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Clinical paper

Slow infusion of calcium channel blockers compared with intravenous adenosine in the emergency treatment of supraventricular tachycardia☆

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ABSTRACT

Introduction: The emergency treatment of supraventricular tachycardia (SVT) has, over the last two decades, changed from verapamil to adenosine primarily owing to documented hypotensive episodes occurring with rapid bolus infusions of the calcium channel blocker. Slow infusions of calcium channel blockers have not previously demonstrated hypotension to any significant degree. The aim of this study was to compare the efficacy and safety of bolus intravenous adenosine and slow infusion of the calcium channel blockers verapamil and diltiazem in the emergency treatment of spontaneous SVT.

Methods: A prospective randomized controlled trial with one group receiving bolus intravenous adenosine 6 mg followed, if conversion was not achieved, by adenosine 12 mg; and the other group receiving a slow infusion of either verapamil at a rate of 1 mg per minute up to a maximum dose of 20 mg, or diltiazem at a rate of 2.5 mg per minute up to a maximum dose of 50 mg. These infusions would be stopped at time of conversion of the SVT or when the whole dose was administered. Heart rate and blood pressure was continuously monitored during drug infusion and for up to 2 h post-conversion.

Results: A total of 206 patients with spontaneous SVT were analysed. Of these, 102 were administered calcium channel blockers (verapamil = 48, diltiazem = 54) and 104 were given adenosine. The conversion rates for the calcium channel blockers (98%) were statistically higher than the adenosine group (86.5%), $p = 0.002$, RR 1.13, 95% CI 1.04–1.23. The initial mean change in blood pressure post-conversion in the calcium channel blocker group was −13.0/−8.1 mmHg (verapamil) and −7.0/−9.4 mmHg (diltiazem) and 2.6/−1.7 mmHg for adenosine. Only one patient in the calcium channel group (0.98%) (95% CI 0.025–5.3) developed hypotension, and none in the adenosine group.

Conclusion: Slow infusion of calcium channel blockers is an alternative to adenosine in the emergency treatment of stable patients with SVT. Calcium channel blockers are safe and affordable for healthcare systems where the availability of adenosine is limited.

1. Introduction

Paroxysmal supraventricular tachycardia (SVT) is a common cardiac emergency presenting to the Emergency Department (ED). Since the 1970s intravenous verapamil has been the drug of choice[1,2] for the treatment of SVT. The 1986 American Heart Association guidelines for Cardiopulmonary Resuscitation and Emergency Cardiac Care recommended that verapamil be given as a 2.5–5 mg intravenous bolus over 2 min and 5–10 mg over 2 min to be given after 15–30 min of the first dose if the SVT persisted[3] or recurred and if blood pressure remains acceptable. For the 1992 American Heart Association Guidelines, adenosine was recommended as the initial drug of choice for haemodynamically stable paroxysmal SVT. The sequence of agents recommended was adenosine twice (6 mg followed by 12 mg). If the blood pressure had not dropped and the SVT persisted up to two doses of verapamil (2.5–5 mg) intravenous over 2 min followed by 5–10 mg over 2 min could be given. When treating the elderly or when blood pressures were within the lower range of normal, smaller doses (2–4 mg) of verapamil over a longer period (3–4 min) were recommended for the first dose.[4] The main reason given for adenosine as the first choice drug was that adenosine does not cause hypotension to the same degree as verapamil because adenosine has a very short half-life (<10 s).

A previous randomized controlled trial (161 patients) by our group compared intravenous verapamil and intravenous diltiazem[5] given as slow infusions (verapamil at a rate of 1 mg per minute and

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diltiazem at a rate of 2.5 mg per minute). This showed a conversion rate of more than 97% with only one patient (1%) developing hypotension. This finding suggests that the haemodynamic instability previously attributed to verapamil may be related to the speed of verapamil administration.

There are few studies directly comparing the effectiveness of adenosine and calcium channel blockers. Most of these studies recruited subjects with laboratory-induced SVT.[6–8] In addition, they used a rapid bolus of intravenous calcium channel blocker given over 15 s (except for the study by Hood and Smith).[7] These studies generally conclude that adenosine and verapamil are both highly effective in the termination of SVT.

There has been no previous large prospective, randomized controlled trial comparing the usefulness of intravenous adenosine vs. slow-infusion calcium channel blockers in a clinical patient-care environment. The aim of this study was to compare the efficacy and safety of bolus intravenous adenosine with the slow infusion of verapamil or diltiazem, in the termination of spontaneous SVT in the ED.

2. Methods

This was a prospective, randomized, controlled clinical trial in patients presenting with SVT to an ED. The study was approved by the hospital Ethics Committee.

2.1. Patients

Patients of at least 10 years of age, who presented to the ED of the Singapore General Hospital with a regular narrow complex tachycardia and an electrocardiographic (ECG) diagnosis of SVT, not converted by vagal manoeuvres (Valsalva manoeuvre or carotid sinus massage or both) and who were in SVT at when seen by a doctor were included in the study.

The exclusion criteria were:

- Patients with signs of impaired cerebral perfusion (e.g. altered mental state) or acute pulmonary edema.
- Patients with a subsequent diagnosis of arrhythmias other than SVT (i.e. sinus tachycardia, atrial flutter, atrial fibrillation or idiopathic ventricular tachycardia) were excluded from the analysis if they were initially enrolled.
- Pregnancy by history (urine pregnancy testing was not used to actively exclude the condition in any of the female patients entered into the study).

2.2. Protocol

Once consent was obtained, patients were randomly assigned into two treatment arms:

- The calcium channel blocker group: patients randomized to receiving diltiazem as the first choice were administered diltiazem at a concentration of 0.625 mg/ml by slow intravenous infusion at a rate of 4 ml per minute (equivalent to 2.5 mg per minute) up to a maximum dose of 50 mg. Those randomized to receiving verapamil as the first choice were administered verapamil at a concentration of 0.25 mg/ml by slow intravenous infusion at a rate of 4 ml per minute (equivalent to 1 mg per minute) up to a maximum dose of 20 mg. Both infusions were given using a Terumo infusion pump. During intravenous infusion, the patient's vital signs (heart rate, systolic and diastolic blood pressures) were monitored using a Propaq® vital sign monitor at 2-min intervals up to the completion of infusion or conversion from SVT, whichever was the earlier. At the time of conversion to sinus rhythm, the infusion was stopped and the amount of drug infused recorded.
- The adenosine group were administered adenosine as a rapid bolus within a 2 s time frame through an 18G intravenous cannula placed in the antecubital fossa, followed by a 10 ml saline push and elevation of that upper limb. Initially a 6 mg bolus was administered, and if there was no conversion of the SVT within 2 min of the administration, a further 12 mg bolus was administered.

If the SVT was not converted by the end of the verapamil or diltiazem infusion, the patients in these groups were then given intravenous adenosine as described above. For patients randomized to receive adenosine initially, and remaining in SVT after the first two boluses, they were again randomized to receive either verapamil or diltiazem slow infusion as described above.

There were four treatment arms as follows:

1. Verapamil infusion → adenosine
2. Diltiazem infusion → adenosine
3. Adenosine → verapamil infusion
4. Adenosine → diltiazem infusion

Patients were randomized using sealed envelopes. Each of these four choices were written on a card and placed in a sealed envelope. The nurse in charge of patients would perform the randomization by drawing the serialized sealed envelope to decide the order of treatment.

If the tachycardia was not converted at the end of the study protocol, patients were managed with synchronized electrical cardioversion if the patient was haemodynamically unstable, or further pharmacotherapy if the patient was haemodynamically stable. This was at the discretion of the treating physician.

Following successful conversion, patients were closely monitored for the next 30 min with measurement of vital signs at 1 min (immediate post-conversion), 5, 10, 15 and 30 min post-conversion, following which, if they remained stable, they were monitored for 2 h in the Department's Emergency Observation Ward with telemetry. If there were no recurrences during the period of observation, they were discharged with an appointment to attend the Cardiology Department's Arrhythmia Clinic within a week. Patients with recurrence of SVT during the 2-h observation period were managed at the discretion of the treating physician.

Follow-up records of the Department of Cardiology were reviewed for a period of up to 1 year.

2.3. Statistical analysis

The association between the success rate of conversion with slow verapamil or diltiazem infusion and adenosine bolus was assessed using chi-square or Fischer's exact test. Normality assumptions of the quantitative variables (age, blood pressure and heart rate) was checked using the Kolmogorov Smirnov 1 sample test. Differences within treatment groups were assessed using paired *t*-tests if normality assumptions were satisfied; otherwise the Wilcoxon Signed Rank test was applied. Differences between treatment groups were determined using ANOVA or Kruskal–Wallis tests with bonferroni adjustments applied. Statistical significance was set at $p < 0.05$.

2.4. Sample size calculation

Our local studies on conversion of spontaneous SVT showed that: