ORIGINAL ARTICLE

Efficacy and safety of antazoline vs propafenone for conversion of paroxysmal atrial fibrillation to sinus rhythm: a randomized, double-blind study (AnProAF)

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KEY WORDS

antazoline, antiarrhythmic drugs, atrial fibrillation, pharmacologic cardioversion, randomized controlled trial

EDITORIAL

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ABSTRACT

INTRODUCTION Antazoline is a frequently used antiarrhythmic drug (AAD); however, to date, no randomized controlled trial has evaluated its efficacy and safety for cardioversion of recent-onset atrial fibrillation (AF) in comparison with other approved AADs.

OBJECTIVES This study aimed to compare clinical efficacy and safety of antazoline and propafenone for a rapid conversion of nonvalvular paroxysmal AF to sinus rhythm in patients without heart failure.

PATIENTS AND METHODS This was a single-center, randomized, double-blind study. It included patients with AF (lasting <48 hours) who were in a stable cardiopulmonary condition and eligible for cardioversion. The individuals who fulfilled the inclusion criteria were randomly assigned to receive either antazoline (up to 300 mg) or propafenone (up to 140 mg) intravenously. The primary end point was conversion of AF to sinus rhythm confirmed on electrocardiography.

RESULTS Overall, 94 participants (46 [48.9%] in the antazoline group and 48 [51.1%] in the propafenone group) were included. The mean (SD) age was 67.5 (14) years, and 40 participants (42.5%) were men. Successful AF conversion was observed in 29 patients (63%) from the antazoline group and 25 individuals (52.1%) from the propafenone group ($P = 0.39$). The median time to conversion was 10 minutes in the antazoline group and 30 minutes in the propafenone group ($P = 0.03$). Severe adverse events were observed in 5 patients (10.8%) treated with antazoline and 5 individuals (10.4%) who received propafenone.

CONCLUSIONS Intravenous antazoline demonstrated efficacy and safety comparable to those of intravenous propafenone for acute conversion of nonvalvular paroxysmal AF to sinus rhythm in patients without heart failure.

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INTRODUCTION Atrial fibrillation (AF) is the most common type of arrhythmia, occurring in approximately 3% of the population over 20 years of age and 9% of those over 80 years of age.[1] Restoration of sinus rhythm (SR) remains an integral part of treatment for this type of arrhythmia. Early pharmacologic cardioversion (PCV) or electrical cardioversion (ECV) is necessary to alleviate the symptoms, prevent side effects of prolonged arrhythmia, and avoid hospitalization.[2,3] ECV requires general sedation and does not protect from immediate AF recurrence. Therefore, a majority of patients are referred for PCV to terminate the arrhythmia. Early PCV of AF may be achieved through administration of class IA, IC, and III antiarrhythmic drugs (AADs; according to the Vaughan–Williams classification): flecainide, ibutilide, dofetilide, propafenone, amiodarone, or a novel agent, vernakalant. These AADs have limitations, such as proarrhythmic side effects in patients with structural heart disease (class IC drugs), delayed onset of action (amiodarone), or high cost and low availability (vernakalant).[4-6]

WHAT'S NEW?

Antazoline is commonly used for intravenous termination of atrial fibrillation (AF) in the emergency setting in Poland. However, this drug is not listed in any of the formal guidelines owing to a lack of randomized controlled trials (RCTs) comparing it with other antiarrhythmic drugs used for sinus rhythm (SR) restoration. This is the first RCT that compares the clinical efficacy and safety of antazoline and propafenone for a rapid conversion of nonvalvular paroxysmal AF to SR. Successful AF conversion occurred in 63% of cases in the antazoline group and 52.1% of cases in the propafenone group. The median time to conversion was significantly shorter in the antazoline group (10 minutes vs 30 minutes). The incidence of adverse events was comparable between the 2 drugs. Antazoline seems a good option for acute conversion of uncomplicated AF in an emergency department considering its rapid onset of action, high efficacy, and good tolerance.

Therefore, identification of an efficacious, well-tolerated, and less expensive AAD with a rapid onset of action is necessary. Antazoline mesylate is an antihistamine agent with antiarrhythmic quinidine-like properties, which were first documented in the 1960s.[7,8] Electrophysiologically, antazoline prolongs action potential duration and lowers its amplitude, prolongs phase 0 duration, shortens phase 4 of the resting potential, and reduces excitability of the cardiac tissue. Anticholinergic action of this drug causes a transient increase in heart rate (HR), improving atrioventricular conduction and increasing the corrected QT (QTc) interval, left atrial refractory period, and interatrial conduction time.[9-11] In healthy human volunteers, the terminal elimination half-life of antazoline was 2.29 hours, with a mean residence time of 3.45 hours.[5] In clinical practice, the drug can be administered intravenously in boluses of 50 to 100 mg every 3 to 5 minutes, either until successful cardioversion or up to a cumulative dose of 250 to 350 mg.[6,8,12]

In Poland, antazoline has been registered for intravenous termination of supraventricular arrhythmias.[13,14] However, it is not listed in any of the formal guidelines due to a lack of large randomized controlled trials (RCTs) comparing this drug with other AADs with respect to SR restoration. To the best of our knowledge, only 1 RCT evaluated the antiarrhythmic effect of antazoline in comparison with placebo.[15] In the antazoline group (38 patients), the rate of successful AF conversion to SR was 72.2%, with a median time to conversion of 16 minutes. Other published observational studies showed high efficacy of antazoline, ranging between 50% and 80%, and its rapid onset of action, with time to cardioversion between 7 and 20 minutes.[8,12,16-20] This study is the first RCT aiming to compare the efficacy and safety of intravenous antazoline and propafenone for cardioversion of recent-onset AF.

PATIENTS AND METHODS We report on outcomes of 94 participants included in the AnProAF study (FIGURE 1). It was a single-center, randomized, double-blind, superiority trial conducted in accordance with the Declaration of Helsinki, approved by the local ethics committee (85/PB/2019), and registered under Clinical Trials number NCT05720572. All participants provided their written informed consent before inclusion.

Study design We enrolled consecutive patients with AF lasting less than 48 hours, treated at the emergency department or clinical ward of the Department of Heart Diseases, Medical Centre of Postgraduate Education in Warsaw, Poland between September 2019 and September 2022 (FIGURE 2). The inclusion criteria were age between 18 and 90 years and a stable cardiopulmonary condition, defined as an absence of symptoms of acute coronary syndrome or heart failure (HF) exacerbation. The exclusion criteria were a lack of written consent, AF lasting more than 48 hours, AF related to a clinically significant valvular disease, allergy to antazoline or propafenone, clinically significant HF or ejection fraction below 50%, resting ventricular rate of less than 80 bpm without pacemaker backup, HR greater than 140 bpm, QT interval greater than 440 ms, systolic blood pressure (BP) below 100 mm Hg, a history of acute coronary syndrome, coronary artery bypass grafting, stroke, or transient ischemic attack within 30 days before enrollment, advanced liver or kidney failure, pre-excitation on electrocardiography (ECG), signs and symptoms of ischemia related to the current episode of AF, pregnancy or breastfeeding, and background therapy with any oral AAD.

Randomization The randomization scheme was prepared by an independent statistician using SAS software (SAS Institute Inc., Cary, North Carolina, United States). Once the eligible patients had provided informed consent, they were assigned a specific identifier. Neither the patient nor the researcher knew which group a participant will be assigned to. The patients were randomized according to the implemented random allocation sequence using numbered sealed envelopes, which were opened after inclusion of a patient in the study. The participants were allocated to treatment with antazoline or propafenone at a 1:1 ratio.

Upon patient enrollment to the study, a nurse opened the numbered envelope and prepared 3 20-ml syringes containing the study drugs, according to the randomization sequence. Subsequently, the syringes were given to the enrolling physician and nurse who administered the drugs. The patient, enrolling physician, and nurse who administered the drugs were blinded to the treatment.

Intervention Treatment in the antazoline and propafenone groups did not differ at any time during the study. The decision for intravenous

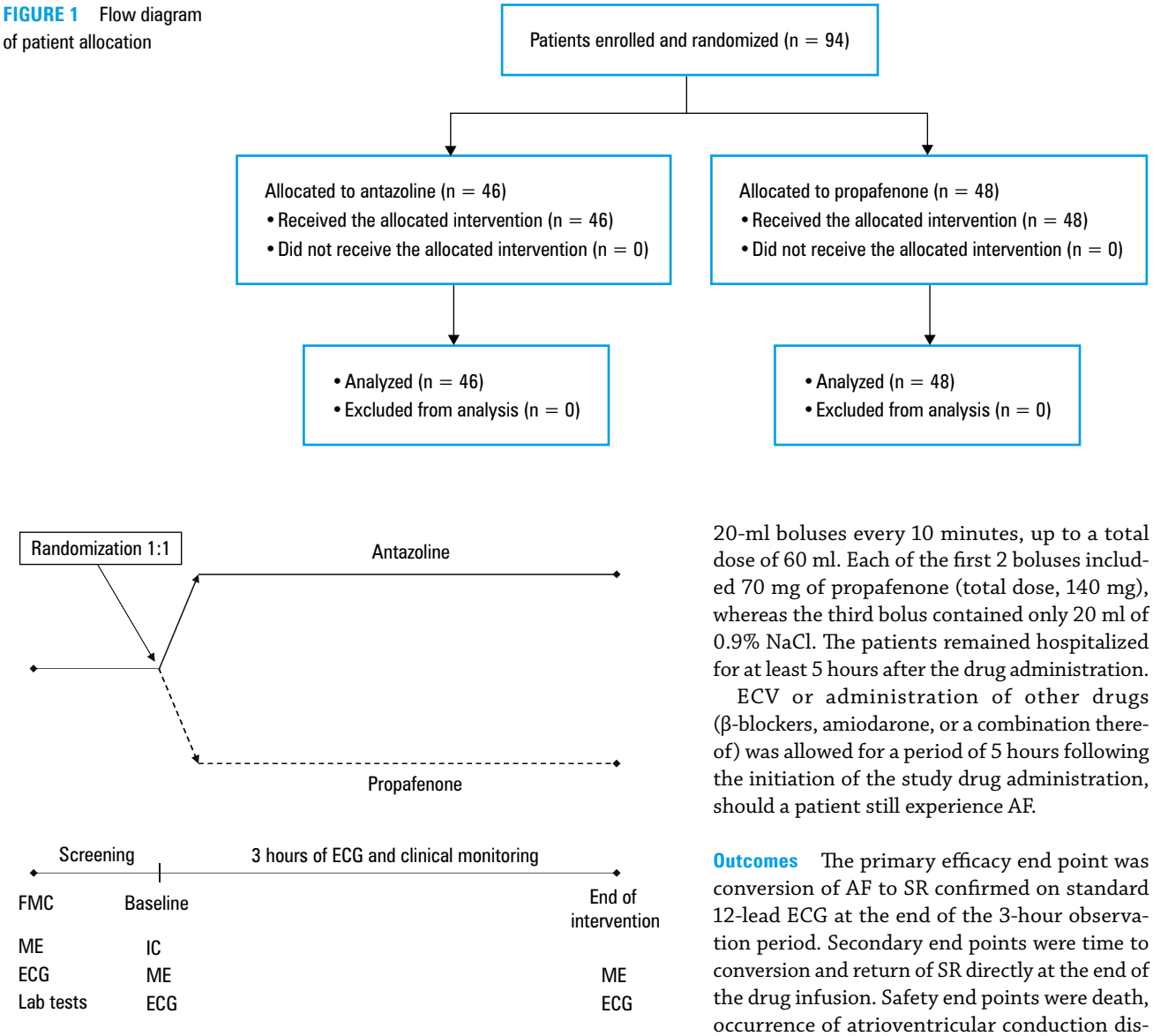

FIGURE 1 Flow diagram of patient allocation

FIGURE 2 Study procedures and treatment assignment
Abbreviations: ECG, electrocardiography; FMC, first medical contact; IC, informed consent; ME, medical examination

administration of β-blockers was made by the physician; the cutoff was a HR greater than 100 bpm. If potassium values were lower than 4 mmol/l, the patients received an electrolyte infusion. The participants were prepared for PCV following a standard clinical care protocol comprising a baseline 12-lead ECG, continuous ECG monitoring, periodic noninvasive BP monitoring, and intravenous line insertion. The study drugs were administered intravenously in boluses by the study nurse under supervision of the enrolling physician, both of whom were blinded to the patient allocation. Drug administration was stopped in the case of conversion of AF to SR, adverse event (AE) occurrence, or conversion of AF to a different supraventricular arrhythmia. The patients assigned to the antazoline group were administered the drug in boluses of 100 mg diluted to 20 ml every 10 minutes, up to a total dose of 300 mg diluted to 60 ml. The patients assigned to the propafenone group were administered 3 20-ml boluses every 10 minutes, up to a total dose of 60 ml. Each of the first 2 boluses included 70 mg of propafenone (total dose, 140 mg), whereas the third bolus contained only 20 ml of 0.9% NaCl. The patients remained hospitalized for at least 5 hours after the drug administration.

ECV or administration of other drugs (β-blockers, amiodarone, or a combination thereof) was allowed for a period of 5 hours following the initiation of the study drug administration, should a patient still experience AF.

Outcomes The primary efficacy end point was conversion of AF to SR confirmed on standard 12-lead ECG at the end of the 3-hour observation period. Secondary end points were time to conversion and return of SR directly at the end of the drug infusion. Safety end points were death, occurrence of atrioventricular conduction disturbances, sustained supraventricular arrhythmia other than AF, new complex ventricular arrhythmia, HR greater than 180 bpm, systolic BP below 90 mm Hg, chest pain, nausea/vomiting, headache, hot flush, drowsiness, and prolongation of QTc (Bazett formula) in comparison with the baseline.

Statistical analysis All analyses were conducted using SAS software (version 9.4, SAS Institute, Inc.). Normally distributed data are presented as mean (SD) and were compared between the groups with the *t* test. Non-normally distributed continuous variables are reported as median with interquartile range and were compared between the groups using the Wilcoxon rank-sum test. Categorical data are expressed as numbers and percentages. Significance of differences for proportions was verified using either the χ^2 test (with the continuity correction) or Fisher exact test. The probability of conversion to SR in the treatment groups was estimated using the Kaplan–Meier method, with a comparison of cumulative events by the log-rank test. All tests were 2-tailed, with a *P* value below 0.05 assumed as significant.

RESULTS A total of 94 patients were included in the analysis. Of them, 46 (48.9%) were allocated to the antazoline group and 48 (51.1%) to the propafenone group (FIGURE 1). Basic epidemiologic and demographic characteristics of the participants on admission are listed in TABLE 1. The groups differed only in sodium concentrations, which were higher in the patients treated with antazoline. The diference was significant, but without clinical relevance.

Efficacy Conversion of AF to SR within the observation period was achieved in 29 patients (63%) treated with antazoline and 25 individuals (52.1%) treated with propafenone (P = 0.39) (TABLE 2). In the antazoline group, the median time to SR restoration was shorter than in the patients receiving propafenone (10 vs 30 minutes; P = 0.03), with greater effectiveness in the first 10 minutes of treatment (30.4% vs 12.5%; P = 0.04) (TABLE 2, FIGURE 3).

Safety The incidence of AEs is outlined in TABLE 3. Serious AEs were equally frequent in both groups (5 cases in each group; TABLES 3 and 4). Pauses in heart rhythm longer than 4 seconds with bradycardia occurred in 3 patients treated with antazoline and 3 patients treated with propafenone. In 1 of the patients who received propafenone, a third-degree atrioventricular block occurred, and a pacing device was implanted. One other patient from the propafenone group was hospitalized for HF exacerbation. This patient did not present any symptoms of HF (eg, peripheral edema, pulmonary crepitations, hepatojugular reflux) before the study drug administration. In the antazoline group, hypotonia with signs of hypoperfusion (cold and sweaty extremities, mental confusion, and dizziness) was observed in a young patient (29 years) without any concomitant diseases or structural heart disease on control echocardiography. These symptoms were transient and resolved after intravenous fluid administration. We also observed 1 case of AF conversion to atrial flutter (AFl) with 1:1 atrioventricular conduction and a HR of 240 bpm. The HR decreased after intravenous metoprolol administration, following which SR returned. Hot flushes were the most common side effect, with higher incidence in the antazoline group (34.8% vs 6.2%; P = 0.001).

DISCUSSION To the best of our knowledge, this is the first RCT comparing the efficacy and safety of antazoline with those of another commonly used AAD, propafenone. We demonstrated that in terms of efficacy, antazoline is comparable to propafenone for conversion of paroxysmal AF to SR, with no differences in the incidence of significant AEs between the drugs.

These results are similar to those reported in previously published observational studies. Wybraniec et al[21] conducted a propensity-score matched (PSM) analysis based on data from a multicenter registry. They revealed that antazoline was comparable to propafenone in terms of successful rhythm conversion (80.9% vs 76.6%; P = 0.61), and that antazoline was more effective than amiodarone (84.1% vs 65.5%; P = 0.001).[21] Another retrospective study including 432 patients with AF demonstrated that antazoline was superior to propafenone in terms of cardioversion success rate (71.6% vs 55.1%).[22]

In our study, antazoline administration resulted in successful PCV of AF in 63% of the participants. This success rate is similar to that reported in a randomized, placebo-controlled trial evaluating antazoline vs placebo for AF termination (AnPAF study[15]), in which the effectiveness of antazoline reached 72.2%. In previous observational studies, the efficacy of antazoline was comparable or slightly higher. In the largest analysis of 1325 patients treated with intravenous antazoline, the drug restored SR in 52% of the patients.[20] Farkowski et al[22] reported that cardioversion with antazoline was successful in 71.6% of the cases. Higher success rates of antazoline were reported in analyses of single-center (CANT study[23]) and multicenter (CANT II study[21]) registries (85.3% and 78.3%, respectively). Studies evaluating the efficacy of antazoline for SR restoration in patients with AF during invasive electrophysiologic procedures showed very high success rates, ranging from 83.6% to 100%.[11,16] Furthermore, the effectiveness of propafenone in the current study (52.1%) was in accordance with the results of previous RCTs, where it ranged from 43% to 89% after intravenous administration.[24-26]

The present findings confirm good tolerance of antazoline-based therapy. Except for hot flushes, the incidence of safety end points was comparable between the study groups. Hot flushes are a typical side effect of antazoline; they were also observed in a high proportion of the AnPAF study participants (19.4%).[15] They were transient, clinically insignificant, and well tolerated. Severe AEs in the present study were documented in 5 patients in each treatment group. The most serious side effect was HF exacerbation with transient severe left ventricular (LV) contractility in a patient from the propafenone group. In this case, 10 mg of intravenous metoprolol were administered before the study drug application. Negative inotropic effects of the drugs could be additive. This observation highlights the need for caution and careful exclusion of features of HF, considering echocardiography in the case of uncertainty. Propafenone (and other class IC agents) are contraindicated in patients with significant LV hypertrophy, LV systolic dysfunction, or ischemic heart disease, and amiodarone is the drug of choice for PCV.[1]

Antazoline is an antihistamine agent with anticholinergic and antiarrhythmic quinidine-like properties. Its action is based on blocking sodium and potassium channels.[9] A previous study conducted in an electrophysiology laboratory revealed that antazoline had no impact on

TABLE 1 Baseline characteristics and clinical presentation of the study population

Parameter		Total (n = 94)	Antazoline (n = 46)	Propafenone (n = 48)	*P* value (antazoline vs propafenone)
Age, y		67.5 (14)	66.8 (15.4)	68.2 (12.6)	0.63
Male sex, n (%)		40 (42.5)	19 (41.3)	21 (43.7)	0.97
First AF episode, n (%)		27 (28.7)	13 (28.3)	14 (29.2)	>0.99
Concomitant diseases, n (%)	Hypertension	70 (74.5)	32 (69.6)	38 (79.2)	0.29
	Thyroid disorders	20 (21.3)	9 (19.6)	11 (22.9)	0.88
	CAD	12 (12.8)	7 (15.2)	5 (10.4)	0.7
	DM	17 (18.1)	8 (17.4)	9 (18.7)	>0.99
	CKD	9 (9.6)	5 (10.9)	4 (8.3)	0.74
	COPD	3 (3.2)	3 (6.5)	0	0.11
Clinical presentation	SBP, mm Hg	135.9 (16)	134.1 (14.2)	137.6 (17.5)	0.3
	DBP, mm Hg	81.6 (10.2)	82.9 (10.3)	80.4 (10)	0.23
	Heart rate, bpm	118.9 (20.1)	117.8 (18.4)	120 (21.7)	0.58
	K, mmol/dl	4.29 (0.4)	4.3 (0.46)	4.28 (0.3)	0.14
	Na, mmol/dl	139.9 (3.2)	140.7 (2.92)	139.3 (3.3)	0.03
Echocardiographic findings	LVEF, %	61.3 (6)	61.6 (5.5)	61 (6.5)	0.68
	LAA, cm^2	22 (4.5)	22.4 (4.8)	21.7 (4.3)	0.53
Background treatment, n (%)	β-Blocker	51 (54.3)	27 (58.7)	24 (50)	0.52
	CCB	22 (23.4)	10 (21.7)	12 (25)	0.9
	Propafenone	0	0	0	–
	Amiodarone	0	0	0	–
	ACEI/ARB	48 (51.1)	25 (54.3)	23 (47.9)	0.68
	Spironolactone	12 (12.8)	6 (13)	6 (12.5)	1

Data are presented as mean (SD) unless otherwise indicated. *P* values <0.05 were considered significant.

SI conversion factors: to convert K and Na to mmol/l, multiply by 10.

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; CAD, coronary artery disease; CCB, calcium channel blocker; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; DM, diabetes mellitus; LAA, left atrial area; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure

TABLE 2 Efficacy of the study drugs and time to sinus rhythm recovery

Parameter		Antazoline (n= 46)	Propafenone (n = 48)	*P* value
SR recovery, n (%)		29 (63)	25 (52.1)	0.39
Time to SR recovery, n (%)	0–10 min	16 (34.8)	8 (16.7)	0.04
	>10 min and ≤60 min	23 (50)	16 (33.3)	0.15
	>60 min and ≤120 min	28 (60.9)	22 (45.8)	0.21
	>120 min and ≤180 min	29 (63)	25 (52.1)	0.39
Time to SR recovery, min, median (IQR)		10 (3–60)	30 (10–105)	0.03

Abbreviations: IQR, interquartile range; SR, sinus rhythm

AH interval, Wenckebach point, atrioventricular (AV) node effective refractory period (AVN-ERP), and sinus node recovery period.[10] Similarly, a study by Farkowski et al[11] showed no impact of antazoline on electrophysiologic parameters, except for AVN-ERP, which was significantly shorter after the drug infusion.[11] In clinical practice, these advantages were associated with antazoline provoking AV disturbances potentially less often than other class I AADs; thus, it became the drug of choice in patients with suspected AV conduction failure not protected with a pacemaker. In our study, a single case of AV disturbance (a third-degree atrioventricular block) was observed among the 48 patients treated with propafenone, and there were no such cases among the 46 patients treated with antazoline.

Three episodes of a pause in heart rhythm lasting more than 4 seconds as an expression of sinus node failure were observed in each study group (6.5% vs 6.3% in the antazoline and propafenone groups, respectively). In line with these findings, bradycardia was documented in 5.6% of cases in the AnPAF study.[15] Wybraniec et al,[21] in their analysis of multicenter registry data, demonstrated a comparable presence of bradycardia below 45 bpm in patients treated with antazoline and propafenone (4.8% vs 5.3%, respectively), with the lowest incidence in those treated with amiodarone (1.7%).[21] The authors explained this phenomenon by a higher rate of intravenous β-blocker administration in the antazoline group, as compared with the amiodarone group. After a PSM analysis adjusted for β-blocker use, bradycardia was observed at a similar rate among the antazoline- and nonantazoline-treated patients (*P* = 0.13).[21] In our study, bradycardia was observed in the antazoline group in the patients

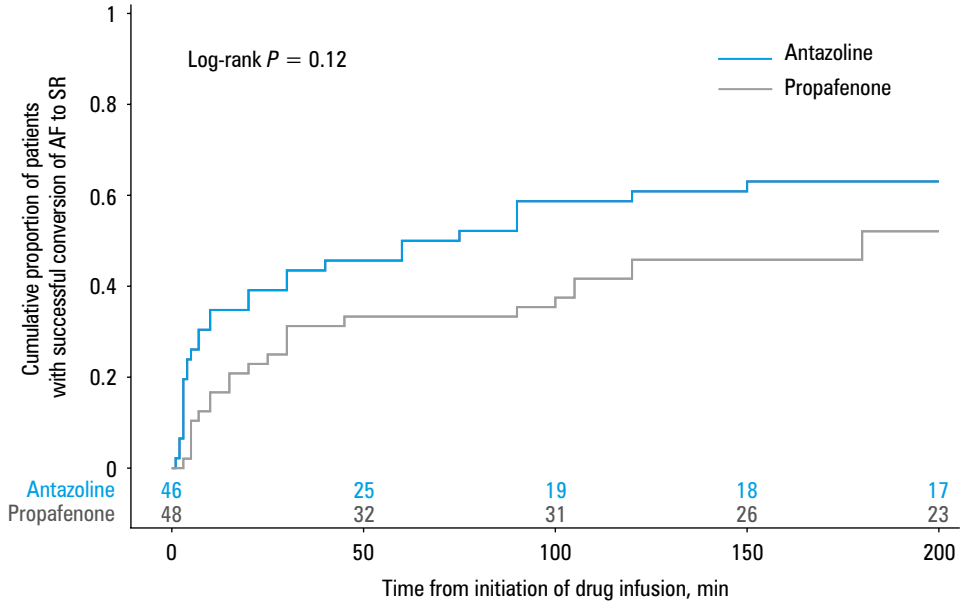

FIGURE 3 Kaplan–Meier curves showing probability of a successful conversion of atrial fibrillation (AF) to sinus rhythm (SR) within 180 minutes in the patients treated with antazoline and propafenone

TABLE 3 Adverse events in the patients treated with antazoline and propafenone

Event	Antazoline (n = 46)	Propafenone (n = 48)	*P* value
Hypotension	1 (2.2)	3 (6.2)	0.62
Tachycardia >180 bpm	1 (2.2)	0	0.49
Pauses in heart rhythm >4 s	3 (6.5)	3 (6.3)	1
HF excerbation	0	1 (2.1)	>0.99
Atrioventricular disturbances	0	1 (1.9)	>0.99
PVC/VT	0	0	–
Hot flush	16 (34.8)	3 (6.2)	0.001
Drowsiness	3 (6.5)	2 (4.2)	0.67
Headache	0	0	–
Nausea	2 (4.4)	0	0.24
Dyspnea/chest pain	0	1 (2.1)	>0.99
Bitter/metallic taste in mouth	4 (8.7)	1 (2.1)	0.2
Anxiety	0	0	–

Abbreviations: HF, heart failure; PVC, premature ventricular contraction; VT, ventricular tachycardia

without background treatment with β-blockers. It is likely that antazoline might have unmasked a previously occurring sick sinus syndrome.

Antazoline use is associated with a transient increase in HR by 8 bpm between 2 and 4 minutes after intravenous bolus administration, and a transient asymptomatic decrease in cardiac output and BP.[9] These properties might explain the episode of hypotension with features of hypoperfusion in a young (29 years) patient treated with antazoline, without any comorbidities or structural heart disease on control echocardiography. Furthermore, in our study, hypotension without hemodynamic instability occurred in 6.25% of the patients treated with propafenone. These findings are in accordance with those presented in other studies, in which hypotension was one of the most common side effects of AADs used for PCV, and occurred within 2 hours in 23.5% of patients treated with flecainide, 15.6% of those receiving amiodarone, and less than 5% of those on propafenone.[27] Hypotension was rarely observed (2.8%) among the antazoline-treated patients in the AnPAF trial.[15] The electrophysiologic properties of antazoline (similar to those typical of class IC AADs) and hemodynamic changes associated with its use suggest that owing to its slightly negative inotropic effect, this drug should not be used in patients with structural heart disease.

In the present study, we observed a single case of AF conversion to AFl with 1:1 conduction after antazoline administration. It could be explained by the effects of antazoline, that is, gradual reduction of the number of fibrillatory waves in the atrium resulting in less concealed conduction in the AV node, improved AV conduction, and increased ventricular rate. In clinical practice, the ability of antazoline to increase HR or convert AF to AFl is prevented by routine β-blocker administration in the absence of signs of AV node failure (eg, AF with slow ventricular rate <80 bpm). AFl occurrence has also been observed after administration of other class I AADs or amiodarone.[28-30]

An interesting finding is a rapid rhythm control in the antazoline group. The median time to conversion to SR in the patients treated with antazoline was 10 minutes, which was 3-fold shorter than in the propafenone group ($P = 0.03$). Comparable results were achieved in the randomized, placebo-controlled AnPAF trial,[15] wherein antazoline terminated AF within a median time of 16 minutes, and in other studies, in which the time to conversion ranged between 7 and 20 minutes.[13,16,22,24] In this important aspect, antazoline is comparable with vernakalant, a modestly faster-acting drug with a median time to rhythm conversion of 8–11

TABLE 4 Clinical characteristics of patients with severe adverse events

Patient No.	Treatment	Event	Age, y; sex	LVEF, %; LAA, cm^2	BP, mm Hg; HR, bpm	Concomitant diseases	Background treatment	Metoprolol IV
1	Antazoline	Hypotonia	29; M	65; 19	145/90; 140	None	None	2.5 mg
2	Antazoline	Pause in heart rhythm, 4523 ms	82; F	57; 35	120/89; 130	Hypertension	NOAC, β-blocker, ACEI	No
3	Propafenone	Pause in heart rhythm, 4600 ms	80; F	62; 17	125/80; 80	Hypertension	NOAC	No
4	Propafenone	HF exacerbation, hypotonia	64; F	50; 29	160/90; 90	Hypertension	ACEI	10 mg
5	Antazoline	Pause in heart rhythm, 4000 ms; bradycardia, 35 bpm	81; F	68; 26	130/70; 100	Hypertension, CAD, thyroid disorders, DM	NOAC, β-blocker, ARB, spironolactone, diuretic, statin	No
6	Antazoline	Pause in heart rhythm, 3600 ms; bradycardia, 40 bpm	83; F	65; 22	164/110; 100	Hypertension, CKD, hyperlipidemia	VKA, β-blocker, statin	No
7	Propafenone	Pause in heart rhythm, 4000 ms	71; F	61; 23	150/90; 120	Hypertension, thyroid disorders	NOAC, β-blocker, ACEI, spironolactone, diuretic	No
8	Propafenone	Pause in heart rhythm, 5000 ms; bradycardia, 30 bpm; hypotonia	72; F	70; 18	155/87; 130	Hypertension, thyroid disorders, hyperlipidemia	NOAC, β-blocker, CCB, ACEI, statin	2.5 mg
9	Propafenone	Third-degree atrioventricular block	69; M	60; 25	130/80; 120	Hypertension	β-blocker	No
10	Antazoline	Atrial flutter with heart rate 240 bpm	30; M	60; 18	156/86; 85	None	None	No

Abbreviations: IV, intravenously; others, see TABLES 1 and 3

minutes; however, use of the latter is limited by the cost of the therapy.[31,32] With respect to other AADs, procainamide has a median time to conversion of 3 hours, while for intravenous propafenone and intravenous flecainide, the reported mean or median time to cardioversion ranges between 14 and 22 minutes.[26,33,34] The advantage of antazoline is its affordable price (approximately 1 EUR per a 200-mg dose), which is much lower than the cost of other AADs.

Certain limitations of the present study need to be acknowledged, the main of which is its single-center design. We enrolled consecutive patients with AF lasting less than 48 hours treated at the emergency department or clinical ward of our center. The sample size calculation was not performed before the beginning of the study. Due to funding constraints, we were not able to perform a multicenter trial. Larger-scale, multicenter RCTs are required in the future.

In conclusion, there were no significant differences between antazoline and propafenone with respect to the efficacy and safety for PCV of AF. Rapid onset of action, high efficacy, and good tolerance make antazoline a suitable alternative to other AADs used for acute conversion of uncomplicated AF in an emergency setting.

ARTICLE INFORMATION

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CONTRIBUTION STATEMENT JK, KW, and JR were responsible for the concept and design of the study. JK, AW, and MB were involved in data collection. KW, KS, and JR prepared the database and performed the statistical analysis. All authors edited and approved the final manuscript.

CONFLICT OF INTEREST None declared.

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