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Recurrent events among Acute Coronary Syndrome patients: gender-specific analysis from Aegean-Islands study

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Abstract

Aim: To evaluate the 12-month recurrent major adverse cardiac events (MACE) in acute coronary syndrome (ACS) patients, in relation to region and clopidogrel treatment separately for men and women.

Material and Methods: During 2015-2016, n=1,194 consecutive ACS patients hospitalized in various Cardiology Clinics in Aegean islands and Attica region, were enrolled. Clopidogrel treatment, on top of aspirin, was recorded either as original product clopidogrel hydrogen sulphate (Plavix®/Iscover®) (branded) or generic clopidogrel besylate formulation (Clovelen®). Six-month follow-up evaluation was performed and recurrent MACE incidence and hemorrhage events were recorded.

Results: The 12-month MACE incidence was 3.9% (4.6% in Aegean islands and 3.5% in Attica area,

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p>0.05). The respective incidence in men was 4.0% and in women 3.8% (p>0.05). Overall generic and branded clopidogrel use was 87% and 13%, respectively. No significant differences were observed between branded and generic clopidogrel use and 12-month MACE incidence; subgroup analysis with gender as strata, did not reveal any significant outcomes as well. Hemorrhage incidence did not exceed the 1% in the total sample.
Conclusions: Lower cost pharmaceutical agents in the CVD primary and secondary prevention spectrum remain a compelling need to address the challenge of such cost and generic drugs are oriented towards this approach; The present study demonstrates that the use of a generic clopidogrel formulation was quite high in both urban and insular areas, having similar efficacy and safety profile with the branded clopidogrel, without any differences observed between genders.

Key words: acute coronary syndrome; cardiovascular disease; clopidogrel; gender; generic clopidogrel; secondary prevention

Introduction

As endorsed by the Institute of Medicine and Healthy People 2020 Agenda, the principle goal is to "improve access to comprehensive, quality health care services" for everyone [1]. During the past years there has been a significant focus on eradicating disparities in healthcare – due to race, sex, region - throughout the world. One area in which such disparities have long being highlighted is related to the medical care of remote areas, such as islands and areas with high altitude, where health care services are less accessible due to geographical particularities, and in many cases due to lower socio-economic status and related financial problems [2, 3]. Despite sex, race, and regional particularities, successful health care systems have to maximize health gain for the entire population and to simultaneously minimize the need for expensive medical care. Off-patent medicines, like generic and bioequivalent medicines, can support this objective offering high-quality treatment at lower costs [4, 5]. In a world with severe resources' constraints, the objective of generic medicines seems more important than ever. Under this perspective, clopidogrel is a first-in-class product with the potential to prevent cardiac episodes in very high CVD risk patients [4]. Currently the clopidogrel-mediated treatment is considered low-cost due to the available generic forms of this drug in the market. However, limited epidemiological data exist to support the therapeutic equivalence of the branded form of this agent with its generic counterparts and even more when it comes to gender-specific conclusions [6].

Thus, the aim of the present work was to evaluate the 12-month incidence of recurrent major adverse cardiac events (MACE) of ACS patients in relation to region, i.e., insular (Aegean Sea islands) and urban areas of Greece (Attica region), gender, and generic medical treatment.

Methods

Sample

The Aegean study is a prospective, observational cohort. Among the goals of the study were to record the incidence of acute coronary syndrome (ACS) in urban, as well as in insular areas of Greece, and the prescription of generic antiplatelet agents, i.e., clopidogrel, as a low-cost medication that could be affordable even by low socio-economic status people. During 2015-2016, n=1,194 consecutive patients with discharge diagnosis of ACS (i.e., acute myocardial infarction (AMI) or unstable angina (UA)) that were hospitalized in the cardiology clinic of Tzaneion Hospital in Piraeus, Attica region and in the cardiology clinics of Aegean Sea islands, were enrolled (participation rate varied 80-95% of the initially approached ACS patients). The particular hospitals were selected to represent both urban areas, as well as insular areas. Of the total enrolled patients, n=740 (69% men and 31% women) were from urban areas and n=454 from insular areas (73% men

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and 27% women).

Defining ACS patients

At hospital entry, as well as during hospitalization biomarkers suggesting cardiac injury and AMI such as, troponin I, creatine kinase (CK) and the MB fraction of total CK (CK-MB) were measured in all patients. Moreover a 12-lead electrocardiogram (ECG) was performed and clinical symptoms were evaluated in all patients, by a cardiologist. AMI was defined by typical rise and gradual fall (for troponin) or more rapid rise and fall (for CK-MB) of biochemical markers of myocardial necrosis with at least one of the following: (a) ischemic symptoms, (b) development of pathologic Q waves on the ECG, (c) ECG changes indicative of ischemia (ST segment elevation or depression), or, (d) coronary artery intervention (e.g. coronary angioplasty) [7]. UA was defined by the occurrence of one or more angina episodes, at rest, within the preceding 48 h, corresponding to class III of the Braunwald classification [8]. Medical information of the patients was retrieved through hospital records.

Measurements at baseline examination

The baseline examination included a range of patients' socio-demographic, clinical, biochemical and lifestyle characteristics, selected through a case report form and including among others: age, gender, smoking habits, alcohol consumption, individual medical history and family history of CVD. Specifically, years of smoking were recorded; current smokers were defined as those who smoked at least one cigarette per day or have stopped smoking during the past 12 months, while the rest were defined as past smokers. The rest of the patients were defined as never or rare smokers. As far as the anthropometric characteristics are concerned, height and weight were measured to the nearest 0.5 cm and 100 g respectively. Body mass index (BMI) was then calculated as weight (in kilograms) divided by height (in meters) squared. Based on the World Health Organization, overweight was defined as BMI between 25 and 29.9 kg/m^2, while obesity as BMI greater than 29.9 kg/m^2.

Using patients' medical files, it was recorded the history of stroke, heart vessels disease, atrial fibrillation, peripheral artery disease, carotid artery disease, heart failure, the New York Heart Association (NYHA) functional classification, liver disease, neoplasm, and thyroid disease. Revascularization in terms of percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) was also recorded. Baseline assessment of other clinical characteristics (i.e., history of hypertension, hypercholesterolemia and diabetes mellitus), was based on the information retrieved through physical examination, as well as patients' medical records and pharmaceutical management. Specifically, participants who had blood pressure levels ≥140/90 mmHg or used antihypertensive medications were classified as hypertensive. Hypercholesterolemia was defined as total serum cholesterol levels >200 mg/dL or the use of lipid-lowering agents according to the National Cholesterol Education Program Adult Treatment Panel III guidelines (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001). As for the diabetes mellitus the American Diabetes Association diagnostic criteria were used i.e. fasting glucose levels ≥126mg/dL or use of anti-diabetic agents. The antiplatelet medical treatment prescribed to patients on top of aspirin was evaluated in terms of: original product clopidogrel hydrogen sulphate (Plavix®/Iscover®) (i.e. branded clopidogrel), generic clopidogrel besylate formulation (Clovelen®) or other P2Y12 receptor antagonists i.e. prasougrel, or ticagrelor. In the sample of the present work, the use of prasougrel or ticagrelor was too low i.e. <5%, while the use of proton pump inhibitors (PPIs) was recorded and presented in **Table 1**. Additionally, the antiplatelet treatment pattern was also evaluated, defined as exclusive use of generic clopidogrel or transition from branded to generic clopidogrel.

Follow-up examination at 12-months

The 12-month follow-up of the study's patients was performed during 2016-2017 and information from all patients was available (i.e., 0% loss to follow up rate). As mentioned above, the combined endpoint studied in the present work was incidence of MACE. In particular, MACE was defined as the development of: AMI, or angina pectoris, or other identified forms of ischemia (WHO-ICD coding 410-414.9, 427.2, 427.6), or heart failure of different types and chronic arrhythmias (WHO-ICD coding 400.0-404.9, 427.0-427.5, 427.9) or the devel-

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Table 1: **Baseline characteristics of Acute Coronary Syndrome patients participated in Aegean epidemiological study and 12-month major cardiac adverse events (MACE) (n=1,194)**

	Aegean Sea Islands (n = 454)			Urban areas (n = 740)		
Baseline characteristics	**Men (n = 335)**	**Women (n = 119)**	**p**	**Men (n = 513)**	**Women (n = 227)**	p
Age (yrs)	65 (12)	69 (13)	0.02	65 (11)	71 (10)	<0.001
Body Mass Index, (kg/m²)	28.4 (4.4)	28.7 (7.4)	0.64	28.2 (4.0)	28.7 (5.6)	0.24
Current smoking, %	52	20	<0.001	58	33	<0.001
Unstable Angina, %	44	58	0.01	49	59	0.01
Acute Myocardial Infarction, %	56	42	0.01	51	41	0.01
STEMI, %	31	22	0.02	30	25	0.02
N-STEMI, %	25	20	0.02	21	16	0.02
Percutaneous coronary intervention, %	46	17	<0.001	64	44	<0.001
Heart Failure, %	18	13	0.13	25	22	0.33
Peripheral artery disease, %	18	27	0.03	12	13	0.67
Carotid artery disease, %	11	15	0.19	16	26	0.01
Heart valve disease, %	13	9	0.23	6	14	0.001
Atrial fibrillation, %	8	11	0.32	6	8	0.28
Generic clopidogrel, %	84	73	0.007	91	89	0.85
Branded clopidogrel, %	15	27	0.002	9	11	0.60
Clopidogrel treatment status						
Exclusive use of generic clopidogrel, %	59	62	0.61	57	65	0.03
Transition from branded to generic clopidogrel, %	41	38	0.61	43	34	0.03
Proton Pump Inhibitors, %	50	45	0.645	50	53	0.637
Hypercholesterolemia, %	66	70	0.49	83	78	0.03
Hypertension, %	63	66	0.59	75	82	0.03
Diabetes mellitus, %	31	33	0.67	33	38	0.15
Family history of CVD, %	18	8	0.009	27	20	0.04
12-month follow-up						
MACE, %	5.0	5.2	0.78	4.3	3.2	0.67
Cardiac deaths, %	1	0	0.30	1	1.3	0.47
Recurrent AMI events, %	2.7	4.2	0.39	1.5	0	0.10
Stroke events, %	0.3	0	0.55	0.8	0.9	0.88
Hospitalization due to hemorrhage, %	1	1	0.75	1	1	0.90

Data are presented as mean (standard deviation, SD). P-values were obtained using the Student's t-test for age and body mass index and the chi-squared test for the rest (categorical) variables. Cardiovascular disease (CVD); New York Heart Association Functional Classification (NYHA)

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opment of stroke (WHO-ICD coding 430-438), or stent thrombosis (WHO-ICD coding T82.868A) or the development of major haemorrhages as classified according to ICD-10-CM. For the participants who died during the follow-up, the information achieved from their relatives, as well as death certificates. As regards individuals who might first suffered from stroke and then had coronary heart disease, it was a-priori decided the first outcome to be considered as the end-point, but also to record the consequent event for further testing of competing risks (however, there were no such cases in the sample).

Bioethics

The study was approved by the Medical Research Ethics Committee of the participated Institutions and carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association. All participants were informed about the aims and procedures of the study and signed an informed consent.

Statistical analysis

Continuous variables are presented as mean, standard deviation (SD), whereas categorical variables as absolute and relative (%) frequencies. The association between normally distributed continuous variables (BMI, age) and patients' gender was evaluated through the Student's t-test for independent samples. Whether these variables were normally distributed was tested through the P-P plot and equality of variances through the Levene's test. Associations between the categorical variables and gender were tested through the chi-squared test. To evaluate the association between antiplatelet treatment (in terms of generic vs. branded clopidogrel and exclusive vs. non-exclusive use of generic clopidogrel) and 12-month MACE, logistic regression analysis was performed, taking into account, among others, the supplementary medical treatment agents other than clopidogrel. Results are presented as odds ratio (OR) and their corresponding 95% confidence intervals (95%CI). Time to event was also taken into account and Cox proportional hazards models were also applied; but it was decided to keep the results from logistic regression as the models had better correct classification rates for the cases and some time points were missing. The STATA software, version 14 (MP & Associates, Sparta, Greece) was used for all statistical analyses.

Results

In **Table 1**, baseline socio-demographic, lifestyle and clinical characteristics of the ACS patients, as well as their 12-month outcome are presented. Out of the n=454 patients of the Aegean islands, 49% were diagnosed with AMI (27% STEMI and 22% N-STEMI, p=0.02) while as for the n=740 patients from the urban region 46% were diagnosed with AMI (28% STEMI and 18% N-STEMI, p=0.02). In particular, overall generic and branded clopidogrel use was 87% and 13%, respectively; the generic drug use in insular areas was 81%, while in urban was higher, i.e., 90% (p<0.001). No significant differences in baseline measurements and the type of clopidogrel treatment have been observed (data not presented in **Table 1**).

During the 12-month follow-up period incidence of MACE was 39 events per 1,000 patients (or 47 patients out of 1,194 (3.9%), 4.6% in Aegean islands and 3.5% in urban areas, p=0.34). Moreover, MACE incidence was similar in both genders, i.e., 4.0% in men and 3.8% in women patients (p=0.86). The distribution of MACE's was: AMI, 43%, followed by cardiac deaths, 21%, stroke events, 15%, and the rest 21% were rehospitalisations due to major haemorrhages. Although no differences were observed between regions and MACE, as regards recurrent AMI events, the 12-month incidence rate was 3.1% in Aegean islands vs. 0.8% in the urban areas (p=0.003). No significant differences were observed between those who developed a MACE and the rest, as regards the type of clopidogrel treatment (p=0.21), or any other medication used (all p's >0.10).

In **Figure 1**, two multi-adjusted models developed to evaluate the association between 12-month MACE incidence and the clopidogrel treatment, are illustrated both for the total sample and separately for men and women patients. As it can be seen, the type of clopidogrel treatment (branded vs. generic form) as well as the transition from branded to generic clopidogrel use did not significantly affect the 12-month MACE risk either in the overall or the gender-stratified analysis (**Figure 1**).

Discussion

The 12 months following a CVD episode are of cru-

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Figure 1 **Gender-specific analysis for the association between A. type (generic vs. branded clopidogrel) and B. pattern of antiplatelet treatment (exclusive use of generic clopidogrel vs. transition from branded to generic clopidogrel) and the 12-month major cardiac adverse events (MACE) in acute coronary syndrome patients of Aegean study.**

Dependent variable	Gender	Cases, % (n)	OR (95%CI)
A. Generic vs. branded clopidogrel	Men	4.0 (34)	0.58 (0.14, 1,45)
	Women	3.8 (13)	1.28 (0.37, 1.94)
	Total	**3.9 (47)**	**1.11 (0.45, 1.71)**
B. Exclusive use of generic clopidogrel, yes vs. no	Men	4.0 (34)	1.09 (0.54, 1.30)
	Women	3.8 (13)	1.25 (0.36, 1.63)
	Total	**3.9 (47)**	**1.13 (0.62, 2.06)**

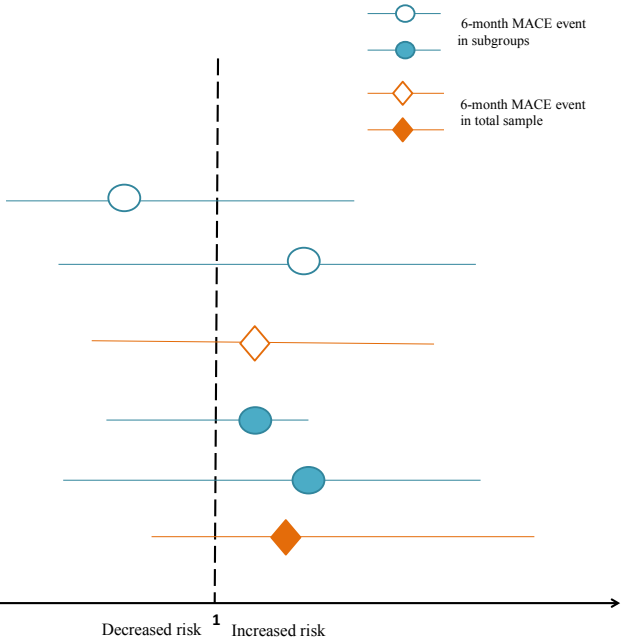

Figure 1. *Odds ratios (dots) and their 95% confidence intervals (horizontal lines) were obtained through multivariate logistic regression analysis adjusted for age, sex, body mass index, region of residence, discharge status, other anticoagulation treatment, percutaneous coronary intervention, history of hypertension, hypercholesterolemia, diabetes mellitus and family CVD history. Vertical and horizontal axes are intersected in the value 1. Odds Ratio (OR); 95% Confidence Interval (95%CI).*

cial importance for the cardiac patient. In this work it was revealed that the 12-month incidence of combined major cardiac events was relatively low and below 4%, without any differences between genders, or between those patients living in mainland urban areas or in the islands. This rate may be quite low compared with the results revealed in other studies with a similar sample e.g., PHAETHON study, yet the fact that the AMI:UA ratio in our study was close to -1- might contribute to this general low 12-month incidence. Moreover, the use of generic form of antiplatelet treatment, i.e., clopidogrel, was quite high (around 85%) in both urban and insular areas. Despite the limitations due to the observational nature of the study, this work comes to support the low CVD incidence in Greek population observed in other similar studies, as well as the routine use of this low cost clopidogrel formulation in the rehabilitation of ACS patients.

A principle target of every health related strategic plan is to suggest cost-effective treatments, maximizing the size of treated population. The "generic" concept is largely oriented towards this approach. In particular, when a branded-name patent expires, generic "equivalent" agents are produced and sold at significantly lower price [4]. Such medicines demand lower health care expenditures to be introduced in the daily clinical practice and in the meanwhile, without compromising health outcomes [9]. Nowadays, market share supply of generic drugs largely contributes to the total market volume; namely in developed countries such as Germany, United Kingdom, France, Canada branded medicines have been substituted by their generic forms even at 90% level [10]. Additionally, between 2008 and 2015, in the wake of global economic recession some governments in Europe, including Greece, implemented generic drug policies, making generic substitution

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and prescription compulsory [10]. Hence, at the same budget, more patients are to have access to an effective medical treatment [9]. However, even if cost-savings and health gain at the same time seem rather important incentives, generic drugs health policy research is usually neglected. In line with this, policy makers in the pharmaceutical field mostly deal with novel treatments policies and how to improve them as a result of the continuous pressures by patients, health care professionals and manufacturers. This depict another reality rarely considered during policy making; to enhance the sustainability of off-patent pharmaceutical agents, physicians' perceptions regarding the efficacy and safety of generic drugs as well as patients' attitude and level of compliance are detrimental factors [9, 10]. In this field, there is much to be done. In the present work, the use of generic clopidogrel, even in overall high levels, was lower in case of insular areas compared with the urban center. This was even more evident in women patients. The expected lower educational level of the islanders compared to the residents in urban centers may mediate this difference; in case of women living off-cities and retaining their feminine role in the household this hypothesis seems more likely. In a recent systematic review acceptance of generics appeared to be higher in patients with higher socioeconomic status while a great mistrust of generics was observed in patients with lower educational level [11]. Subsequently, the vast majority of patients learn about generic drugs from their physician; thereby, the decision to make an off-patent medication is highly dependent on the relevant medical advice [12]. It has been suggested that physicians in Greece away from large urban centers e.g., Athens are as well or even more willing to substitute the branded with off-patent generic drug [13]. This was also highlighted in the present work with similar outcomes between urban and insular areas regarding the substitution level of branded clopidogrel (**Table 1**).

In most countries, the bioequivalence of generic products to the originator or reference product is a mandatory prerequisite for the registration of generic drugs. Nonetheless, this is not the case when it comes to therapeutic equivalence; from this standpoint the studies are more limited and without the potential to draw strong conclusions [14]. Therapeutic equivalence in the context of non-communicable diseases with a large disease burden such as CVDs is rather important, especially when the suggested off-patent therapeutic pattern is to substitute a common effective, yet high cost, treatment [14]. In the present work, the 12-month MACE remained quite low with the use of generic clopidogrel being at high level while multivariate analysis revealed that branded and generic form of clopidogrel exhibited similar efficacy pattern (**Table 2**). At the same time the bleeding events remained extremely low, probably suggesting safety equivalence as well. The clinical usefulness of clopidogrel hydrogen sulfate (i.e. branded form) has been largely proved in large scale clinical trials for patients with high thrombotic risk [6]. With the recent approval of clinical use of several generic clopidogrel formulations, alternative cost-saving treatments in cardiac rehabilitation programs have been introduced [6]. Nonetheless, as in most generic drugs, there is a paucity of therapeutic equivalence studies; in the meanwhile, the hitherto small studies comparing original with specific off-patent clopidogrel forms in ACS patients against hard end points revealed positive outcomes, in line with the outcomes of the present work [6, 15-17].

An equally important aspect in pharmaceutical research is to confirm if the suggested drug is equally effective in different subgroups within a population. In this context and in response to the widely acknowledged under- or mis- representation of women in the medical research that shapes daily clinical practice, large organizations e.g., National Institute of Health (notice, NOT-OD-15-102), required from investigators a sex-specific reporting of the outcomes and the accompanied conclusions; a recommendation established to cover the biological heterogeneities between genders [18]. Subsequently, stratified analyses with gender as strata, is considered of crucial importance to confirm the efficacy of a medicine against major events as well as its safety [19]. In the present work, both the statistical (in terms of p for interaction) and the clinical (in terms of stratified risk analysis) gender–treatment interaction were evaluated yet no significant differences were observed. Clopidogrel-mediated antiplatelet treatment has been well-investigated separately in men and women; non-significant outcomes have been revealed in a meta-analysis of five clinical trials with more than 79,000 participants, 30% of whom were women [20]. However, in these meta-analyzed data men presented

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almost twice as high recurrent CVD risk reduction compared to women (i.e. 16% vs. 7%) while women were related to higher bleeding risk (43% vs. 22%) [20]; besides the non-significance of these discrepancies, the usually suggested hyporesponsiveness of women to clopidogrel raises concerns regarding the actual efficacy of this antiplatelet drug, even more when generic forms of this drug are currently used [21]. In the hitherto literature, 60% of all patients admitted to the hospital for adverse drug effects are women, predominantly attributed to dose-related reasons [21]. Biological factors such body size, lipid maze, hepatic metabolism as well as genetic discrepancies should be considered in relation to gender-specific particularities when original or generic drugs are prescribed.

Limitations

The findings of the present work should be considered with cautiousness and without any causal interpretations, due to the observational nature of the study from which these results were extracted. Another limitation of the study is that, the conditions under which an alternative to clopidogrel antiplatelet treatment was prescribed to the participants of the present study was not examined, which may be considered of some bias.

Conclusions

The principle policy objective of a successful health related strategic plan is to maximize health gain in the entire population through efficiently allocating limited recourses. Drugs account for sizeable shares of overall health care expenditures in CVD which in Europe reach annually the $210 billion [22]. Hence, lower cost pharmaceutical agents in the CVD primary and secondary prevention spectrum remain a compelling need to address the challenge of such numbers and generic drugs are oriented towards this approach. The present study demonstrates that the use of a generic clopidogrel formulation was quite high in both urban and insular areas, having similar efficacy and safety profile with the branded clopidogrel, without any differences observed between genders, or between those patients living in mainland urban areas or in the Aegean islands of Greece. High quality studies that evaluate the clinical/therapeutic and safety equivalence of these antiplatelet agents with the original ones are strongly demanded to demonstrate their routine prescription while gender-specific conclusions are undoubtedly needed to be drawn.

Conflict of interest

None to declare.

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Περίληψη

Νέα καρδιαγγειακά συμβάματα σε ασθενείς με Οξύ Στεφανιαίο Σύνδρομο: η αλληλεπίδραση με το φύλο από την επιδημιολογική μελέτη Aegean

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Σκοπός: Στην παρούσα εργασία εκτιμήθηκε η πιθανότητα εμφάνισης νέου μείζονος καρδιαγγειακού συμβάματος κατά τον 12-μηνιαίο επανέλεγχο ασθενών με Οξύ Στεφανιαίο Σύνδρομο (ΟΣΣ) ανάλογα με την περιοχή διαμονής και τη θεραπευτική αγωγή με κλοπιδογρέλη, διακριτά σε άνδρες και γυναίκες.

Υλικό και Μέθοδος: Την περίοδο 2015-2016, n=1,194 διαδοχικοί ασθενείς με ΟΣΣ Καρδιολογικών Κλινικών σε νησιά του Αιγαίου και στο Νομό Αττικής εντάχθηκαν στη μελέτη. Η θεραπευτική αγωγή –συμπληρωματικά της ασπιρίνης- με κλοπιδογρέλη καταγράφηκε ανάλογα με το αν χρησιμοποιούσαν το πρωτότυπο φάρμακο (Plavix®/Iscover®) ή τη γενόσημη μορφή του βεσυλική κλοπιδογρέλη (Clovelen®). Επανέλεγχος πραγματοποιήθηκε στους 12 μήνες όπου καταγράφηκε το νέο μείζον καρδιαγγειακό συμβάν και πιθανά αιμορραγικά επεισόδια.

Αποτελέσματα: Η επίπτωση νέου μείζονος καρδιαγγειακού συμβάντος στο 12μηνο ανήλθε στο 3,9% (4,6% στο Αιγαίου και 3,5% στην Αττική, p>0,05). Για τους άνδρες τα νέα καρδιαγγειακά συμβάντα ανήλθαν στο 4,0% και για τις γυναίκες στο 3,8% (p>0,05). Συνολικά η χρήση γενόσημου και πρωτότυπου φαρμάκου ανήλθε στο 87% και 13%, αντίστοιχα. Δεν παρατηρήθηκε στατιστικά σημαντική διαφορά με τον τύπο θεραπευτικής αγωγής και την 12μηνη πρόγνωση ασθενών σε όλο το δείγμα και σε διαστρωματοποιημένη ανάλυση ως προς το φύλο. Τα αιμορραγικά επεισόδια ήταν λιγότερα από 1% στο σύνολο του δείγματος.

Συμπεράσματα: Φαρμακευτική αγωγή χαμηλότερου κόστους είναι υψίστης σημασίας στην πρωτογενή και δευτερογενή πρόληψη καρδιαγγειακής νόσου και τα γενόσημα φάρμακα προσανατολίζονται προς αυτήν την κατεύθυνση. Στην παρούσα εργασία, η χρήση γενόσημης κλοπιδογρέλης ήταν υψηλή τόσο στο αστικό όσο και στο νησιωτικό χώρο, με ισοδύναμη αποτελεσματικότητα και ασφάλεια με το πρωτότυπο φάρμακο τόσο για άνδρες όσο και για γυναίκες.

Λέξεις ευρετηρίου: Οξύ Στεφανιαίο Σύνδρομο, καρδιαγγειακή νόσος, κλοπιδογρέλη, φύλο, γενόσημη κλοπιδογρέλη, δευτερογενής πρόληψη

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