**WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care**

**Worksheet author(s)**

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**Clinical question.**

"In infants and children with supraventricular tachycardia with a pulse (P), does the use of any drug or combination of drugs (I) compared with adenosine(C), improve outcomes (termination of rhythm, survival) (O)?"

**Is this question addressing an intervention/therapy, prognosis or diagnosis?** intervention/therapy

**State if this is a proposed new topic or revision of existing worksheet:** update of existing topic (existing worksheets include vagal maneuvers for SVT, amiodarone as an alternative agent for stable SVT, amiodarone for stable wide QRS complex SVT)

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**Conflict of interest specific to this question**

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? NO

**Search strategy (including electronic databases searched).**

- **MEDLINE:** “Supraventricular Tachycardia” or “Paroxysmal Atrial Tachycardia”
  - Limited to: 2003 to current, further limited to “All Child (0-18 years)” – 512 hits.
  - Titles, abstracts reviewed, 43 articles felt to be relevant to topic

- **MEDLINE:** MeSH headings, “Tachycardia, Supraventricular”
  - Limited to: 2003 to current, further limited to “All Child (0-18 years)” – 526 hits
  - Titles, abstracts reviewed, no additional articles felt to be relevant to topic

- **ECC ENDNOTE MASTER LIBRARY:** “Tachycardia” OR “Supraventricular”
  - Limited to: 2003 or later –194 hits
  - Titles reviewed, no additional relevant articles

- **COCHRANE DATABASE** “Supraventricular Tachycardia” – 5 hits, 1 article relevant to topic.

- **EMBASE:** “Supraventricular Tachycardia” or “Paroxysmal Atrial Tachycardia”
  - Titles, abstracts reviewed, an additional 4 articles relevant to topic.

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**State inclusion and exclusion criteria**

Exclusion criteria: single case reports citing positive results, review articles, editorials/letters to the editor, studies with exclusively adult populations (>18 years)

Articles were included if they had pediatric study populations or adult studies which documented participation of some subjects < 18 years.

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**Number of articles/sources meeting criteria for further review: 12**
# Summary of evidence

## Evidence Supporting Clinical Question

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
</table>

A = Conversion to sinus rhythm  
C = Avoidance of adverse effects  
E = Other endpoint  
*Italicics = Animal studies*

## Evidence Neutral to Clinical question

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>A = Conversion to sinus rhythm</td>
<td></td>
<td></td>
<td>Saul 2005-A, B, C</td>
</tr>
</tbody>
</table>

B = Tachycardia rate control  
C = Avoidance of adverse effects  
D = Occurrence of adverse effects  
*Italicics = Animal studies*

## Evidence Opposing Clinical Question

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>A = Conversion to sinus rhythm</td>
<td></td>
<td></td>
<td>Ertan 2008-A, C Riccardi 2008-A</td>
</tr>
</tbody>
</table>

D = Occurrence of adverse effects  
*Italicics = Animal studies*
There are no recent studies regarding hemodynamically stable supraventricular tachycardia which directly compare other drugs (or combination of drugs) to standard treatments--vagal maneuvers, adenosine—in pediatric patients.

Standard treatment:
Adenosine as treatment for SVT continues to be evaluated in retrospective case series involving children. Studies by Dixon, 2005 and Moghaddom, 2008 call into question the appropriate initial dose of adenosine but in their protocols, they started at 50 mcg/kg rather than the recommended 100 mcg/kg per Guidelines 2005. Gagallo, 2007 demonstrated adenosine’s effectiveness for SVT in an ICU setting. Larger retrospective series (Riccardi, 2008 and Ertan, 2008) involving predominantly adults (with a few teenagers) show high efficacy of adenosine. Side effects were common but transient.

One randomized, prospective study in adults, which included some teenagers (Lim, 2009), compared adenosine to calcium channel blockers (CCB)—verapamil or diltiazem. CCB were infused slowly in order to avoid hypotension. CCB had significantly higher conversion rates than adenosine (98% vs 87%) and only 1 patient out of 102 (1%) became hypotensive. A Cochrane meta-analysis (Holdgate, 2006) reviewed seven adult studies and one pediatric study, concluded that adenosine and verapamil are both effective agents in treating SVT, though specifically state that verapamil should not be used in pediatric patients because of the risk of cardiac arrest in infants. Both Lim and Holdgate highlight the cost effectiveness of verapamil over adenosine.

Regarding vagal maneuvers, Diamantis, 2006 add to the literature a case report of subcutaneous fat necrosis in an infant with SVT who was treated with ice to the face.

Other drugs
Recent studies regarding amiodarone (Saul 2005, Haas 2008) document its effectiveness in highly selected populations. The study by Saul raises concerns about the high incidence of side effects (~80%), including hypotension, bradycardia and heart block, while Haas et al claim that hypotension can be minimized by slow intravenous infusion of the amiodarone loading dose over one hour. A case report by Ng relate the occurrence of catastrophic cardiovascular collapse and proarrhythmia in a neonate with stable SVT who did not respond to vagal maneuvers or adenosine. In this case, the amiodarone dose was infused over 30 minutes.

Two small case series on highly selected patients in specific settings show efficacy of esmolol (Adamson 2006) and dexmedetomidine (Chrysostomou 2008). At this point, their findings must be reproduced in larger prospective studies before these drugs can be considered for widespread use.

Acknowledgements:

Citation List


COMMENT: Prospective study in which SVT conversion was a secondary focus of the investigation. Subjects were studied in the EP lab as part of comprehensive electrophysiology study or radiofrequency ablation. Sustained SVT occurred spontaneously or was induced by programmed stimulation. Some subjects required isoproterenol infusion in order for SVT to be induced. In the age group 2-11 years, esmolol successfully converted SVT in 6 of 14 (43%). In the group aged 12-16 years, esmolol successfully converted SVT in 11 of 13 (85%). Overall efficacy was 63%. There was one adverse event: hypotension in a patient in whom the esmolol did not convert the SVT. LOE 4, Evidence NEUTRAL, FAIR quality study.

COMMENT: Manuscript in Spanish. Retrospective analysis of pediatric patients admitted to an ICU for medical treatment. In this series, adenosine was effective in 21 of 35 patients (60%). Interestingly, all patients were admitted after having failed vagal maneuvers from an outpatient (ED?) setting and so were admitted for further therapy. Vagal maneuvers were then attempted in the ICU and subsequently successfully converted 15 (25%) of the 61 pts. Other antiarrhythmics used in smaller numbers of patients were: esmolol (8 pts, successful in 3) and amiodarone, propafenone, verapamil, lidocaine and magnesium sulfate (1 pt each). LOE 4, Evidence OPPOSING, POOR quality study.


COMMENT: Small retrospective non-randomized, uncontrolled case series for a variety of substrates of SVT. All patients had to be free of “hemodynamic instability” and required sedation/analgesia/anxiolysis in order to included in the study. All patients were hospitalized in an ICU and several were on inotropic or ventilatory support. 4 of 4 patients with reentrant SVT were successfully converted to sinus rhythm. LOE 4, Evidence NEUTRAL, POOR quality study.


COMMENT: Based on their report of 23 infants (median effective dose 200 mcg/kg) and 12 children (median effective dose of 150 mcg/kg), as well as a review of the literature, the authors recommend an initial dose of 200 mcg/kg for infants and 150 mcg/kg for children. However, their starting dose for their protocol was only 50 mcg/kg and so they would likely have had more initial success if they had started at the AHA Guidelines recommendation of 100 mcg/kg, with less impetus to “improve” on initial conversion rates. LOE 4, Evidence OPPOSING, POOR quality study.


COMMENT: Mostly-adult series which included patients as young as 16 years old. 43 of 46 patients had successful termination with up to two doses of adenosine (1st dose = 6 mg, 2nd dose = 12 mg). About half of patients had ventricular ectopy, which was always transient in nature. LOE 5, Evidence OPPOSING, FAIR quality study.


COMMENTS: Another retrospective study in a highly select population of patients with various arrhythmias in the post-operative cardiac ICU setting. The authors uniformly observed improvement (rate response) though not necessarily conversion to sinus rhythm. They emphasize slow intravenous infusion of amiodarone 5 mg/kg administered over 1 hour. LOE 4, Evidence NEUTRAL, POOR quality study.


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. They also comment on the relative costs of verapamil and adenosine.

COMMENT: The only meta-analysis in the literature reviewed 8 trials published between 1982 and 2003. One of these trials was an exclusively pediatric study (Greco R, Musto B, Arienzo V, Alborino A, Garofalo S, Marsico F. Treatment of paroxysmal supraventricular tachycardia in infancy with digitalis, adenosine-5’-triphosphate and verapamil: a comparative study. Circulation 1982;66:504-508), in which 2 of 9 infants receiving verapamil had cardiac arrest. Because of this, in the Discussion, the authors specifically state “pediatric patients should not be treated with verapamil.” LOE 5, Evidence NEUTRAL, GOOD quality study.

COMMENT: A well-designed, prospective, randomized study evaluating adenosine vs. calcium channel blockers (CCB) – verapamil or diltiazem. Impressive conversion rates for CCB of 98% vs. 87% for adenosine. Blood pressures were significantly lower after CCB infusion (even after conversion of SVT) but only one patient became truly hypotensive. The authors also quoted costs of CCB vs. adenosine with adenosine being roughly 2.3 times more costly than verapamil and 1.5 times more so than diltiazem. The authors stated that inclusion criteria for the study were patients >10 years of age but in their results, did not state the actual age range of the study population, nor how many patients were less than 18 years. LOE 5, Evidence NEUTRAL, GOOD quality study.


COMMENT: Another retrospective study examining the effective dose of adenosine. In contrast to the previously cited study, infants responded to a lower dose than did older children. They had poor conversion rates (<50%) regardless of the dose given, which raises the question of whether they were actually administering the drug properly. LOE 4, Evidence OPPOSING, POOR quality study.


COMMENT: Single case report citing a catastrophic adverse reaction and warning that hemodynamically stable SVT was made remarkably unstable by infusion of amiodarone. The authors concede that the IV loading dose, given over 30 minutes, may have been given too rapidly. LOE 5, Evidence OPPOSING, POOR quality study.


COMMENT: Large retrospective series included a few teenagers in their experience. Side effects were common but transient, including the “major” adverse effect that they cited. LOE 5, Evidence OPPOSING, FAIR quality study.


COMMENT: A well designed, multicenter, semi-blinded study as to dosing regimen (either low, medium or high doses infused over a 48 hour period). Very highly selected study population with incessant SVT substrates. Higher rates of efficacy were seen in the medium and high dosing regimens. The authors emphasized the high numbers of adverse events and suggest that previously published non-controlled case series in pediatric patients have significantly overestimated the safety profile for amiodarone. LOE 4, Evidence NEUTRAL, GOOD quality study.