acetylosalicylowy (ASA) jest podstawowym lekiem przeciwpłytkowym stosowanym w okresie okołooperacyjnym u chorych poddawanych operacjom pomostowania tętnic wieńcowych (CABG). Operacja pomostowania tętnic wieńcowych bez użycia krążenia pozaustrojowego (OPCAB) prawdopodobnie w mniejszym stopniu zaburza funkcję płytek krwi (PLT) niż operacja wykonywana w krążeniu pozaustrojowym i może być przyczyną wysokiej reaktywności płytek mimo leczenia ASA (HAPR) w okresie pooperacyjnym.

Materiały i metody. Celem badania była prospektywna analiza zmienności stężenia tromboksanu B_2 (TXB_2) w surowicy krwi i reaktywności PLT zależnej od ASA u pacjentów ze stabilną chorobą wieńcową, poddanych OPCAB, leczonych standardową, pojedynczą dawką dobową 75 mg ASA. Próbki krwi do analizy pobierano po 2 i 24 h od przyjęcia porannej dawki ASA w dobie poprzedzającej operację, a następnie w 2. i 7. dobie po operacji.

Wyniki. W 2. dobie po OPCAB obserwowano istotne zmniejszenie liczby PLT oraz zwiększenie średniej objętości płytek krwi. W 7. dobie pooperacyjnej stwierdzono zwiększenie liczby PLT wobec wartości przed operacją. W 7. dobie po OPCAB obserwowano istotne zwiększenie w odniesieniu do wartości przed operacją odsetka pacjentów z niedostateczną w analizie laboratoryjnej skutecznością leczenia przeciwpłytkowego ASA (definiowaną jako stężenie TXB_2 w surowicy krwi ≥ 7,2 ng/ml), odpowiednio 52% w porównaniu z 20%; p = 0,02. W 7. dobie pooperacyjnej stwierdzono znamienny wzrost mediany reaktywności PLT oraz odsetka pacjentów z HAPR (wynik testu VerifyNow® Aspirin ≥ 550 ARU) w porównaniu z wartościami przed OPCAB (odpowiednio 48% *v.* 12%; p = 0,007).

Wnioski. W grupie pacjentów stosujących pojedynczą, dobową dawkę 75 mg ASA u istotnego odsetka badanych (p = 0,03) przed operacją oraz w 7. dobie po OPCAB stwierdzono suboptymalne zahamowanie syntazy TXB_2 oraz HAPR. Znamienne obniżenie stężenia TXB_2 w surowicy krwi w 2. dobie pooperacyjnej nie korelowało z reaktywnością PLT. W przyszłych badaniach dotyczących efektywności leczenia przeciwpłytkowego oraz wyników klinicznych po OPCAB należy zwrócić szczególną uwagę na optymalizację dawkowania ASA.

Słowa kluczowe: kwas acetylosalicylowy, pomostowanie tętnic wieńcowych, tromboksan, reaktywność płytek krwi

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