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

C Demircan, H I Cikriklar, Z Engindeniz, H Cebicci, N Atar, V Guler, E O Unlu, B Ozdemir

**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.

**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 °C, 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). All the enrolled patients received information about the study and gave written informed consent. The study was conducted in accordance 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. 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
Accepted as a complication of treatment. 13 14 If the initial was no significant difference between the groups as regards men, 10 women; mean age 64.0 years, range 31–82). There enrolled in the study (fig 1). Twenty patients were initially evaluated, 40 (18 men, 22 women; mean (SD) age 62.1 (12.9) years) met all the inclusion criteria and were to be given treatment the top most envelope was opened 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. 11 Hypotension (systolic blood pressure <90 mm Hg) was accepted as a complication of treatment. 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 χ² 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 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. 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 1 Flow chart of the numbers of patients at different time points in the study.

Figure 2 Mean ventricular rate in relation to time after treatment in the two treatment groups.
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 tachyarrhythmias. 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. 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. 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>
<thead>
<tr>
<th>Table 2</th>
<th>Mean (SD) percentage decrease in ventricular rate in relation to time in both treatment groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment groups</td>
<td>Time (minutes after administration of treatment)</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>25.6 (12)</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>17.5 (11.6)</td>
</tr>
<tr>
<td>p value</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Treatment success ratios (%) in relation to time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment groups</td>
<td>Time (minutes after administration of treatment)</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>50</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>15</td>
</tr>
<tr>
<td>p value</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Mean (SD) blood pressure in both treatment groups in relation to time. Values are mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment group</td>
<td>Time (minutes after administration of treatment)</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>SBP</td>
</tr>
<tr>
<td></td>
<td>DBP</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>SBP</td>
</tr>
<tr>
<td></td>
<td>DBP</td>
</tr>
<tr>
<td>p value</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>
ventricular rate at different time intervals in the diltiazem group was higher in the metoprolol group.

Authors’ affiliations
C Demircan, H I Cikriklar, Z Engindeniz, H Cebicci, N Atar, V Guler, E O Unlu, B Ozdemir, Uludag University Medical Faculty Hospital, Bursa, Turkey

Competing interests: none declared

REFERENCES
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’.

Clinical Evidence—Call for contributors

Clinical Evidence is a regularly updated evidence-based journal available worldwide both as a paper version and on the internet. Clinical Evidence needs to recruit a number of new contributors. Contributors are healthcare professionals or epidemiologists with experience in evidence-based medicine and the ability to write in a concise and structured way.

Areas for which we are currently seeking authors:
- Child health: nocturnal enuresis
- Eye disorders: bacterial conjunctivitis
- Male health: prostate cancer (metastatic)
- Women’s health: pre-menstrual syndrome; pyelonephritis in non-pregnant women

However, we are always looking for others, so do not let this list discourage you.

Being a contributor involves:
- Selecting from a validated, screened search (performed by in-house Information Specialists) epidemiologically sound studies for inclusion.
- Documenting your decisions about which studies to include on an inclusion and exclusion form, which we keep on file.
- Writing the text to a highly structured template (about 1500–3000 words), using evidence from the final studies chosen, within 8–10 weeks of receiving the literature search.
- Working with Clinical Evidence editors to ensure that the final text meets epidemiological and style standards.
- Updating the text every six months using any new, sound evidence that becomes available. The Clinical Evidence in-house team will conduct the searches for contributors; your task is simply to filter out high quality studies and incorporate them in the existing text.
- To expand the topic to include a new question about once every 12–18 months.

If you would like to become a contributor for Clinical Evidence or require more information about what this involves please send your contact details and a copy of your CV, clearly stating the clinical area you are interested in, to Klara Brunnhuber (kbrunnhuber@bmjgroup.com).

Call for peer reviewers

Clinical Evidence also needs to recruit a number of new peer reviewers specifically with an interest in the clinical areas stated above, and also others related to general practice. Peer reviewers are healthcare professionals or epidemiologists with experience in evidence-based medicine. As a peer reviewer you would be asked for your views on the clinical relevance, validity, and accessibility of specific topics within the journal, and their usefulness to the intended audience (international generalists and healthcare professionals, possibly with limited statistical knowledge). Topics are usually 1500–3000 words in length and we would ask you to review between 2–5 topics per year. The peer review process takes place throughout the year, and our turnaround time for each review is ideally 10–14 days.

If you are interested in becoming a peer reviewer for Clinical Evidence, please complete the peer review questionnaire at www.clinicalevidence.com or contact Klara Brunnhuber (kbrunnhuber@bmjgroup.com).