Adenosine versus intravenous calcium channel antagonists for the treatment of supraventricular tachycardia in adults (Review)

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[Intervention Review]

Adenosine versus intravenous calcium channel antagonists for the treatment of supraventricular tachycardia in adults

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ABSTRACT

Background

Patients with paroxysmal supraventricular tachycardia frequently present to the Emergency Department. Where vagal manoeuvres fail, the two most commonly used drugs are adenosine and calcium channel antagonists. Both are known to be effective but both have a significant side-effect profile.

Objectives

To examine the relative effects of adenosine and calcium channel antagonists and, if possible, to determine which is most appropriate for the management of supraventricular tachycardia.

Search methods

Studies were identified from The Cochrane Central Register of Controlled Trials (CENTRAL), Issue 3 2006, MEDLINE (1966 to June 2006), Pre-MEDLINE and EMBASE (1980 to June 2006). Bibliographies of identified studies were also examined. No language restrictions were applied.

Selection criteria

Inclusion criteria: randomised trials comparing adenosine and a calcium channel antagonist in patients of any age with supraventricular tachycardia, where one of the defined outcomes was reported. Outcomes of interest were: reversion rate, mortality, time to reversion, rate of relapse, minor adverse events, major adverse events, length of hospital stay and patient satisfaction. Major adverse events were defined as cardiac arrest, prolonged hypotension, symptomatic bradycardia requiring treatment and acute cardiac failure. Minor adverse events were any other reported event.

Data collection and analysis

Two reviewers independently checked the results of searches to identify relevant studies. Dichotomous outcomes were reported as Peto Odds ratios and continuous outcomes as weighted mean differences.

Main results

Eight trials were identified. In the pooled analysis there was no significant difference in reversion rate or relapse rate between the two drugs. Time to reversion was slower for verapamil than adenosine in all studies that reported this outcome, but the data were not suitable for combining. Minor adverse events such as nausea, chest tightness, shortness of breath and headache were reported much more frequently in patients treated with adenosine with 10.8 % of patients reporting at least one of these events, compared with 0.6% of those treated with verapamil (OR 0.15, 95% CI 0.09 to 0.26, P<0.001). There was no significant difference in the rate of major adverse events between the two groups, although hypotension was reported exclusively in the verapamil treatment group (3/166 patients treated with verapamil, 0/171 treated with adenosine).

Authors' conclusions

Adenosine and verapamil are both effective treatments for supraventricular tachycardia in the majority of patients. However, given the high incidence of minor but unpleasant side effects in patients treated with adenosine and the potential for hypotension with verapamil, patients should be fully informed of these risks prior to treatment.

PLAIN LANGUAGE SUMMARY

Adenosine versus intravenous calcium channel antagonists for tachycardia in adults

Supraventricular tachycardia (SVT)is a common abnormal rhythm of the heart resulting in a very rapid heart beat. This rhythm problem usually occurs in otherwise healthy people and common symptoms include palpitations, light headedness, and chest pain. Occasionally, SVT may also cause confusion or loss of consciousness. SVT can sometimes be treated with simple physical manoeuvres such as forced breath holding. When simple manoeuvres fail, supraventricular tachycardia can be treated in the Emergency department with a variety of different drugs. The two most commonly used drug types are adenosine and calcium channel antagonists (verapamil is the most frequently used drug in this class). This review compares the relative effectiveness and side effects of these two drugs.

Eight trials involving 577 patients were included in the review. Combined analysis of these trials showed no difference in the effectiveness of adenosine and verapamil in successfully treating supraventricular tachycardia, with an overall success rate of approximately 90% for both drugs. Adenosine took less time than verapamil to work, but when effective, both drugs worked within 15 minutes. Adenosine was associated with more side effects than verapamil, with approximately one in ten patients treated with adenosine experiencing chest pain, nausea, shortness of breath or headache, while these symptoms occurred in less than 1% of patients treated with verapamil. However these side effects lasted for only a short time, usually less than a few minutes. Very low blood pressure which required treatment was reported in three out of 166 patients treated with verapamil, while no patients treated with adenosine experienced low blood pressure.

Overall, both drugs appear to be similarly effective but adenosine is associated with a relatively high incidence of 'minor' side effects and verapamil is associated with infrequent 'major' side effects. None of the trials examined patient satisfaction with treatment or how long patients had to stay in hospital, and this somewhat limits the significance of the findings as these issues are probably most important in deciding which drug is the 'best' treatment.

BACKGROUND

Paroxysmal supraventricular tachycardia (PSVT) is one of the most common arrhythmias presenting to the Emergency Department. Common symptoms include palpitations, light headedness, and chest pain and in a small proportion of patients PSVT may also cause confusion or loss of consciousness. The majority of patients are relatively young and healthy, and can be treated and discharged from the Emergency Department. Most narrow complex PSVTs are due to re-entry circuits within the AV node (60-90%) or via a bypass tract with anterograde conduction through the AV node (Bolton 2000; Cameron 2000). For the majority of patients, PSVT is not acutely life threatening but causes significant symptoms and requires treatment to terminate the tachyarrhythmia. Treatment in stable, symptomatic patients is aimed at terminating the abnormal rhythm by decreasing conduction through the AV node. Increas-

ing vagal tone by the Valsalva manoeuvre (forced expiration against a closed glottis) or carotid sinus massage (firm unilateral pressure over the carotid artery in the neck for 5-10 seconds) has been reported to be effective in 17 to 53% of patients (Lim 1998; Ornato 1990; Wen 1998). Lower success rates may be related to variability in instructions given to patients on the correct technique for performing a Valsalva manoeuvre (Taylor 2004). For patients in whom vagal manoeuvres are not effective, calcium channel antagonists, adenosine, sotalol, beta-blockers and magnesium sulphate have been shown to be more effective than placebo (Dougherty 1992; Gupta 1999; Jordaens 1991; Joshi 1995). In small studies magnesium sulphate is effective in converting approximately 33% of PSVT (Joshi 1995), sotalol is effective in 83% of patients but is associated with an adverse event rate of 14% (Jordaens 1991) and short acting beta-blockers such as esmolol are effective in only 25% of patients (Gupta 1999). Therefore, calcium channel antagonists and adenosine are the most commonly recommended therapies (AHA 2005a; Bolton 2000; Cameron 2000; Harrison 2003) because of their relatively high efficacy and low side effect profile.

Calcium channel antagonists have been used in PSVT for many years, are effective in up to 90% of patients (Bolton 2000) and are relatively cheap. As their name suggests, they act by blocking voltage-dependent calcium channels thus reducing intracellular calcium resulting in blockade of calcium dependent conduction through the AV node. However, calcium channel blockade also causes negative inotropy and peripheral vasodilation which may result in hypotension, particularly in patients with impaired left ventricular function. They have a relatively long half-life of three to six hours and thus adverse effects may be prolonged. They are also relatively contraindicated in patients who are already on beta-blockers as the combined effect may lead to significant bradycardia (Katzung 1995). Calcium antagonists are contraindicated in the presence of wide complex tachycardia and with atrial fibrillation or flutter associated with Wolf-Parkinson-White syndrome (AHA 2005a).

Adenosine has been widely used in PSVT in recent years with reported efficacy similar to calcium channel antagonists (Bolton 2000). It is an endogenous nucleoside with a half-life of less than a minute, which acts by inhibiting cAMP-mediated calcium influx and enhancing potassium conduction. This leads to inhibition of AV nodal conduction and increase in the AV nodal refractory period. Because of the short half-life, reversion to sinus rhythm may be short lived as a subsequent ectopic beat may re-initiate SVT. Many patients experience short-lived but very unpleasant side effects following administration of adenosine, including dyspnoea, flushing and a sense of impending death or doom which can be very frightening (Bolton 2000; Hourigan 2001; Katzung 1995). Adenosine is significantly more costly than most intravenous calcium channel antagonists but if it is more effective and/or associated with fewer side effects, the additional cost of adenosine would be less important.

Both these agents are reasonably effective but have significant side effects. Several small studies have examined the effectiveness of these agents individually and comparatively but the decision as to which agent to use is usually determined by personal experience of both the patient and the clinician.

OBJECTIVES

The aim of this review is to examine the relative efficacy and adverse event rates of adenosine and calcium channel antagonists and, if possible, to determine which of these drug types is most appropriate for the management of PSVT.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) or quasi-RCTs comparing any intravenous calcium antagonist with intravenous adenosine.

Types of participants

Patients of any age with narrow complex SVT diagnosed on 12-lead ECG within 24 hours of onset. SVT was defined as a regular, narrow complex tachycardia at a rate of 150-220 beats/minute.

Types of interventions

All interventions that directly compare any intravenous calcium channel antagonist with intravenous adenosine, in any dosage of either drug.

Types of outcome measures

Studies reporting any one of the following were eligible for inclusion:
(1) Reversion rate to sinus rhythm;
(2) Mortality within 12 hours of drug administration;
(3) Time to immediate reversion to sinus rhythm;
(4) Rate of relapse to SVT within 2 hours following reversion ;
(5) Length of stay in hospital;
(6) Major adverse events (defined as cardiac arrest, prolonged hypotension, symptomatic bradycardia requiring treatment, acute cardiac failure);
(7) Minor adverse events (defined as any reported adverse event other than those defined above);

(8) Patient satisfaction as measured on any validated scale.

Search methods for identification of studies

Relevant trials were identified from the following sources:
(1) Cochrane Central Register of Controlled Trials (CENTRAL), Issue 3 2006 (see Table 1);
(2) MEDLINE (1966 to June 2006) and Pre MEDLINE combined with the optimally sensitive strategy for the identification of RCTs (Dickersin 1994);
(3) EMBASE (1980 to June 2006) using terms similar to those used for MEDLINE and combined with a search strategy for the identification of RCTs (Lefebvre C 1996) (see Table 2);
(4) Reference lists of relevant textbooks, review articles and relevant trials;
(5) Conference proceedings and abstracts from cardiac and emergency medicine scientific meetings;
(6) Letters seeking information about unpublished or incomplete trials to investigators known to be involved in previous trials.
Studies in any language were included. Search strategy for MEDLINE is detailed below.

Ovid MEDLINE search strategy

1 exp Adenosine/
2 adenosin$.tw.
3 1 or 2
4 exp Tachycardia, Supraventricular/
5 supraventricular tachycardia$.tw.
6 supraventricular arrhythmia$.tw.
7 supraventricular tachyarrhythmi$.tw.
8 sinus tachycardia$.tw.
9 svt.tw.
10 psvt.tw.
11 or/4-10
12 3 and 11

Data collection and analysis

This review was undertaken by two reviewers (AH and AF). The results from the search strategy are presented as a flowchart based on the Quorom statement (Moher 1999). Titles and abstracts identified by the search strategy described were screened independently by both reviewers. All potentially relevant reviews were retained and the full text of these studies examined to determine which studies satisfied the inclusion criteria. Data extraction was carried out independently by the same reviewers using pre-defined data extraction forms. Studies reported in languages other than those familiar to the authors were translated and evaluated in the presence of a native speaker of the language. Where important data was not reported, we attempted to contact the original authors to get the necessary information.

Study quality

The quality of studies was assessed independently by AH and AF without blinding to authorship or journal. Quality assessment was performed according to the guidelines in the Cochrane Handbook aiming to identify the four main sources of systematic bias in trials: selection bias, performance bias,attrition bias and detection bias. Each of the following criteria was coded as adequate, unclear, inadequate or not used:
(1) Allocation concealment - did the described method ensure that allocation of treatment was concealed up to the point of assignment;
(2) Blinding to outcome assessment - was the method of blinding described adequate to ensure that (1)patients (2)caregivers and (3) investigators remained unaware of treatment assignment;
(3) Adequacy of controls - were the treatment and control groups comparable at entry;
(4) Adequacy of follow-up - did the described method identify all participants including withdrawals, dropout and protocol deviations;
(5) Intention to treat analysis. Control of selection bias after treatment allocation: was there intention to treat analysis, were withdrawals and completeness to follow-up reported, were the results analysed both by the original treatment assignment and by treatment received (yes/no/not stated).
Similarly, the following characteristics were coded to determine external validity:
(1) Clear definition of inclusion and exclusion criteria at entry;
(2) Clear definition of outcome measures;
(3) Reporting of accuracy, precision and observer variation of outcome measures;
(4) Appropriateness of timing of outcome measures;
(5) Clarity of reporting of outcome measures.
Any disagreements were resolved by discussion, including a third party if necessary.

Statistical assessment

Dichotomous outcomes results were expressed as Peto Odds ratios with 95% confidence intervals (CI). Where continuous scales of measurement were used to assess the effects of treatment the weighted mean difference (WMD) was used, or the standardised mean difference (SMD) if different scales were used. Statistical heterogeneity was analysed using a Chi squared test on N-1 degrees of freedom, with $p<0.1$ defined as substantial heterogeneity. If no heterogeneity was present, analysis was performed using a fixed effects model. Where substantial heterogeneity was detected, further analysis was used to explore possible sources of heterogeneity (e.g. study quality, outcome measures, participants and interventions). When the source of heterogeneity could not be explained we did not combine study results. Subgroup analysis was to be used to look for different effects amongst different groups where numbers allowed. Relevant subgroup analysis based on participants' age, gender, duration of symptoms, intercurrent drug therapy, presence of underlying heart disease, prior treatments and drug dosage was explored if possible.

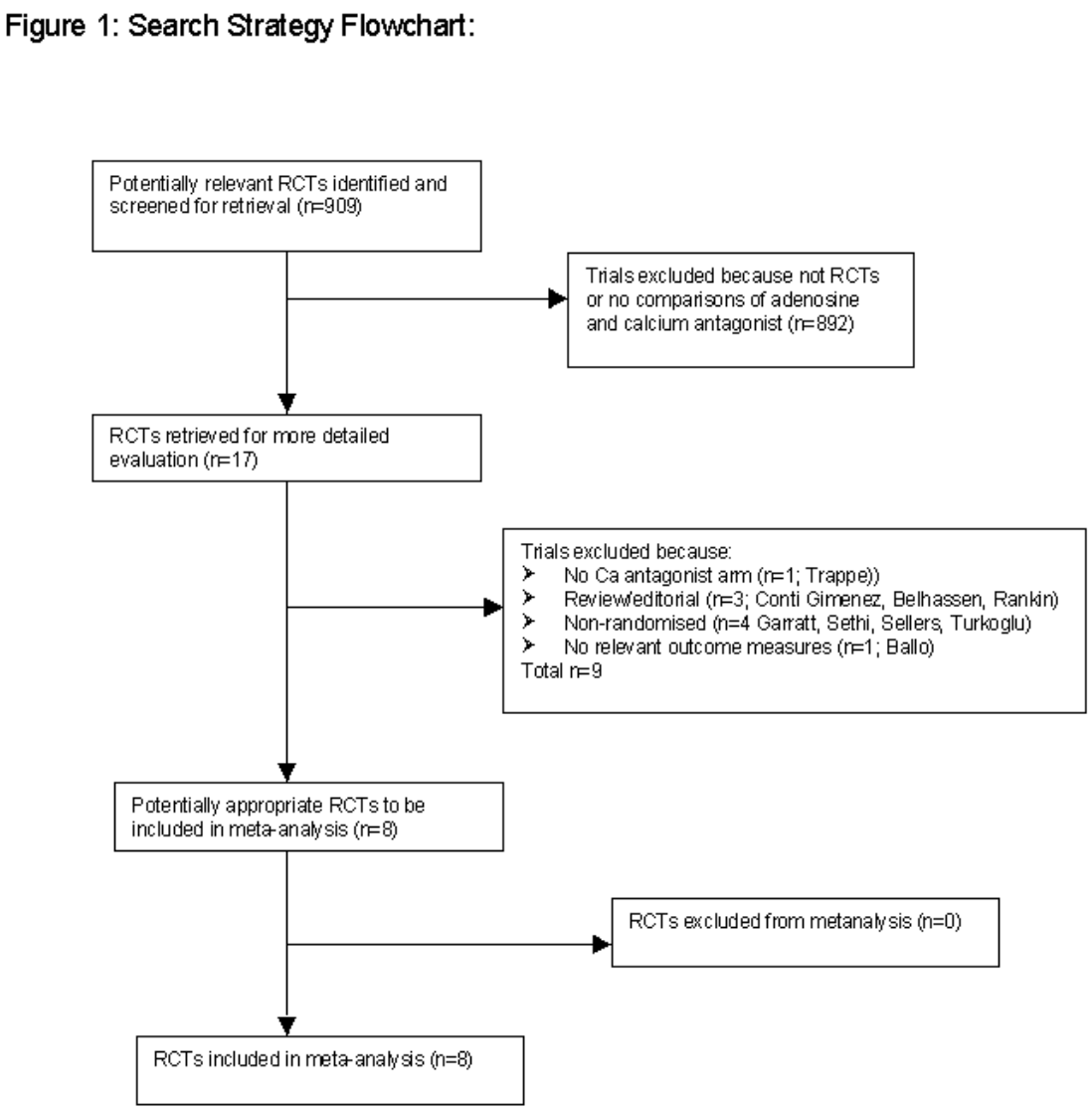
RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

The literature search identified 909 potentially relevant studies. The majority were excluded on abstract review because they were not RCTs or did not compare adenosine and a calcium antagonist (Figure 1). Seventeen articles were retrieved for more detailed evaluation, of which a further nine were excluded because they did not meet our inclusion criteria. No studies were excluded on the basis of quality assessment alone. Thus eight trials were available for inclusion in the review (Cabrera-Sole 1989; Cheng 2003; DiMarco 1990; Ferreira 1996; Gil Madre 1995; Greco 1982; Hood 1992; Kulakowski 1998). Several studies included a crossover component where the alternate study drug was administered if the first drug was unsuccessful (DiMarco 1990; Ferreira 1996; Gil Madre 1995; Greco 1982; Hood 1992). As the time between the drugs was short and did not allow drug washout (particularly for verapamil), we included only data from the pre-crossover phase of these trials. One study (DiMarco 1990) included adenosine versus placebo phase and another study (Greco 1982) had a third treatment arm with digitalis, data from these components of the trials was not included.

Figure 1. Figure 1 - Flowchart.



The eight trials were conducted in 10 different countries and published between 1982 and 2003, with 577 participants. Four of the trials used adenosine in the form of ATP (adenosine tri-phosphate) (Cabrera-Sole 1989; Ferreira 1996; Gil Madre 1995; Greco 1982), the remaining four used adenosine. ATP is rapidly converted to adenosine (the free base form) following exogenous administration, with 10 mg ATP equipotent to 6 mg adenosine, and a linear dosage relationship between the two forms of the drug (Belhassen 1984; Faulds 1991). Verapamil was the calcium antagonist used in all trials. All studies but one (Greco 1982) were conducted in adults.

Two studies enrolled only patients with spontaneous SVT (Ferreira 1996; Greco 1982) and two enrolled patients with both spontaneous and induced SVT (DiMarco 1990; Hood 1992). The remaining trials did not specify whether SVT was spontaneous or induced. None of the studies had a defined maximum length of time for duration of SVT as an inclusion criterion, thus all papers that report 'acute' or 'paroxysmal' SVT as an inclusion criterion were included .

No studies reported length of stay in hospital or outcomes from patient satisfaction surveys.

Risk of bias in included studies

Only one trial (Hood 1992) specified a method of randomisation which demonstrated adequate allocation concealment. One trial (Kulakowski 1998) randomised patients into two groups, but patients then received the alternate study drug (rather than the allocated drug) if they had contraindications to the drug allocated by randomisation. The remaining six trials did not give sufficient information to determine whether allocation concealment was adequate, though these trials stated that patients were 'randomly' allocated to either study arm.

None of the eight trials provided specific information regarding blinding of patients, caregivers or investigators. As the two drugs are usually given by different methods (one as a rapid bolus and one as a slower IV push or infusion) it would only be possible to achieve blinding by using a double dummy method which would require substantial resources. However, this issue was not discussed by any of the investigators.

All studies provided data which demonstrated that patients in both drug groups had similar age and physiological parameters at the time of enrolment. No studies specifically reported completeness to follow-up with withdrawals, dropouts and protocol deviations unreported except where patient had reverted to sinus rhythm prior to treatment. Intention to treat analysis was clearly documented in only one trial (DiMarco 1990) and, as outlined above, the study by Kulakowski did not undertake intention to treat analysis. The remaining trials did not clearly state whether intention to treat analysis was undertaken.

Inclusion criteria were described in all trials, though most studies stated a diagnosis of SVT as the main inclusion criteria without defining SVT by rate or QRS width and with no time limit on duration of symptoms. Exclusion criteria were well described in all but one study, patients with cardiac failure or evidence of shock were excluded except in this one trial (Cabrera-Sole 1989) where exclusion criteria were not defined. All trials reported reversion to sinus rhythm as the main outcome,although this was not defined by ECG criteria.

Effects of interventions

All eight studies gave adequate data on at least one of the stated outcomes for further analysis, thus further contact was not sought with any investigators.

REVERSION RATE

All eight studies reported reversion rate or 'efficacy' of adenosine versus verapamil as an outcome measure. All but one study (Cabrera-Sole 1989) used sequentially increasing doses of each trial drug until reversion occurred or the predetermined maximum dose was reached, whichever occurred first. In these seven trials, reversion rate as an overall cumulative reversion for subjects who received one or more dose of each drug was reported. Some of these trials also reported reversion rates at each drug dose (see below). The remaining trial used a fixed dose of each drug with no escalation of drug dosage in the absence of reversion.

In the pooled analysis of these eight trials, successful reversion in the adenosine group occurred in 273/296 episodes (92.2%) compared with 260/293 (89.0%) in the verapamil group. This difference was not significant (Outcome 01: OR 0.67; 95% CI 0.38 to 1.16; P = 0.15). There was no significant heterogeneity between these trials (P = 0.5).

Reversion rates at different drug doses within each study are summarised in the tables (Table 3 - adenosine; Table 4 - verapamil).

TIME TO REVERSION

Average time to reversion was reported in four studies (Cheng 2003; Ferreira 1996; Hood 1992; Kulakowski 1998). Each study showed a statistically significant shorter time to reversion with adenosine compared with verapamil. However there was significant heterogeneity demonstrated (P < 0.00001) and therefore results could not be combined. The reason for the heterogeneity may relate to the differences in timing and dosing protocols between these trials. The study by Hood reported time from 'effective dose given' and Cheng reported 'average time after dose' whilst the Kulakowski trial timed from the onset of the drug infusion. Adenosine was given in successive 40 ug/kg increments in one study (Hood 1992), in sequential 3mg-6mg-9mg-12mg doses in another study (Kulakowski 1998), in doubling doses (3mg-6mg-12mg) in a third study (Cheng 2003) and with dosing starting at 10mg ATP (equivalent to 6mg adenosine) followed by 20mg ATP in the fourth study (Ferreira 1996). All four studies gave verapamil in 5mg boluses. In two studies (Cheng 2003; Hood 1992) the drug was given as a 5 minute infusion whilst the other two studies(Ferreira 1996; Kulakowski 1998) infused the 5mg over 1 minute and 30 seconds respectively. The longest average times were reported in Cheng's study with 414.4 seconds (6min 54sec) in the verapamil group and 34.2 seconds in the adenosine group. Because of small study numbers, subgroup analysis to examine the cause of heterogeneity was not possible.

RELAPSE RATE

Four studies reported rate of relapse to SVT following reversion to sinus rhythm (DiMarco 1990; Ferreira 1996; Gil Madre 1995; Hood 1992). The study by DiMarco et al was not included in the pooled analysis as it combined results from their adenosine-only dose-ranging protocol with their adenosine versus verapamil protocol. In the remaining three studies there was no evidence of heterogeneity (P=0.51). There was a relapse rate of 1.9% (1 of 51) in the verapamil group compared with 10.2% (6 of 59) in those given adenosine, this difference was not significant (Outcome 03: OR 0.27, 95% CI 0.06 to 1.23, P = 0.09). The time period of observation following drug administration was not documented in any of these studies. Hood reported re-initiation of SVT in two patients at 4.3 and 7.3 seconds. Ferreira reported relapse at 10 minutes in one case given adenosine but did not mention time to relapse for the other case given verapamil.

DiMarco reported relapse to SVT in 8.6% of 210 patients who

received and responded to adenosine either as part of a placebo controlled dose-ranging trial or in the adenosine vs verapamil protocol.

MINOR ADVERSE EVENTS

All studies reported minor adverse events, but the specific events recorded varied between trials. No trial pre-defined minor adverse events. Studies reported the total number of patients with any adverse event, the total number of patients reporting specific adverse events, or both. Reported events included chest tightness, nausea, shortness of breath, headache and flushing.

Three studies reported the total number of patients with any adverse event (Cabrera-Sole 1989; DiMarco 1990; Hood 1992), with most of these events described as one or more of transient flushing, chest discomfort and dyspnoea. Two of these studies included data from both the pre and post crossover phases of their trials (DiMarco 1990; Hood 1992), and thus the results could not be pooled as patients in the post-crossover phase had received verapamil immediately prior to adenosine. Allowing for the most extreme scenario, where all crossed-over patients experienced an adverse event, we removed the number of crossed-over patients from both the numerator and denominator. After this adjustment, all of these trials reported significantly more minor adverse events in patients receiving adenosine, with 0 to 16.3% of patients treated with verapamil experiencing an event, compared with at least 36.9% and up to 97.7% of those treated with adenosine.

Chest tightness was reported by four trials (Cheng 2003; Ferreira 1996; Gil Madre 1995; Kulakowski 1998), and occurred in 15.3% of patients receiving adenosine compared with no patients treated with verapamil. This difference was significant (Outcome 04-01: OR 0.13, 95% CI 0.05 to 0.29, P<0.001). There was no evidence of statistical heterogeneity between these trials (P=1.0).The two trials reporting nausea (Cheng 2003; Gil Madre 1995) demonstrated significantly higher rates in patients receiving adenosine compared with verapamil (Outcome 04-02: 1.1% vs 16.3%, OR 0.12, 95% CI 0.04 to 0.37, P<0.001), with no evidence of heterogeneity (P=0.11). Pooled results for the three trials reporting shortness of breath and headache (Cheng 2003; Gil Madre 1995; Kulakowski 1998) showed a significantly higher rate of dyspnoea (Outcome 04-03: OR 0.20, 95% CI 0.06 to 0.60, P=0.004) and a non-significant increase in headache (Outcome 04-04: OR 0.29, 95% CI 0.06 to 1.46, P=0.13) in patients receiving adenosine.

Flushing was reported in two trials (Gil Madre 1995; Kulakowski 1998) and was significantly higher in the adenosine group in both studies but because the trial by Gil included patients from the cross-over phase, this data could not be pooled.

Greco (Greco 1982) also reported nausea, chest tightness, shortness of breath and headache at higher rates in patients treated with adenosine but this data included results from a non-randomised component of the study and therefore these outcomes were not included in the pooled analysis.

MAJOR ADVERSE EVENTS

Hypotension was a reported outcome in 5 studies (Cabrera-Sole 1989; DiMarco 1990; Ferreira 1996; Hood 1992; Kulakowski 1998) with a total of 3 episodes of hypotension in 166 patients treated with verapamil, and no episodes in 171 patients in the adenosine group (Outcome 05: OR 8.6, 95% CI 0.88 to 83.86, P = 0.06). There was no evidence of heterogeneity between these trials (P=0.99). Four of the five studies reporting hypotension specifically excluded patients with a systolic BP <90mm Hg at enrolment, while the fifth study (Cabrera-Sole 1989) did not specify whether or not hypotension was an exclusion criteria. Two of the three hypotensive episodes occurred at doses of verapamil <10mg, the dose in the third case (Kulakowski 1998) was not reported. Two of the patients subsequently reverted with adenosine and did not require any other specific treatment for their hypotension, the outcome and interventions for the third case were not reported. From this data, 55 additional patients would need to be treated with adenosine to avoid one episode of hypotension.

Only one study (Ferreira 1996) specifically reported an absence of major bradycardia in either group, and no studies reported acute heart failure.

The one paediatric study (Greco 1982) reported two patients who experienced cardiac arrest after treatment with verapamil. One was an infant with cyanotic heart disease and electrolyte disturbances, the other was an infant already being treated with a B-blocker for Wolff Parkinson White syndrome. Both children were successfully resuscitated.

DISCUSSION

Our review aimed to examine the relative efficacy and safety of adenosine and calcium channel antagonists in patients presenting with PSVT. The trials in this analysis included patients with both spontaneous and induced SVT, and patients treated in both the Emergency Department and specialised cardiac laboratories. Thus our findings may be of limited applicability in patients presenting *de novo* with spontaneous PSVT.

We used three outcomes to explore the efficacy of these agents: reversion rates, time to reversion and relapse rates. Overall there was a non-significant difference in reversion rates with approximately 90% of patients reverting with both drugs, suggesting that either drug can be effectively used to treat PSVT in the majority of patients. None of the studies was adequately powered to detect whether the observed differences were significant, and the pooled analysis of 589 patients had a power of only 22% to detect a difference of 3.2% at a significance level of 5%. Approximately 1400 patients in each group would be required to determined whether the observed difference was significant at the 5% level with a power of 80%. The rate of relapse to SVT, following initially successful treatment, was also not significantly different between the two drug types. This outcome was also relatively underpowered and would have required approximately three times as many patients

to achieve a power of 80%. Although these results were not statistically significant, amongst the three studies reporting relapse rates there was only one patient (2.0%, 95%CI: 0.4 -10.0%) who relapsed after successful reversion with verapamil compared with six patients (10.2%, 95%CI 4.8 -20.5%) treated with adenosine.

Time to reversion could not be examined in the pooled analysis due to heterogeneity but was longer for patients treated with verapamil in all four studies. However, the average time to reversion was less than 10 minutes even in the verapamil group and the difference between the two drugs is probably of little clinical significance in patients who are haemodynamically stable.

Minor adverse events occurred far more frequently in patients receiving adenosine with approximately one third of patients reporting an event. Given that minor adverse events were not specifically defined in any of the studies and relied on ad hoc reporting, it is possible the actual rate was higher than reflected in the data. Most of the adverse events related to adenosine were reported as transient and, from a medical perspective, short lived symptoms such as chest pain, dyspnoea and flushing may be perceived as minor. No studies explored the patients' perception of the relative severity of these events.

Although the major adverse event rate was not significantly different between the two treatments, major adverse events were seen exclusively in patients treated with verapamil, with three episodes of hypotension and two cardiac arrests. The cardiac arrests both occurred in a paediatric study published in the 1980s, in clinical circumstances where current practice guidelines would not recommend verapamil (AHA 2005b).

The decision as to which drug is the best option for PSVT in stable adults remains unclear. Both drugs are readily available and simple to administer by intravenous bolus injection. Adenosine costs substantially more than verapamil at $13.89 AUD (US$10.56) per 6mg ampoule compared with $0.96 AUD (US$ 0.73) for a 5mg verapamil ampoule. Of those patients who responded to adenosine 16% required more than 2 ampoules to achieve reversion, whereas patients who responded to verapamil did so at doses of 10mg (2 ampoules) or less. Both drugs appear to have similar efficacy in terms of reversion to sinus rhythm, but adenosine is associated with a relatively high incidence of 'minor' adverse events and verapamil is associated with infrequent 'major' adverse events. The two outcomes for which we could find no data i.e. patient satisfaction and length of hospital stay, may be crucial in the clinical decision as to which treatment to use. From the patient's perspective, the high risk of brief but unpleasant side effects may be unacceptable and, in the authors' experience, patients often find these 'minor' side effects extremely unpleasant.

AUTHORS' CONCLUSIONS

Implications for practice

Both adenosine and verapamil are effective treatments for PSVT in the majority of patients. However, given the small risk of significant hypotension in patients treated with verapamil, and the high incidence of minor but unpleasant side effects in patients treated with adenosine, patients should be fully informed of these risks prior to treatment. There are clinical situations where verapamil is clearly contraindicated such as in patients who have hypotension, poor left ventricular function, are already taking beta-blockers, or who have other tachyarrhythmias such as broad complex tachycardia or atrial fibrillation with underlying accessory pathway. Adenosine is the safer option in these situations. Similarly, paediatric patients should not be treated with verapamil.

Given the proven effectiveness of simple vagal manoeuvres in many patients, these should always be attempted as first line treatment prior to drug administration, unless contraindicated by underlying conditions such as carotid artery disease. While adenosine and verapamil are the most commonly used drugs for PSVT, there are many other therapeutic agents available such as beta-blockers, magnesium and sotalol which have been shown to be effective in some patients in small studies. However these agents are less well studied with few randomised controlled trials comparing them with the commonly used drugs.

Implications for research

Larger studies comparing reversion rates, defined adverse events, length of hospital stay and patient experiences would be required to fully answer whether one treatment is preferable in the management of SVT. As the difference in reversion rate is very small (3.2%) it is unlikely that this difference is of any real clinical significance and a larger study in this area is not warranted. Given that the adverse event rate for adenosine is high, but most events are relatively minor and transient, the main gap in current knowledge is which treatment patients prefer.

Studies regarding other alternative drug therapies are limited and further research is needed to address the safety and efficacy of these agents.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Cabrera-Sole 1989

Methods	Country: Spain Randomisation method: not stated
Participants	Age not stated, presumed adult. Group 1: 44 participants Group 2: 43 participants Inclusion criteria: SVT. Exclusion criteria: not stated
Interventions	Group 1: ATP 20mg bolus. Group 2: Verapamil 10mg bolus
Outcomes	Reversion rate Minor adverse events
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Cheng 2003

Methods	Country: China Randomisation method not stated
Participants	Adults 18-75 years Group 1:60 participants (29 male) Group 2:61 participants (25 male) Inclusion criteria: PSVT. Exclusion criteria: heart block; asthma; emhysema; tea/coffee; taking B-blocker, Ca antagonist or other antihypertensives or antiarrhythics; pregnancy or breast feeding
Interventions	Group 1: Adenosine 3mg then 6mg then 9mg every 1-2 min if no response to previous dose. Mean dose 9.63mg Group 2: Verapamil 5mg over 5min, repeated if no reversion by 15 min. Mean dose 7.15mg
Outcomes	Reversion rate Time to reversion Minoradverse events
Notes	

Cheng 2003 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

DiMarco 1990

Methods	Country: multicentre UK, USA, Canada Randomisation method not stated
Participants	Adults >18years Group 1: 61 participants Group 2: 70 participants Inclusion criteria: induced or spontaneous SVT , SBP >90 Exclusion criteria: severe congestive cardiac failure (CCF), unstable angina (UAP), recent myocardial infarction (MI), severe mitral regurgitation (MR), intracardiac shunt, sleep apnea
Interventions	Group 1: Adenosine 6mg, then 12mg if needed Group 2: Verapamil 5mg, then 7.5mg if needed
Outcomes	Reversion rate Minor adverse events Serious adverse events
Notes	2 part study, first part not included as no Ca antagonist arm. Outcomes for minor adverse events, time to reversion and relapse rate not included as adenosine data from first and second parts combined

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Ferreira 1996

Methods	Country: Brazil Randomisation method: not stated
Participants	Adults Group 1: 25 participants (8 Male) Group 2: 25 participants (9 Male) Inclusion criteria: PSVT presenting to emergency department. Exclusion criteria: systolic blood pressure (SBP)<90, low output state, CCF, UAP, recent MI, taking dipyridamole or methylxanthine

Ferreira 1996 (*Continued*)

Interventions	Group 1: ATP 10mg then 20mg bolus if needed. Mean dose 10.8mg Group 2: Verapamil infused at 5mg/min up to 15mg if needed. Mean dose 9.38mg
Outcomes	Reversion rate Time to reversion Recurrence rate Minor adverse events Major adverse events
Notes	Crossover trial

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Gil Madre 1995

Methods	Country: Spain Randomisation method: not stated
Participants	Adults (25 male,25 female) Group 1: 26 participants Group 2: 24 participants Inclusion criteria: SVT without haemodynamic instability, unresponsive to vagal manouevres. Exclusion criteria: SBP <80, current treatment with B-blockers or Ca antagonists, know ventricular dysfunction, asthma, recent treatment with dipyridamole
Interventions	Group 1: ATP 5mg then 10mg then 20mg every 1min if previous dose not effective. Group 2: 5mg over 3mins, repeated after 10min if no response to first dose
Outcomes	Reversion rate Relapse rate Minor adverse events
Notes	Crossover trial

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Greco 1982

Methods	Country:Italy Randomisation method: random numbers table
Participants	Children <13years Group1: 16 participants Group2: 16 participants Inclusion criteria:presentation with PSVT Exclusion criteria: shock or response to vagal manoeuvre
Interventions	Group1: ATP titrated to effect, mean dose 7.46mg Group2:Verapamil titrated to effect, mean dose 2.09mg
Outcomes	Reversion rate Minor adverse events
Notes	2 part study, only participants in 2nd part included as no randomisation in 1st part

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Hood 1992

Methods	Country: NZ Randomisation method: 'envelope method'
Participants	Adults >16years Group 1: 14 participants (5 male) Group 2: 11 participants (2 male) Inclusion criteria: spontaneous (19 pts) or induced (6 pts) narrow complex SVT, SBP>90 Exclusion criteria: recent B-blocker, Ca antagonist, dipyridamole, methylxanthine; sinus node dysfunction; CCF
Interventions	Group 1: Adenosine 40ug/kg boluses (equivalent to 3mg in 75kg pt) every 2 mins to max 20mg. Mean effective dose 7.8mg Group 2: Verapamil 70ug/kg (equivalent to 5mg in 70kg patient) infused over 5min, repeated at 5 min intervals to max 15mg. Mean effective dose 4.3mg
Outcomes	Reversion rate Relapse rate Time to reversion Major adverse events Minor adverse events Change in SBP
Notes	Some pts had SVT >12 hours

Hood 1992 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Kulakowski 1998

Methods	Country: Poland Randomisation method: not stated
Participants	Adults>= 16years Group 1:46 participants (14 male) Group 2:35 participants (11male) Inclusion criteria: SVT. Exclusion criteria (applied AFTER randomisation): asthma, dipyridamole (for adenosine); hypotension, CCF, Wolff Parkinson White Syndrome (WPW), paroxysmal atrial fibrillation (for Verapamil)
Interventions	Group 1: Adenosine 3mg then 6mg then 9mg then 12mg every 2-3 min if no reversion with previous dose. Group 2: Verapamil 5mg bolus repeated in 3 mins if no reversion
Outcomes	Reversion rate Time to reversion Minor adverse events Major adverse events
Notes	Patients re-allocated to alternate group AFTER randomisation if contraindications to allocated drug

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	No	C - Inadequate

mg=milligrammes
min=minute

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ballo 2004	Retrospective chart review and no relevant outcomes measured
Belhassen 1984	Review article, not a trial.
Conti 1995	Editorial only.
Garratt 1989	Not a randomised trial. Patients with induced SVT given adenosine, then re-induced and given verapamil
Rankin 1991	Review article, not a trial.
Sellers 1987	Retrospective chart review.
Sethi 1994	Not a randomised trial. Patients with induced SVT given adenosine, then re-induced and given verapamil
Trappe 1997	Comparison of adenosine and ajmaline (class 1A anti-arrhythmic). No calcium antagonist arm
Turkoglu 1996	Not a randomised trial.

DATA AND ANALYSES

Comparison 1. Adenosine vs Ca Blockers

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Reversion rate	8	589	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.67 [0.38, 1.16]
2 Time to reversion (seconds)	4	278	Mean Difference (IV, Fixed, 95% CI)	156.07 [133.99, 178.16]
3 Relapse to SVT post-reversion	3	110	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.27 [0.06, 1.23]
4 Minor Adverse events	4	979	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.15 [0.09, 0.26]
4.1 chest tightness	4	303	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.13 [0.05, 0.29]
4.2 Nausea	2	172	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.12 [0.04, 0.37]
4.3 Shortness of breath	3	252	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.20 [0.06, 0.60]
4.4 Headache	3	252	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.29 [0.06, 1.46]
5 Hypotension	5	337	Peto Odds Ratio (Peto, Fixed, 95% CI)	8.60 [0.88, 83.86]

Analysis 1.1. Comparison 1 Adenosine vs Ca Blockers, Outcome 1 Reversion rate.

Review: Adenosine versus intravenous calcium channel antagonists for the treatment of supraventricular tachycardia in adults

Comparison: 1 Adenosine vs Ca Blockers

Outcome: 1 Reversion rate

Study or subgroup	Verapamil n/N	Adenosine n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Cabrera-Sole 1989	39/43	42/44		11.2 %	0.48 [0.09, 2.50]
Cheng 2003	54/62	52/60		27.8 %	1.04 [0.36, 2.96]
DiMarco 1990	64/70	57/61		18.4 %	0.75 [0.21, 2.73]
Ferreira 1996	23/25	24/25		5.7 %	0.50 [0.05, 5.03]
Gil Madre 1995	20/24	21/26		14.9 %	1.19 [0.28, 4.95]
Greco 1982	21/23	18/20		7.3 %	1.16 [0.15, 8.93]
Hood 1992	8/11	14/14		5.4 %	0.08 [0.01, 0.91]
Kulakowski 1998	31/35	45/46		9.3 %	0.21 [0.03, 1.27]
Total (95% CI)	**293**	**296**		**100.0 %**	**0.67 [0.38, 1.16]**

Total events: 260 (Verapamil), 273 (Adenosine)

Heterogeneity: Chi^2 = 6.36, df = 7 (P = 0.50); I^2 =0.0%

Test for overall effect: Z = 1.44 (P = 0.15)

Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Adenosine vs Ca Blockers, Outcome 2 Time to reversion (seconds).

Review: Adenosine versus intravenous calcium channel antagonists for the treatment of supraventricular tachycardia in adults

Comparison: 1 Adenosine vs Ca Blockers

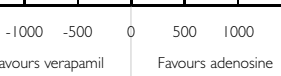
Outcome: 2 Time to reversion (seconds)

Study or subgroup	Verapamil N	Mean(SD)	Adenosine N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Cheng 2003	62	414.4 (191.2)	60	34.2 (19.5)		21.3 %	380.20 [332.35, 428.05]
Ferreira 1996	25	248 (152.5)	25	29.6 (11.6)		13.6 %	218.40 [158.45, 278.35]
Hood 1992	11	306 (234)	14	21.9 (10.2)		2.5 %	284.10 [145.71, 422.49]
Kulakowski 1998	35	85 (84)	46	24 (8)		62.6 %	61.00 [33.08, 88.92]
Total (95% CI)	**133**		**145**			**100.0 %**	**156.07 [133.99, 178.16]**

Heterogeneity: Chi^2 = 136.26, df = 3 (P<0.00001); I^2 =98%

Test for overall effect: Z = 13.85 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 1.3. Comparison 1 Adenosine vs Ca Blockers, Outcome 3 Relapse to SVT post-reversion.

Review: Adenosine versus intravenous calcium channel antagonists for the treatment of supraventricular tachycardia in adults

Comparison: 1 Adenosine vs Ca Blockers

Outcome: 3 Relapse to SVT post-reversion

Study or subgroup	Verapamil n/N	Adenosine n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Ferreira 1996	1/23	1/24		29.8 %	1.04 [0.06, 17.23]
Gil Madre 1995	0/20	3/21		43.4 %	0.13 [0.01, 1.31]
Hood 1992	0/8	2/14		26.8 %	0.19 [0.01, 3.68]
Total (95% CI)	**51**	**59**		**100.0 %**	**0.27 [0.06, 1.23]**

Total events: 1 (Verapamil), 6 (Adenosine)

Heterogeneity: Chi^2 = 1.34, df = 2 (P = 0.51); I^2 =0.0%

Test for overall effect: Z = 1.69 (P = 0.090)

Test for subgroup differences: Not applicable

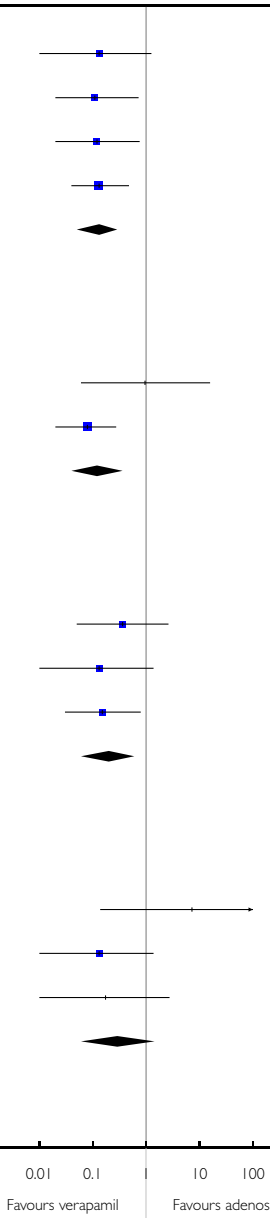
Analysis 1.4. Comparison 1 Adenosine vs Ca Blockers, Outcome 4 Minor Adverse events.

Review: Adenosine versus intravenous calcium channel antagonists for the treatment of supraventricular tachycardia in adults

Comparison: 1 Adenosine vs Ca Blockers

Outcome: 4 Minor Adverse events

Study or subgroup	Verapamil n/N	Adenosine n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
1 chest tightness					
Cheng 2003	0/62	3/60		5.7 %	0.13 [0.01, 1.24]
Ferreira 1996	0/25	5/25		8.9 %	0.11 [0.02, 0.71]
Gil Madre 1995	0/24	5/26		8.9 %	0.12 [0.02, 0.77]
Kulakowski 1998	0/35	11/46		18.4 %	0.13 [0.04, 0.48]
Subtotal (95% CI)	**146**	**157**		**41.9 %**	**0.13 [0.05, 0.29]**
Total events: 0 (Verapamil), 24 (Adenosine)					
Heterogeneity: Chi^2 = 0.02, df = 3 (P = 1.00); I^2 =0.0%					
Test for overall effect: Z = 4.81 (P < 0.00001)					
2 Nausea					
Cheng 2003	1/62	1/60		3.9 %	0.97 [0.06, 15.65]
Gil Madre 1995	0/24	13/26		19.0 %	0.08 [0.02, 0.27]
Subtotal (95% CI)	**86**	**86**		**22.9 %**	**0.12 [0.04, 0.37]**
Total events: 1 (Verapamil), 14 (Adenosine)					
Heterogeneity: Chi^2 = 2.61, df = 1 (P = 0.11); I^2 =62%					
Test for overall effect: Z = 3.65 (P = 0.00027)					
3 Shortness of breath					
Cheng 2003	1/60	3/61		7.6 %	0.36 [0.05, 2.65]
Gil Madre 1995	0/24	3/26		5.6 %	0.13 [0.01, 1.36]
Kulakowski 1998	0/35	6/46		10.7 %	0.15 [0.03, 0.81]
Subtotal (95% CI)	**119**	**133**		**23.9 %**	**0.20 [0.06, 0.60]**
Total events: 1 (Verapamil), 12 (Adenosine)					
Heterogeneity: Chi^2 = 0.56, df = 2 (P = 0.75); I^2 =0.0%					
Test for overall effect: Z = 2.86 (P = 0.0042)					
4 Headache					
Cheng 2003	1/61	0/60		1.9 %	7.27 [0.14, 366.38]
Gil Madre 1995	0/24	3/26		5.6 %	0.13 [0.01, 1.36]
Kulakowski 1998	0/35	2/46		3.8 %	0.17 [0.01, 2.81]
Subtotal (95% CI)	**120**	**132**		**11.3 %**	**0.29 [0.06, 1.46]**
Total events: 1 (Verapamil), 5 (Adenosine)					
Heterogeneity: Chi^2 = 3.16, df = 2 (P = 0.21); I^2 =37%					



(*Continued* . . .)

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Study or subgroup	Verapamil n/N	Adenosine n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Test for overall effect: Z = 1.50 (P = 0.13)					
Total (95% CI)	**471**	**508**		**100.0 %**	**0.15 [0.09, 0.26]**
Total events: 3 (Verapamil), 55 (Adenosine)					
Heterogeneity: Chi² = 7.50, df = 11 (P = 0.76); I² =0.0%					
Test for overall effect: Z = 6.76 (P < 0.00001)					
Test for subgroup differences: Chi² = 1.15, df = 3 (P = 0.77), I² =0.0%					

Analysis 1.5. Comparison 1 Adenosine vs Ca Blockers, Outcome 5 Hypotension.

Review: Adenosine versus intravenous calcium channel antagonists for the treatment of supraventricular tachycardia in adults

Comparison: 1 Adenosine vs Ca Blockers

Outcome: 5 Hypotension

Study or subgroup	Verapamil n/N	Adenosine n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Cabrera-Sole 1989	0/25	0/25			Not estimable
DiMarco 1990	1/70	0/61		33.6 %	6.50 [0.13, 330.51]
Ferreira 1996	0/25	0/25			Not estimable
Hood 1992	1/11	0/14		33.3 %	9.71 [0.19, 503.30]
Kulakowski 1998	1/35	0/46		33.1 %	10.12 [0.19, 528.94]
Total (95% CI)	**166**	**171**		**100.0 %**	**8.60 [0.88, 83.86]**
Total events: 3 (Verapamil), 0 (Adenosine)					
Heterogeneity: Chi² = 0.03, df = 2 (P = 0.99); I² =0.0%					
Test for overall effect: Z = 1.85 (P = 0.064)					
Test for subgroup differences: Not applicable					

ADDITIONAL TABLES

Table 1. Search methods for CENTRAL on The Cochrane Library

Terms in capitals are exploded MeSH terms and those in lower case are textword searches:
#1 ADENOSINE
#2 adenosin*
#3 (#1 or #2)
#4 TACHYCARDIA SUPRAVENTRICULAR
#5 (supraventricular next arrhythmia*)
#6 tachycardia*
#7 tachyarrhythmi*
#8 (idioventricular next rhythm*)
#9 supraventric*
#10 svt
#11 psvt
#12 (#4 or #5 or #6 or #7 or #8 or #9 or #10 or #11)
#13 (#3 and #12)

Table 2. Search Strategy for EMBASE

1 exp Adenosine/
2 adenosin$.tw.
3 1 or 2
4 Heart Supraventricular Arrhythmia/
5 Supraventricular Tachycardia/
6 Paroxysmal Supraventricular Tachycardia/
7 supraventricular tachycardia$.tw.
8 supraventricular arrhythmia$.tw.
9 supraventricular tachyarrhythmi$.tw.
10 sinus tachycardia$.tw.
11 svt.tw.
12 psvt.tw.
13 or/4-12
14 3 and 13

Table 3. Rate of reversion to sinus rhythm for adenosine, by dose

Study	<6mg; 5mg ATP	6 to <9mg; 10mg ATP	9 to <12 mg; 20mg ATP	>=12mg	Cumulative % reversion rate for all doses	Mean effective dose
Cabrera-Sole*			42/44		96%	

Table 3. Rate of reversion to sinus rhythm for adenosine, by dose (*Continued*)

Cheng^		17/60		35/60	87%	9.63+/-2.74mg
Di Marco^		35/61		22/61	93%	
Ferreira*			22/25	2/25	96%	
Gil Madre*	13/25	8/25	4/25		100%	
Hood (ug/kg)^ $	3/14	6/14	3/14		86%	
Kulakowski^	12/46	22/46	3/46	8/46	98%	0.09+/-0.04mg/kg
* ATP used; ^ adenosine used; $ for 70kg person - 40mcg/kg equiv 3mg, 80mcg/kg equiv 6mg, 120mcg/kg equiv 9mg adenosine						

Table 4. Rate of reversion to sinus rhythm for verapamil, by dose

Study	<=5mg	>5 to 10mg	Cumulative reversion rate	Mean effective dose
Cabrera-Sole		39/43	91%	
Cheng	30/62	24/62	87%	7.15+/-2.67mg
Di Marco	56/70	8/70	91%	
Ferreira				9.38+/-3.9mg
Gil Madre	16/25	9/25	96%	
Hood	6/11	1/11	64%	
Kulakowski	24/35	7/35	89%	

WHAT'S NEW

Last assessed as up-to-date: 1 August 2006.

Date	Event	Description
8 September 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 1, 2005

Review first published: Issue 4, 2006

CONTRIBUTIONS OF AUTHORS

A Holdgate conceived the review

A Holdgate and A Foo developed the protocol and search strategy in conjunction with the Cochrane Heart Group. Both reviewers screeened papers for inclusion, extracted data from included papers, participated in data analysis and drafted the review

DECLARATIONS OF INTEREST

None known

SOURCES OF SUPPORT

Internal sources

- St George Hospital, Australia.
- Liverpool Hospital, Australia.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

Adenosine [adverse effects; *therapeutic use]; Calcium Channel Blockers [adverse effects; *therapeutic use]; Randomized Controlled Trials as Topic; Tachycardia, Supraventricular [*drug therapy]; Verapamil [adverse effects; therapeutic use]

MeSH check words

Adult; Humans