Research Paper for a Medication Training Gap

Drug: Adenosine

Name:

DOB:

For Application of ACP

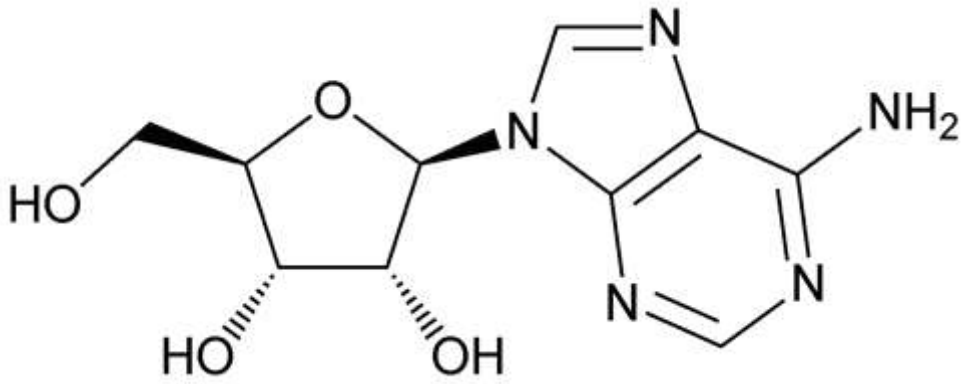
DRUG: Adenosine (Adenocard)

Classification:

Class 5 Anti-arrhythmic - Prescription only medicine (POM)

Pharmacodynamics:

Adenosine is a product of the enzymatic breakdown of intra- and extra-cellular adenine nucleotides and intracellular S-adenosylhomocysteine (Conti, 1991). It is an endogenous nucleoside and is chemically described as 6-Amino-9-β-D-ribofuranosyl-*9H*-purine and has the following structural formula:



(Drugs.com, 2015)

It stimulates specific Adenosine receptors which results in activation of acetylcholine sensitive potassium channels (efflux of potassium) and blocks the calcium influx in the sinoatrial (SA) node, atrium and atrioventricular (AV) node. The cells therefore become hyperpolarized leading to blunting of the SA node discharge, slowing AV conduction and increasing the AV node refractory period (Bctg.bcas.ca, 2015).

Adenosine produces a direct negative chronotropic, dromotropic and inotropic effect on the heart, due to A1 -receptor agonism. A1 receptors are located in cardiomyocytes of heart muscle cells. Binding to these receptors inhibits adenyl cyclase activity which lowers cyclic adenosine monophosphate (cAMP). It therefore causes peripheral vasodilation, due to A2-receptor agonism. The A2 receptors are found in endothelial cells and smooth muscle cells that line the blood vessels. These work in contrary to the A1 receptors by enhancement of adenylyl cylase activity and increased cyclic AMP (cAMP) (Mandal, 2013). The overall effect of Adenosine on patients is characteristically a mild to moderate reduction in systolic, diastolic and mean arterial blood pressure associated with a reflex increase in heart rate (Drugs.com, 2015).

In relation to the drug concentration and effect, Adenosine is initially given as a standard dose of 6mg in a bolus and should be followed by a large flush of 0.9% normal saline. Regardless of adult size or weight, literature suggests the dose is not titrated to effect like analgesia may be. Rather a blous is given, and can be increased further if ineffective the first time.

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Pharmacokinetics:

The following is based on intra-venous administration:

- The onset of action = less than 20 seconds
- The peak effect is estimated to be between 20-30 seconds.
- The duration of action has been found to be variable but is estimated to be around 1-2 minutes.
- The half-life is around 6-10 seconds

Interaction / toxicity:
Can cause prolonged bradycardia in patients with toxic concentration of calcium channel blockers
It is antagonized competitively by methylxanthines (e.g. theophylline, caffeine).
It is potentiated by blockers of nucleoside transport (e.g. dipyridamole).
Higher degrees of heart block in the presence of carbamazepine (Dorsy, 2004)

Intravenously administered adenosine is rapidly cleared from the body's circulation via cellular uptake, predominantly by erythrocytes and vascular endothelial cells, with a half-life of less than 10 seconds. The intracellular adenosine is quickly metabolised either via phosphorylation to adenosine monophosphate by adenosine kinase, or via deamination to inosine by adenosine deaminase in the cytosol. Adenosine monophosphate formed by phosphorylation of adenosine is incorporated (Health Canada, 2015).

Indications:

Adenosine is indicated for use in pharmacologic/chemical conversion of supraventricular tachycardia (SVT) / paroxysmal supraventricular tachycardia (PSVT) in British Columbia (Bctg.bcas.ca, 2015).

It is indicated in the rapid reversion to sinus rhythm of paroxysmal supraventricular tachycardias, including those associated with accessory conducting pathways (e.g. Wolff-Parkinson-White syndrome) in the UK (Medicines Complete, 2015).

Contraindications:

As listed by RxList, (2009)

- Second degree (Type 1&2) or third-degree A-V block (except in patients with a functioning artificial pacemaker)
- Sick sinus syndrome
- Symptomatic bradycardia (except in patients with a functioning artificial pacemaker).
- Known hypersensitivity to adenosine

Having reviewed literature, there is also a suggestion that known or suspected bronchoconstrictive or bronchospastic lung disease can be a contraindication.

The BCAS treatment guidelines acknowledge this only as a caution however.

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Cautions:

Pregnancy
As Adenosine is naturally present in the body no foetal effects would be anticipated. However, as there is no evidence to suggest it will not cause foetal harm when administered to pregnant women, it should not be used during pregnancy unless potential benefits outweigh the potential risks to the foetus.

Bronchoconstriction
As previously mentioned, most literature including the BCAS treatment guidelines caution the use of adenosine with patients suffering from this condition.

Use in Children
Whilst paediatric doses can be calculated some literature offers a caution when doing so.

Use in Elderly
Some literature suggests the use of adenosine in geriatric patients should be used with caution as this population may have a diminished cardiac function, nodal dysfunction, concomitant diseases or drug therapies that may change hemodynamic function and produce severe bradycardia or AV block.

Health Canada (2015), (Drugs.com, 2015), (Bctg.bcas.ca, 2015).

Side Effects:

Cardiovascular:
Facial flushing, headache, sweating, palpitations, chest pain, and hypotension. A variety of arrhythmias and conduction disturbances such as, atrial fibrillation ,prolonged asystole, ventricular tachycardia, ventricular fibrillation, transient increase in blood pressure, bradycardia and torsade's de pointes.

Respiratory:
Dyspnoea, chest pains, chest tightness and hyperventilation.

Central Nervous System:
An infusion of adenosine causes increased cerebral blood flow, which can cause the following: Headaches, light-headedness, dizziness, tingling in arms, numbness, blurred vision, burning sensation, heaviness in arms, and neck and back pain. Seizureal activity, including tonic clonic and (grand mal) seizures have also been reported.

Gastrointestinal:
Adenosine can cause renal and hepatic arterial vasoconstriction. Nausea and metallic taste, tightness in throat, and pressure in groin have also been recorded as side effects.

(Smith et al., 2011), (RxList, 2009), (Medicines Complete, 2015), (Health Canada, 2015), (Drugs.com, 2015)

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Drug interactions:

Cardioactive Drugs:
Adenosine has been successfully administered in the presence of other cardioactive drugs, such as quinidine, beta-adrenergic blocking agents, calcium channel blocking agents and angiotensin converting enzyme inhibitors, without any change in the adverse reaction profile.

However, because of the synergistic depressant effects on the SA and AV nodes caused by Digoxin and Verapamil adenosine should be used with caution as the use may be rarely associated with ventricular fibrillation when combined (RxList, 2009).

Methylxanthines:
The effects of adenosine are antagonised by methylxanthines (such as caffeine and theophylline). In the presence of methylxanthines, larger doses of adenosine may be required as the normal dose of adenosine may not be effective (Health Canada, 2015).

Dipyridamole:
Adenosine effects are increased by dipyridamole. Therefore smaller doses may be effective in the presence of dipyridamole medications (Health Canada, 2015).

Carbamazepine:
Carbamazepine has been reported to increase the degree of heart block produced by other medications. As the main effect of adenosine is to decrease conduction through the AV node, higher degrees of heart block may be produced in the presence of carbamazepine (Drugs.com, 2015).

Parenteral Administration:

Administration of this medication is given via the intra-venous route. Ideally through a large bore cannula situated in the most central position available.
(Bctg.bcas.ca, 2015)

Dosage:

Adult Patients
The recommended intravenous doses for adults from both Health Canada (2015) and BCAS (2015) are as follows:

- 6 mg administered as a rapid intravenous bolus given over a 1- to 2-second time period followed by a large flush of normal saline between 20-30ml.
- Further doses can be administered if the initial dose does not terminate supraventricular tachycardia within 1 - 2 minutes.
- 12 mg dose should be given as a rapid intravenous bolus followed by a large flush.

The 12 mg dose may be repeated a second time if required after 1-2 minutes if the first 12mg dose is ineffective or the rhythm does not slow enough to allow diagnosis.

Note: No bigger bolus than 12mg should be administered.

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Dosage:

Paediatric Patients

The recommended intravenous doses for paediatrics from both Health Canada (2015) and BCAS (2015) are as follows:

Patient with a body weight ≥ 50 kg:
Administer as per the adult dose guidelines.

Paediatric patients with a body weight < 50 kg:

Initial doses vary based on the calculations from literature: Give between (0.05 & 0.1mg/kg) to (0.10 & 0.2mg/kg) as a rapid intravenous bolus given either centrally or peripherally. Flush with 2-20mls of IV fluid depending weight of child.

If conversion of PSVT is not successful within 1 - 2 minutes, additional bolus injections of adenosine can be administered at incrementally higher doses, increasing the amount given by 0.05 - 0.10 mg/kg.

Follow each bolus with a saline flush. This process should be continued until sinus rhythm is established or up to a maximum dose of 0.3 mg/kg.

How Supplied:

Presentations can vary between areas and suppliers.

The most common presentation found in the literature suggests that it is supplied in the form of 6mg/2ml vials.

(Health Canada, 2015)

Special Considerations:

None found

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Patient Application

Conditions Medication could be used In:

Adenosine combines with phosphate to form various chemical compounds including adenosine monophosphate (AMP) and adenosine triphosphate (ATP).

It can be used for treatments of multiple conditions. AMP is used orally for treating shingles and a blood disorder called porphyria cutanea tarda which is a type of porphyria in which affected individuals are sensitive to sunlight.

ATP is used as a sublingual medication to increase physical energy. It is also administered intravenously for treating acute kidney failure, multiple organ failure, high blood pressure in lung arteries (pulmonary hypertension), cystic fibrosis, lung cancer, weight loss associated with cancer, and controlling blood pressure during anaesthesia and surgery. It is also used for cardiac stress tests.

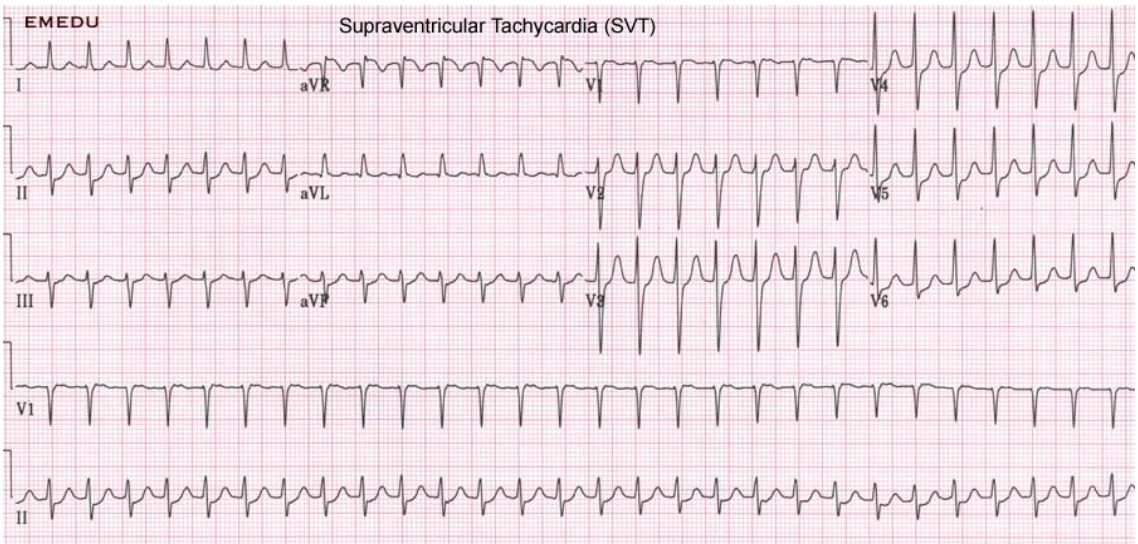
It is also used intravenously for treating surgical pain and nerve pain and certain types of irregular heartbeat such as SVT.

(Webmd.com, 2015)

Indication for use:

Within British Columbia treatment guidelines, the indication for use is as follows:

For the conversion of supraventricular tachycardia (SVT) / paroxysmal supraventricular tachycardia (PSVT) as part of a management process



(Emedu.org, 2015)

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Indication for use:

Symptomatic but stable patients with PSVT can be treated within the pre-hospital setting with adenosine after consultation with an emergency department Doctor. Patients who present with borderline unstable findings can be treated with Adenosine if it can be administered with no delay. The patient should always be prepared and be ready to cardiovert these patients. Patients who are haemodynamically unstable should be cardioverted (Following protocol sequencing for cardioversion).

(Bctg.bcas.ca, 2015)

Treatment Contraindications:

As listed by the British Columbia Treatment Guidelines:

- Second degree (Type 1&2) or third-degree A-V block (except in patients with a functioning artificial pacemaker)
- Sick sinus syndrome
- Symptomatic bradycardia (except in patients with a functioning artificial pacemaker).
- Known hypersensitivity to adenosine

Protocol Sequencing:

Adenosine sits within a protocol structure for the management of regular narrow-complex tachyarrhythmia. However, it is advised if a patient has adverse features (Unstable Presentation) and is at risk of deterioration, perform a synchronised cardioversion. It is reasonable to attempt vagal and chemical conversions while preparations are being made for cardioversion.

In the absence of adverse features (Stable Presentation) to sequencing is as follows:

Vagal Manoeuvres – Carotid sinus massage or a Valsalva manoeuvre will terminate up to 25% of paroxysmal SVT. Recording of a 12 lead ECG is advised through this procedure.

If the arrhythmia persists and is not atrial flutter discuss the case with the ED Doctor who may allow the move to administer 6mg of Adenosine as per dosage guidelines. Record a 12 Lead ECG during this process.

If this fails to terminate administer a further 12mg of Adenosine as per guidelines may be required.

Vagal manoeuvres or Adenosine will terminate almost all PSVTs. Failure to terminate with these actions suggest an atrial tachycardia such as atrial flutter.

Guiding Principles:

Symptomatic but stable patients with PSVT can be treated pre-hospital with adenosine after consultation with the ED Doctor.

Borderline unstable patients with PSVT can be treated with Adenosine pre-hospital if it can be achieved with no delay. Patients who are haemodynamically unstable should be cardioverted.

(Bctg.bcas.ca, 2015), (Nolan, 2011).

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Treatment Objectives:

To correct rhythm disturbance and restore the patient's heart rate to a normal sinus rhythm, providing effective relief of symptoms. The patient must also be treated in a time critical manor and provided with rapid transport to the most appropriate hospital.

Vital Sign Requirements:

As within any clinical patient presentation and treatment, vital signs are required.

Given this is a significant cardiac event and the treatment can impact the cardiovascular system with potentially life threatening complications, cardiac monitoring is advised as best practice. A 12 lead ECG must also be undertaking throughout the patients management and throughout key stages of the protocol sequencing.

Other observations (including time taken) as well as a physical assessment should include:

Pulse rate
Respiratory Rate
Blood Pressure
Sp02
Glasgow Coma Scale (GCS)
Pupils
Blood Sugar

(Fisher, 2013).

Treatment Exit Requirements:

As with any clinical intervention, a full reassessment of the patient must be undertaken. As mentioned previously, a full set of observations should be ascertained as part of this re-assessment along with a full ECG recording and 12 Lead ECG.

As Adenosine is part of a larger patient management plan, clinicians should be prepared for cardioversion/arrest and have all medications and equipment available to aid in the efficient management of the patient.

If the patient has been successfully managed with Adenosine and has returned to NSR, they should be made comfortable, continuously monitored and taken to the most appropriate receiving ED.

If the patient remains in SVT, and the management protocol has not been successful, the patient should be rapidly transferred to the ED and handed over.

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