ORIGINAL ARTICLE

# Comparison of the effectiveness of intravenous diltiazem and metoprolol in the management of rapid ventricular rate in atrial fibrillation

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**Objective:** To compare the effectiveness of intravenous (IV) diltiazem and metoprolol in the management of rapid ventricular rate in atrial fibrillation (AF).

**Methods:** This prospective, randomised study was conducted in the Emergency Department of the Uludag University Medical Faculty Hospital, Bursa, Turkey. Forty AF patients with a ventricular rate ⩾120/minute and systolic blood pressure ⩾95 mm Hg were included and randomised to receive IV diltiazem 0.25 mg/kg (maximum 25 mg) or metoprolol 0.15 mg/kg (maximum 10 mg) over 2 minutes. Blood pressures and heart rate were measured at 2, 5, 10, 15, and 20 minutes. Successful treatment was defined as fall in ventricular rate to below 100/minute or decrease in ventricular rate by 20% or return to sinus rhythm.

**Results:** Between January 2000 and July 2002, 40 patients (18 men, 22 women) met the inclusion criteria. Of these 20 (8 men, 12 women; mean age 60.2 years, range 31–82) received diltiazem and 20 (10 men, 10 women; mean age 64.0 years, range 31–82) received metoprolol. The success rate at 20 minutes for diltiazem and metoprolol was 90% (n = 18) and 80% (n = 16), respectively. The success rate at 2 minutes was higher in the diltiazem group. The percentage decrease in ventricular rate was higher in the diltiazem group at each time interval. None of the patients had hypotension.

**Conclusion:** Both diltiazem and metoprolol were safe and effective for the management of rapid ventricular rate in AF. However, the rate control effect began earlier and the percentage decrease in ventricular rate was higher with diltiazem than with metoprolol.

Atrial fibrillation (AF) is the commonest chronic arrhythmia, and its prevalence increases with age.[1 2] AF is a potential risk factor for stroke by predisposing to thrombus formation, it may exacerbate heart failure due to loss of effective atrial contraction in compensated patients, and it may cause tachycardia induced cardiomyopathy when ventricular rate is not controlled.[2–4] The goals of treatment for AF are to maintain effective cardiac output either by conversion to sinus rhythm when appropriate or by controlling ventricular rate and preventing embolic complications.[5 6] Recent trials (the rate control versus electrical cardioversion for persistent atrial fibrillation (RACE) study and the atrial fibrillation follow-up investigation of rhythm management (AFFIRM) study) have demonstrated that therapies directed towards maintenance of sinus rhythm have no survival advantage over ventricular rate controlling strategies and that there is a lower risk of adverse drug effects with the rate control strategy.[7 8]

The rapid ventricular rate increases the oxygen demand of the myocardium and may cause myocardial ischaemia and heart failure in the patients who have limited myocardial reserve. Symptoms including palpitation, angina, dyspnoea, and anxiety may be seen in patients with AF. To prevent complications and relieve the symptoms ventricular rate should be controlled in AF patients with a rapid ventricular rate.

Digitalis, β blockers and calcium channel blockers (verapamil and diltiazem) are all used in the treatment of rapid ventricular rate in AF.[5 6 9–11] However, there has been no study comparing the effectiveness of these agents. Therefore, we conducted the present study to compare the effectiveness of intravenous (IV) diltiazem and metoprolol (the only parenteral β blocker preparation available in Turkey) in the management of rapid ventricular rate in AF in an emergency department (ED) setting.

## METHODS

This prospective, double blind, randomised study was planned and conducted in the ED of the Uludag University Medical Faculty Hospital, Bursa, Turkey. The mean number of annual admissions to the ED is 24 000. We enrolled patients >18 years of age who had AF with a ventricular rate ⩾120/minute and systolic blood pressure ⩾95 mm Hg. Patients were excluded if they had history of allergic reactions to diltiazem and metoprolol, congestive heart failure (New York Heart Association Class IV), systolic blood pressure <95 mm Hg, sick sinus syndrome, atrioventricular (AV) block (2nd or 3rd degree), pre-excitation syndromes, ventricular rate >220/min, QRS >0.08 s, unstable angina pectoris, acute myocardial infarction, hyperthyroidism, temperature >38.0 ℃, haemoglobin <11.0 g/dl, bronchial asthma, chronic obstructive pulmonary disease, diabetes mellitus, peripheral vascular disease, pregnancy, history of use of diltiazem, verapamil, digoxin, β blockers, theophylline, or β mimetics within the last five days (these drugs are cleared from the body within this time).[12–14] All the enrolled patients received information about the study and gave written informed consent. The study was conducted inaccordance with the Declaration of Helsinki.

All patients had a 12-lead electrocardiogram at the beginning of the trial. We recorded and monitored their heart rate and blood pressures. The patients were randomly assigned to IV diltiazem 0.25 mg/kg (maximum 25 mg) or metoprolol 0.15 mg/kg (maximum 10 mg), which was administered by the nursing staff in the ED.[12–15] For randomisation, we used cards with "metoprolol" or "diltiazem" put in sealed, opaque envelopes. The envelopes were

**Abbreviations:** AF, atrial fibrillation; ED, emergency department; IV, intravenous

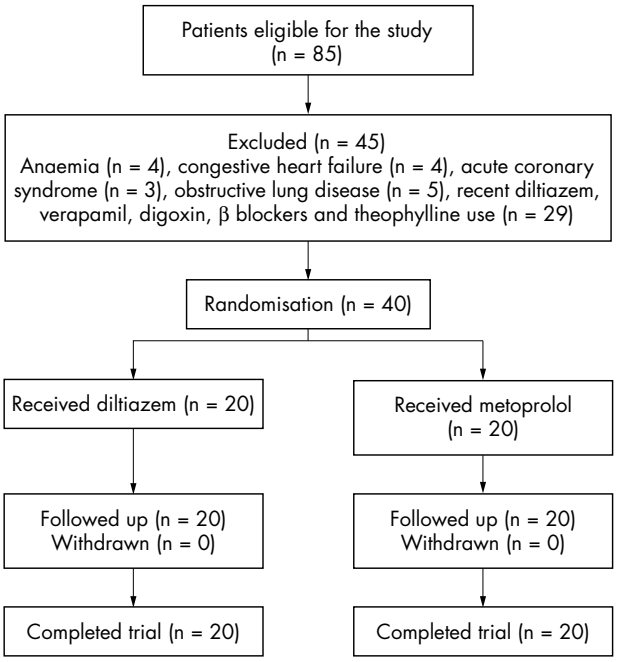


**Figure 1** Flow chart of the numbers of patients at different time points in the study.

shuffled to achieve randomisation. When an eligible patient was to be given treatment the top most envelope was opened by a nurse who was not taking part in the study. Then the drug was prepared by the nurse and the amount of the injection equalised with normal saline. The drug was administered to the patient in the presence of an observer (one of the authors) who was blinded to the contents of the injection. The patient's heart rate (with a rhythm strip at least 30 s long) and blood pressures were measured and recorded by a blinded observer at 2, 5, 10, 15, and 20 minutes to evaluate the effect of the treatment.

We defined successful treatment as achievement of a ventricular rate <100/min or a decrease in ventricular rate by 20% (<120/min at least) or conversion to sinus rhythm.[13] Hypotension (systolic blood pressure <90 mm Hg) was accepted as a complication of treatment.[13 14] If the initial therapy was unsuccessful, an additional dose of IV diltiazem (0.35 mg/kg in diltiazem group and 0.25 mg/kg in the metoprolol group) was given as rescue treatment at the end of the study period. At this time point the observer was not blinded.

We analysed the data with SPSS for Windows (version 10.0). We used the *t* test for statistical comparisons of the differences between the two groups with regard to mean age, sex, pretreatment ventricular rate, systolic and diastolic blood pressures, treatment success ratios, and percentage decrease in ventricular rate. The paired *t* test was used for comparing within group changes at different time point. Differences in categorical variables were analysed with $\chi^2$ square test.

## RESULTS

Between January 2000 and July 2002, of 85 patients who were initially evaluated, 40 (18 men, 22 women; mean (SD) age 62.1 (12.9) years) met all the inclusion criteria and were enrolled in the study (fig 1). Twenty patients were randomised to receive diltiazem (8 men, 12 women; mean age 60.2 years, range 31–82) and 20 to receive metoprolol (10 men, 10 women; mean age 64.0 years, range 31–82). There was no significant difference between the groups as regards age and sex.

**Table 1** Ventricular rate at the different time points of the study for each patient in both treatment groups

| Treatment group and patient no. | Age | Sex | Minutes after administration of treatment 0 | 2 | 5 | 10 | 15 | 20 | Result |
|---|---|---|---|---|---|---|---|---|---|
| Diltiazem | | | | | | | | | |
| 1 | 65 | F | 145 | 112 | 105 | 102 | 102 | 100 | Successful |
| 2 | 72 | F | 150 | 96 | 75 | 68 | 72 | 76 | Successful |
| 3 | 70 | M | 140 | 94 | 103 | 90 | 85 | 80 | Successful |
| 4 | 41 | M | 178 | 101 | 94 | 93 | 95 | 99 | Successful |
| 5 | 50 | M | 150 | 85 | 90 | 92 | 98 | 96 | Successful |
| 6 | 64 | M | 146 | 105 | 108 | 108 | 108 | 98 | Successful |
| 7 | 70 | F | 192 | 132 | 120 | 118 | 117 | 118 | Successful |
| 8 | 56 | F | 174 | 170 | 132 | 136 | 138 | 124 | Unsuccessful |
| 9 | 69 | M | 128 | 107 | 103 | 100 | 96 | 98 | Successful |
| 10 | 67 | F | 124 | 68 | 74 | 72 | 80 | 72 | Successful |
| 11 | 73 | F | 146 | 112 | 94 | 98 | 100 | 98 | Successful |
| 12 | 63 | F | 160 | 132 | 104 | 108 | 106 | 98 | Successful |
| 13 | 60 | M | 160 | 43 | 139 | 108 | 105 | 98 | Successful |
| 14 | 47 | F | 170 | 154 | 142 | 124 | 116 | 112 | Successful |
| 15 | 31 | M | 158 | 145 | 124 | 120 | 95 | 96 | Successful |
| 16 | 66 | F | 162 | 122 | 120 | 118 | 116 | 115 | Successful |
| 17 | 50 | F | 186 | 130 | 126 | 130 | 140 | 130 | Unsuccessful |
| 18 | 82 | F | 169 | 121 | 108 | 104 | 104 | 99 | Successful |
| 19 | 68 | M | 140 | 98 | 96 | 93 | 95 | 103 | Successful |
| 20 | 40 | F | 150 | 105 | 108 | 92 | 80 | 90 | Successful |
| Mean | | | 156.4 | 116.6 | 108.2 | 103.7 | 102.4 | 100 | |
| Metoprolol | | | | | | | | | |
| 1 | 62 | M | 166 | 148 | 144 | 135 | 138 | 142 | Unsuccessful |
| 2 | 66 | F | 161 | 121 | 120 | 118 | 116 | 112 | Successful |
| 3 | 64 | M | 132 | 108 | 110 | 102 | 104 | 93 | Successful |
| 4 | 82 | M | 124 | 120 | 106 | 98 | 94 | 98 | Successful |
| 5 | 65 | F | 150 | 92 | 102 | 112 | 104 | 98 | Successful |
| 6 | 64 | F | 124 | 100 | 90 | 96 | 90 | 96 | Successful |
| 7 | 74 | F | 156 | 140 | 132 | 130 | 129 | 115 | Successful |
| 8 | 76 | F | 138 | 118 | 108 | 106 | 110 | 107 | Successful |
| 9 | 40 | F | 130 | 128 | 128 | 126 | 128 | 122 | Unsuccessful |
| 10 | 69 | M | 141 | 116 | 98 | 104 | 104 | 98 | Successful |
| 11 | 31 | F | 170 | 120 | 122 | 122 | 116 | 118 | Successful |
| 12 | 52 | M | 150 | 150 | 150 | 130 | 130 | 128 | Unsuccessful |
| 13 | 73 | M | 140 | 126 | 114 | 104 | 108 | 98 | Successful |
| 14 | 70 | M | 160 | 128 | 114 | 112 | 110 | 98 | Successful |
| 15 | 56 | M | 168 | 97 | 92 | 88 | 89 | 90 | Successful |
| 16 | 60 | M | 142 | 122 | 119 | 65 | 65 | 68 | Successful |
| 17 | 80 | F | 150 | 108 | 94 | 106 | 94 | 90 | Successful |
| 18 | 70 | F | 160 | 141 | 144 | 132 | 126 | 114 | Successful |
| 19 | 75 | M | 198 | 183 | 190 | 185 | 163 | 150 | Unsuccessful |
| 20 | 52 | F | 180 | 130 | 140 | 130 | 128 | 115 | Successful |
| Mean | | | 152 | 124.8 | 120.8 | 115 | 112.3 | 107.5 | |

Table 1 gives the changes in ventricular rate following treatment for all patients in both study groups. The changes in mean ventricular rate are shown in fig 2 and the percentage decrease in ventricular rate in relation to time in table 2. The rate of success of the treatments at 2, 5, 10, 15, and 20 minutes are given in table 3 and table 4 shows the changes in blood pressure with time in both the study groups. There were no significant differences between the mean

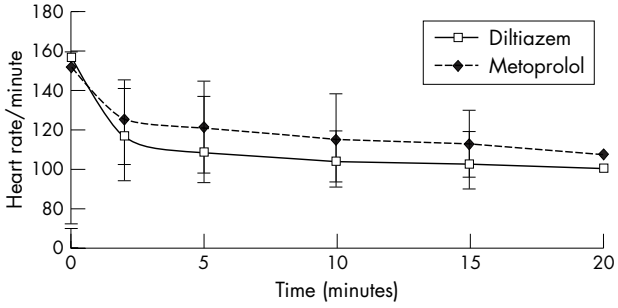


**Figure 2** Mean ventricular rate in relation to time after treatment in the two treatment groups.

**Table 2** Mean (SD) percentage decrease in ventricular rate in relation to time in both treatment groups

| Treatment groups | Time (minutes after administration of treatment) | | | | |
|---|---|---|---|---|---|
| | 2 | 5 | 10 | 15 | 20 |
| Diltiazem | 25.6 (12) | 30.7 (9.7) | 33.6 (8.4) | 34.5 (8) | 35.9 (6.6) |
| Metoprolol | 17.5 (11.6) | 20.4 (11.8) | 24.3 (11.6) | 25.9 (11.5) | 28.9 (10.9) |
| p value | p<0.05 | p<0.01 | p<0.01 | p<0.01 | p<0.05 |

**Table 3** Treatment success ratios (%) in relation to time

| Treatment groups | Time (minutes after administration of treatment) | | | | |
|---|---|---|---|---|---|
| | 2 | 5 | 10 | 15 | 20 |
| Diltiazem | 50 | 60 | 75 | 90 | 90 |
| Metoprolol | 15 | 35 | 60 | 65 | 80 |
| p value | p<0.05 | p>0.05 | p>0.05 | p>0.05 | p>0.05 |

ventricular rate and the systolic and diastolic blood pressures of the two treatment groups before treatment.

None of the patients achieved sinus rhythm. A significant decrease in the ventricular rate was observed in both treatment groups after at 2 minutes ($p<0.01$). The percentage decrease in ventricular rate was significantly higher in the diltiazem group than in the metoprolol group at 2, 5, 10, 15, and 20 minutes. Diltiazem was found to have a significantly higher success rate at 2 minutes than metoprolol. The success rate in the diltiazem group appeared to be higher than metoprolol group at each time interval, however, there was no statistically significant difference between the two groups at 5, 10, 15, and 20 minutes.

At 20 minutes, a mean decline of 15.5/9.8 mm Hg and 22.3/11.5 mm Hg in the systolic/diastolic blood pressures was observed in the diltiazem and metoprolol groups, respectively. There was no significant difference between the decrease of blood pressure in the two treatment groups. None of the patients had hypotension.

## DISCUSSION

Diltiazem is a calcium channel blocker classified as a class IV antiarrhythmic in the Vaughan–Williams classification. It slows the conduction through the AV node and prolongs AV nodal refractoriness when the AV nodal conduction rates are high. Hence it is commonly used in supraventricular tachycardias.[12–14] In a study comparing the efficacy of diltiazem and digoxin in 30 patients with AF and atrial flutter with rapid ventricular rate, Schreck *et al* reported that the mean heart rate decreased significantly (from 150/min to 111/min) after IV diltiazem at 5 minutes and that IV diltiazem was more effective than IV digoxin for emergent control of ventricular rate.[14] In an out-of-hospital study on 43 patients (38 AF, 4 atrial flatter, 1 supraventricular tachycardia), Wang *et al* reported that sinus rhythm returned in four patients, ventricular rate decreased to $\leqslant$100/min in 20 patients, heart rate decreased >20% in 11 patients, and the overall success rate was 81% with IV diltiazem.[16] Goldenberg *et al*, in a study of patients with AF, atrial flutter, and moderate to severe congestive heart failure, reported a high therapeutic response (83.7% with 0.25 mg/kg and 97.3% with an additional 0.35 mg/kg) with IV diltiazem in controlling rapid ventricular rate.[17]

In our study, successful ventricular rate control was achieved in 18/20 patients (90%) in the diltiazem group at 20 minutes. The remaining two patients required an additional dose of 0.35 mg/kg diltiazem for rate control. Half of the patients had a rapid response to diltiazem at 2 minutes. None of the patients had hypotension.

β Blockers are class II antiarrhythmic drugs whose physiological effects are a result of their competitive inhibition of catecholamine binding to β-adrenoceptor sites. They slow AV nodal conduction and prolong AV nodal refractoriness, so they are useful in supraventricular tachyarrhythmias. The effect of metoprolol, which is the only parenteral β blocker preparation available in Turkey, on ventricular rate has been proved in several studies.[15 18 19] In a study on the patients with supraventricular tachyarrhythmias, Amsterdam *et al* reported that the mean heart rate decreased by more than 15% in 11 of 16 patients (69%) (9 of 11 patients with AF (82%)) with a mean dose of 9.5 mg metoprolol. Hypotension was observed in five patients.[18]

In our study the desired ventricular rate control was achieved in 16 of 20 patients (80%) in the metoprolol group at 20 minutes. In the remaining four patients the therapeutic effect was achieved with IV diltiazem, 0.25 mg/kg (only one of these patients needed an additional dose of diltiazem, 0.35 mg/kg). None of the patients had hypotension.

In conclusion, our study showed both diltiazem and metoprolol were effective and safe in controlling rapid ventricular rate in AF. However, the rate control effect of diltiazem began earlier and the percentage decrease in

**Table 4** Mean (SD) blood pressure in both treatment groups in relation to time. Values are mm Hg

| Treatment group | Time (minutes after administration of treatment) | | | | | |
|---|---|---|---|---|---|---|
| | 0 | 2 | 5 | 10 | 15 | 20 |
| Diltiazem | | | | | | |
| SBP | 136.5 (29.8) | 128.7 (24.8) | 124.5 (22.6) | 122 (21.9) | 121 (21.4) | 121 (19.9) |
| DBP | 86 (15.1) | 81.7 (12.9) | 78.5 (12.2) | 77.5 (11.3) | 76.5 (11.2) | 76.2 (11.3) |
| Metoprolol | | | | | | |
| SBP | 143 (22.5) | 134 (22.2) | 129.2 (19.0) | 125.5 (19.9) | 124.2 (18.0) | 81.5 (10.1) |
| DBP | 93 (13.8) | 88 (13.3) | 85 (11.3) | 84 (11.4) | 82 (10.5) | 120.7 (18.1) |
| p value | p>0.05 | p>0.05 | p>0.05 | p>0.05 | p>0.05 | p>0.05 |

SBP, systolic blood pressure; DBP, diastolic blood pressure.

ventricular rate at different time intervals in the diltiazem group was higher in the metoprolol group.


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Competing interests: none declared

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# PostScript

## CORRECTIONS

doi: 10.1136/emj.2004.015586corr1

In the short report titled, Not all cases of neck pain with/without torticollis are benign: unusual presentations in a paediatric accident and emergency department (*Emerg Med J* 2005; **22**:645–8) two errors have occurred. The corresponding address for A Natarajan is incorrect and should be Consultant Paediatrician, anatarajan@hotmail.com. The second error is in the legend for figure 1. It should read 'T1-weighted MRI scan of the cervical spine showing a large intramedullary tumour in the cervical and upper thoracic region C1-T2.' The journal apologises for these errors.

doi: 10.1136/emj.2003.11403corr1

An author's error occurred in the paper titled Hazardous drinkers in the accident and emergency department—Who accepts advice? (*Emerg Med J* 2004;**21**:491–2). Incorrect proportions for 'Believed initial AED attendance related to drinking' appear in table 1 (A). The figures were calculated using a denominator based on the number of responses to that item, rather than the number of patients who were offered advice. The correct proportions are 49.9 for 'Accepted advice' and 45.9 for 'Did not accept advice' (not 70.1 and 69.8 as stated in the text). The difference in proportion (95% CI) should read 4.0 (-2.1 to 10.1).

doi: 10.1136/emj.2003.10247corr1

In the paper titled, Comparison of the effectiveness of intravenous diltiazem and metoprolol in the management of rapid ventricular rate in atrial fibrillation (*Emerg Med J* 2005;**22**:411-4) an error has occurred in table 4. At 20 minutes, places of systolic and diastolic pressures were exchanged. The author apologises for this error.

doi: 10.1136/emj.2005.002005

In part 15 of the ABC of community emergency care (*Emerg Med J* 2005;**22**: 564–71) the legend for figure 2 is incorrect. It should read 'Sixth nerve palsy right eye: failure of abduction. Courtesy of Dr P Marazzi/SPL model released'.

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