VIA MEDICA

RESEARCH LETTER

Cardiology Journal
2024, Vol. 31, No. 3, 499–501
DOI: 10.5603/cj.96610

ISSN 1897–5593
eISSN 1898–018X

Effectiveness of antazoline versus amiodarone, flecainide, and propafenone in restoring sinus rhythm at the Emergency Department — case-match study

Janusz Springer[1], Michalina Pejska[2], Dariusz Kozłowski[3]

[1]Department of Cardiology, J.K. Łukowicz Memorial Specialist Hospital, Chojnice, Poland
[2]Department of Internal Medicine, Provincial Specialist Hospital in Słupsk, Poland
[3]Department of Cardiology and Electrotherapy, Medical University of Gdańsk, Gdańsk, Poland

Atrial fibrillation (AF) is the most common arrhythmia among adults worldwide [1]. It is estimated that 19.2% of people ≥ 65 years of age in Poland have AF, most frequently paroxysmal [2]. As the incidence and prevalence of AF rise (due to increases in AF risk factors: age, heart failure, hypertension, obesity, sleep apnea), so is the number of Emergency Department (ED) visits due to AF [3]. For example, in the years 2007–2014 in the United States the number of ED visits due to AF increased by 30.7% [4]. The ED physician has 2 methods of restoring sinus rhythm (SR) in a patient with paroxysmal AF: electric cardioversion or pharmacological (chemical) cardioversion (PCV) using an anti-arrhythmic drug (AAD) [5].

In our previous study, we retrospectively analyzed the hospital records of 1878 ED patients who underwent PCV with AADs commonly available in Poland: antazoline (± β-blocker), amiodarone, flecainide, or propafenone [6]. We found that that antazoline is more effective in terminating AF than the 3 other AADs and that antazoline did so significantly faster than amiodarone or propafenone. The aim of the current study was to use case-matching analysis to verify the results of our previous study, with the hope of overcoming the biases and limitations of its retrospective design.

We described the details about the data collection and results of our study in another article [6]. To summarize, we conducted a single-center retrospective analysis of patients' records from an ED at a large hospital in Poland (Provincial Specialist Hospital in Słupsk). The inclusion criteria were as follows: > 18 years of age, hemodynamically stable, without respiratory distress, an episode of AF (*de novo* or paroxysmal) lasting < 48 hours, and having undergone PCV at the ED. The diagnosis of AF upon admission to the ED was made in accordance with the current literature [1, 7]. The exclusion criteria were as follows: hemodynamic instability (as defined by the current ESC guidelines) [1], respiratory distress or with an AF episode secondary to acute coronary syndrome, heart valve disease, or hyperthyroidism. The success of PCV was defined as termination of AF and return to SR confirmed with a 12-lead electrocardiogram. All patients had their vital signs and EKG monitored before, during, and after PCV.

The choice of the administered AAD was based on the ED physician's discretion. Antazoline was administered intravenously (IV) in 50 mg or 100 mg doses. If SR was not restored after the initial bolus of antazoline, additional 50 mg boluses were administered every 15 minutes until the SR was restored or the maximum dose of 300 mg was reached. The initial dose of amiodarone was 300 mg iv diluted with 50 ml 5% glucose solution administered via infusion pump over 1 hour (maximum dose 1200 mg IV

Address for correspondence: Janusz Springer MD, Department of Cardiology, J.K. Łukowicz Memorial Specialist Hospital, ul. Leśna 10, 89-600, Chojnice, Poland, tel: + 48 698 954 941, fax: + 48 52 395 6639; e-mail: janusz.springer@gumed.edu.pl

Received: 22.07.2023 Accepted: 10.04.2024 Early publication date: 21.05.2024

Table 1. Demographic and clinical parameters of the patients included in the case-match analysis.

	"Antazoline" group	"Not antazoline" group
Female	15 (45.5%)	16 (48.5%)
Male	18 (54.5%)	17 (51.5%)
Age (years) mean (SD)	64.1 (10.4)	64.8 (12.1)
Weight (kg) mean (SD)	79.1 (9.1)	81.8 (20.0)
Height (cm) mean (SD)	167.6 (7.0)	170.2 (9.9)
BMI mean (SD)	28.3 (3.8)	28.1 (6.2)
Total cholesterol (mg/dL) mean (SD)	168.8 (32.5)	176.1 (37.0)
LDL (mg/dL) mean (SD)	87.9 (27.5)	101.6 (34.3)
HDL (mg/dL) mean (SD)	48.3 (19.1)	47.7 (8.8)
Triacylglycerols (mg/dL) mean (SD)	139.3 (42.5)	139.1 (59.2)
Glucose (mg/dL) mean (SD)	108.2 (28.9)	116.1 (37.0)

in 24 hours). The initial dose of flecainide was 150–300 mg per os (maximum dose 300 mg). The initial dose of propafenone was 70 mg IV over 10 minutes (maximum dose 140 mg IV). If SR was not restored after the initial dose, each drug was administered again until the maximum dose was reached or SR was restored.

The study protocol was approved by the Local Ethics Committee (decision number NKEBN/151/2008). In accordance with the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, all patients gave informed consent to participate in this study. All the patient data were anonymized and protected in accordance with the European Union's General Data Protection Regulation.

All data were entered into Microsoft Excel spreadsheets (Microsoft Corp., Redmond, USA). In all calculations, the significance level was $p = 0.05$. All statistical calculations were performed using Statistica software version 12.0 (StatSoft Inc., Tulsa, OK, USA).

Using the logistic regression model and 10 demographic/clinical parameters (sex, age, weight, height, BMI, total cholesterol, LDL, HDL, triacylglycerols, glucose), the probability of belonging to the 'antazoline' or 'not antazoline' group was calculated. Then, using the propensity score matching method, 33 patients were included in the "antazoline" group (15 females, 18 males) and 33 in the "not antazoline" group (16 females, 17 males). Their average age was 64 years (Table 1).

The effectiveness of PCV among patients treated with antazoline versus "not antazoline" were 63.6% and 61.3%, respectively (chi-square test), and no statistically significant differences were found (Mann-Whitney U test). The mean time to restore SR in the antazoline group was 31.7 (38.5) minutes versus 120.3 (136.1) minutes in the "not antazoline" group, and this difference was statistically significant ($p = 0.0011$, Mann-Whitney U test).

In the literature we found only one case-matching study regarding PCV using antazoline in the ED [8]. In their propensity score-matched sample of 165 patients in the antazoline and non-antazoline groups each, Wybraniec *et al.* reported that antazoline was significantly more effective in terminating AF than amiodarone or propafenone (84.2% vs. 66.7%; RR, 1.26; 95% CI, 1.11–1.43; $p < 0.001$). As noted above, our analysis did not reveal statistical significance of that parameter. Unfortunately, the authors did not measure the time elapsed from administering an AAD to successful restoration of SR; therefore, we could not compare those results. Another notable difference is that Wybraniec *et al.* [8] did not seem to include patients with heart failure (which coexists in up to 1/3 of patients with AF). Furthermore, they did not include in their non-antazoline group any patients who were administered flecainide.

The fundamental limitations of our study are its small sample and the small number of clinical parameters used for the case matching. This was because all patient management was performed by a team of physicians, which lead to inconsistencies in the patient data collection. Finally, our patient sample is not diverse because the intravenous form of antazoline seems to be currently available only in Poland.

Our case-matching analysis revealed that PCV with antazoline is faster than with the other drugs we compared: amiodarone, flecainide, and propafenone. More and higher-quality evidence is needed to decisively assess the effectiveness of antazoline in terminating paroxysmal AF episodes.

Acknowledgments: We would like to thank Dariusz Świetlik, PhD for his expert guidance regarding the statistical analysis.

Funding: None.

Conflict of interest: None to report.

References

1. Hindricks G, Potpara T, Dagres N, et al. ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the european association for cardio-thoracic surgery (EACTS): The task force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021; 42(5): 373–498, doi: 10.1093/eurheartj/ehaa612, indexed in Pubmed: 32860505.
2. Kalarus Z, Średniawa B, Mitręga K, et al. Prevalence of atrial fibrillation in the 65 or over polish population. Report of cross-sectional NOMED-AF study. Kardiol Pol. 2023; 81(1): 14–21, doi: 10.33963/KP.a2022.0202, indexed in Pubmed: 36043418.
3. Colilla S, Crow A, Petkun W, et al. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. Am J Cardiol. 2013; 112(8): 1142–1147, doi: 10.1016/j.amjcard.2013.05.063, indexed in Pubmed: 23831166.
4. Rozen G, Hosseini S, Kaadan M, et al. Emergency department visits for atrial fibrillation in the United States: Trends in admission rates and economic burden from 2007 to 2014. Journal of the American Heart Association. 2018; 7(15), doi: 10.1161/jaha.118.009024, indexed in Pubmed: 30030215.
5. Springer J, Szmuda T, Kozłowski D. Does the choice of drug in pharmacologic cardioversion correlate with the guidelines? Systematic review. Advances in clinical and experimental medicine. 2021; 30(3): 331–348, doi: 10.17219/acem/130592, indexed in Pubmed: 33757165.
6. Springer J, Pejska M, Homenda W, et al. Effectiveness of antazoline versus amiodarone, flecainide and propafenone in restoring sinus rhythm at the emergency department. Adv Med Sci. 2024 [Epub ahead of print]; 69(2): 248–255, doi: 10.1016/j.advms.2024.04.003, indexed in Pubmed: 38649031.
7. Kozłowski D. Method in the Chaos – a step-by-step approach to ECG Interpretation.Eur J Transl Clin Med. 2018; 1(1): 76–92, doi: 10.31373/ejtcm/92255 (28.07.2023).
8. Wybraniec MT, Maciąg A, Miśkowiec D, et al. Efficacy and safety of antazoline for cardioversion of atrial fibrillation: propensity score matching analysis of a multicenter registry (CANT II Study). Pol Arch Intern Med. 2022; 132(6), doi: 10.20452/pamw.16234, indexed in Pubmed: 35293200.