DOWNLOAD PDF ADENOSINE MECHANISM OF ACTION

Chapter 1 : [Cardiac effects of adenosine. Mechanism of action, pathophysiologic and clinical significance]

Adenosine can bind to purinergic receptors in different cell types where it can produce a number of different physiological actions. One important action is vascular smooth muscle relaxation, which leads to vasodilation.

Second- or third-degree heart block without a pacemaker Severe hypotension Sick sinus syndrome without a pacemaker When administered via a central lumen catheter, adenosine has been shown to initiate atrial fibrillation because of its effect on atrial tissue. In individuals with accessory pathways , the onset of atrial fibrillation can lead to a life-threatening ventricular fibrillation. However, adenosine may be administered if equipment for cardioversion is immediately available as a backup. Side effects[edit] Many individuals experience facial flushing, a temporary rash on the chest, lightheadedness, diaphoresis , or nausea after administration of adenosine due to its vasodilatory effects. Metallic taste is a hallmark side-effect of adenosine administration. These symptoms are transitory, usually lasting less than one minute. It is classically associated with a sense of "impending doom", more prosaically described as apprehension. This lasts a few seconds after administration of a bolus dose, during transient asystole induced by intravenous administration. Pharmacological effects[edit] Adenosine is an endogenous purine nucleoside that modulates many physiological processes. Thus, in regard to stress or injury, the function of adenosine is primarily that of cytoprotection preventing tissue damage during instances of hypoxia , ischemia , and seizure activity. Activation of A2A receptors produces a constellation of responses that in general can be classified as anti-inflammatory. The four receptor subtypes are further classified based on their ability to either stimulate or inhibit adenylate cyclase activity. Researchers at Cornell University have recently shown adenosine receptors to be key in opening the blood-brain barrier BBB. This causes dilation of the "normal" segments of arteries, i. This feature allows physicians to use adenosine to test for blockages in the coronary arteries, by exaggerating the difference between the normal and abnormal segments. The administration of adenosine also reduces blood flow to coronary arteries past the occlusion. Other coronary arteries dilate when adenosine is administered while the segment past the occlusion is already maximally dilated. This leads to less blood reaching the ischemic tissue, which in turn produces the characteristic chest pain. Metabolism[edit] Adenosine used as a second messenger can be the result of de novo purine biosynthesis via adenosine monophosphate AMP , though it is possible other pathways exist. Dipyridamole , an inhibitor of adenosine nucleoside transporter , allows adenosine to accumulate in the blood stream. This causes an increase in coronary vasodilatation.

Chapter 2 : Adenosine | C10H13N5O4 - PubChem

Mechanism of Action Adenosine injection slows conduction time through the A-V node, can interrupt the reentry pathways through the A-V node, and can restore normal sinus rhythm in patients with paroxysmal supraventricular tachycardia (PSVT), including PSVT associated with Wolff-Parkinson-White Syndrome.

This is an open access article distributed under the Creative Commons Attribution License , which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Abstract Caffeine is the most widely consumed stimulating substance in the world. It is found in coffee, tea, soft drinks, chocolate, and many medications. Caffeine is a xanthine with various effects and mechanisms of action in vascular tissue. In endothelial cells, it increases intracellular calcium stimulating the production of nitric oxide through the expression of the endothelial nitric oxide synthase enzyme. Nitric oxide is diffused to the vascular smooth muscle cell to produce vasodilation. In vascular smooth muscle cells its effect is predominantly a competitive inhibition of phosphodiesterase, producing an accumulation of cAMP and vasodilation. In addition, it blocks the adenosine receptors present in the vascular tissue to produce vasoconstriction. In this paper the main mechanisms of action of caffeine on the vascular tissue are described, in which it is shown that caffeine has some cardiovascular properties and effects which could be considered beneficial. Introduction Coffee is one of the most frequently consumed beverages in the world. It represents a culture and an economy. It has been produced in Colombia since the nineteenth century and is the main export to more than 36 countries; in it represented close to There are approximately coffee growing municipalities, , coffee growers, , direct employees, and more than a million indirect employees, which means approximately 2 million people dependent on coffee cultivation [1] Over 2, substances have been isolated from coffee. They also contain minerals, aliphatic and chlorogenic acids, trigonellines, and volatile aromas. Of the alkaloids, the most studied and recognized one is caffeine, which makes up 1. Coffee consumption is generally associated with a large number of diseases and health alterations. However, the majority of epidemiological studies regarding this relationship have not yielded a clear conclusion, mainly due to the lack of concrete and continuous information regarding the frequency of consumption, the exact composition of the beverage, and factors associated with an unhealthy lifestyle cigarette smoking, alcohol, and sedentarism. These aspects in combination could lead to diseases or health problems [3]. Many epidemiologic studies have studied the relationship between coffee consumption and the risk of heart disease. An analysis [4] of the coffee-mortality relationship states that there is no direct relationship between coffee consumption and an increase in mortality; on the contrary, the authors describe a slightly Inverse relationship between the consumption of coffee and their benefits related to the inflammatory process, endothelial function, and the risk of developing type 2 diabetes. According to Yukawa et al. Additionally, caffeine increases the production of urine with water and electrolyte secretion patterns very similar to those seen with the thiazides [8]. The underlying mechanisms may depend on various factors such as dose, chronic exposure, genetic and enzymatic factors, among others. In animal studies with caffeine exposure, an increase in glomerular filtration and kidney blood flow, especially in the renal medulla, is seen. In a study of the intrarenal mechanisms responsible for the natriuretic effect of caffeine, the renal secretion of sodium increased, and the glomerular filtration rate remained the same, suggesting that diminished fractional sodium reabsorption, both in the proximal and distal tubule of the nephron, contributes to the natriuretic effect of caffeine [8] Caffeine is the psychoactive substance most widely consumed in the world, it is found not only in coffee but also in tea, carbonated beverages or soft drinks, chocolate, and a wide variety of medications, including appetite suppressants, diuretics, analgesics, and decongestants; the majority of which are sold over the counter and do not have a regulatory control [9 , 10]. If you combine the consumption of coffee, tea, chocolate, and soft drinks, the general population consumes a considerable amount of caffeine per day. Adults over the age of 25 have an estimated consumption of approximately 2. In addition, it has been confirmed that theobromine and theophylline are alkaloids also found naturally in green tea, black coffee, and cacao [11] however, the direct effect of these substances on physiological responses to the ingestion of foods and beverages containing these types of alkaloids, and the

role of each, is not clear. There are five main metabolic pathways which contribute to caffeine metabolism in adults [13 , 14]. The first three consist of demethylization of N-3 to form Paraxanthine, N-1 to form Theophylline vasodilator, increased cerebral and muscular blood flow , and N-7 to form Theophylline vascular, bronchiole, muscular, and respiratory relaxant. The fourth pathway results in the formation of uracil metabolites, and the fifth consists of renal elimination of the remaining percentage of caffeine that was not able to be degraded in the process. The large interindividual differences observed in plasmatic concentration of caffeine following the administration of an equal dose are mainly due to variations in metabolism. These variations depend on four factors: The time in which maximum plasmatic concentration is obtained Tmax is 30â€”45 minutes [11 , 14 , 16 , 17] fasting and is delayed with food ingestion; it has an average metabolic half life in humans of 2. Vascular Effects of Caffeine Numerous studies have been carried out to determine the effect of caffeine on the cardiovascular system, with inconclusive results. Some have found that the consumption of caffeine increases cardiovascular risk [19 â€” 21] while others have described a beneficial or neutral effect on the same [22 â€” 24]. It is evident that the cardiovascular response to this substance depends on a variety of factors such as the amount ingested, the time of consumption, the frequency, degree of absorption, and hepatic metabolism, all aspects which cause a unique response of each individual to caffeine [25]. In addition to these factors, it is believed that some substances found in caffeinated beverages theobromine and theophylline active substances in bronchodilator medications used in the treatment of respiratory diseases could have some effects on the variability of these particular physiologic responses. It intervenes as an antagonist of the adenosine receptors, inhibitor of phosphodiesterase enzymes, sensitizer of calcium liberation channels, and GABA receptor antagonist [26]. In this paper, the main mechanisms of action of caffeine on the vascular tissue are described, and we will try to break a series of myths and paradigms that have negatively influenced the consumption of coffee. These mechanisms are summarized in Table 1. Summary of the vascular effects of caffeine. Mechanisms of Action of Caffeine at the Endothelial Level The endothelium is probably the most extensive tissue in the human body. It forms an anatomic and functional barrier covering the arterial walls which is highly selective and permeable through a continuous, uninterrupted, and soft surface. It synthesizes and releases a broad spectrum of vasoactive substances, intervening in the regulation of VSMC tone through an interaction between vasoconstrictor renin, angiotensin, ET-1, etc. Caffeine acts directly on the endothelial cell, stimulating the production of NO [40]. This effect was evaluated by blocking the NO pathway with NG-nitro-L-arginine, oxyhemoglobin, and methylene blue [47]. Some authors argue that caffeine produces greater vasodilation by acting on the endothelium than on the VSMC [33]. However, in in vitro studies carried out by our group, using rabbit arteries[52] and human internal mammary arteries, we observed that caffeine induces a potent arterial vasodilator effect in the presence or absence of preserved endothelial function Figure 1. Relaxation of human arteries in the presence of increasing doses of caffeine. The data are presented as average standard error of the media, which is presented in only one direction to facilitate the reading of the figure. Direct Effects Caffeine, by acting on the VSMC, generates a minimal initial contraction and then a significant vasodilator effect. There are various mechanisms that explain these effects. It is interesting to note that in the experiments carried out with caffeine in our laboratory [54], in human arteries and animal models, this contraction was not seen, which leads us to believe that it is probably a very slight vasoconstrictor effect Figure 2. Typical in vitro vascular response curve of caffeine produced in rabbit aortas with three accumulated caffeine doses corresponding to the plasmatic concentration obtained upon consumption of one, two, and three espressos. Vasodilation induced by the administration of caffeine without prior contraction is shown. Caffeine is a nonselective competitive inhibitor of the phosphodiesterase enzymes [40]. These enzymes have the capacity to degrade the phosphodiesterase bond in some compounds such as cAMP and cyclic guanosine monophosphate cGMP. One of the main enzymes inhibited by caffeine is - AMP phosphodiesterase [31 , 32], whose function is to degrade cAMP, causing its local accumulation. In addition, it is time dependent, generating a greater accumulation of cAMP the longer the incubation time [28]. As the enzyme is inhibited, the MLC phosphorylation is diminished and the actin-myosin interaction is inhibited. Up until now, the kinase enzyme of the myosin light chain in smooth muscle is the enzyme that activates the MLC through phosphorylation to a specific domain. However, more

recent studies have shown that this mechanism is not the only regulator of the myosin-actin interaction [58]. However, the effects of caffeine described cannot be attributed solely to the increase in cAMP. In , Ozaki et al. Given that the xanthenes contain an adenine ring identical to that of ATP, it has been postulated that they can interact competitively with the ATP binding site on the IP3 receptor [60]. The direct mechanisms of vasodilation are illustrated in Figure 3. Vasodilation produced by the direct effects of caffeine on the VSMC. Therefore MLC phosphatase predominates and there is vasodilation. Caffeine also directly inhibits MLC Kinase and the actin-myosin interaction. More recently, Sandow et al. These effects are illustrated in Figure 4. Indirect effects of caffeine on VSMC. Caffeine acts on the endothelial cell increasing cytoplasmic which will form the calcium-calmodulin complex which activates the nitric oxide synthase enzyme to produce nitric oxide. This diffuses to the VSMC. Caffeine, in turn, competitively inhibits 3 5 cGMP phosphodiesterase [20], stimulating even more accumulation of cGMP. Other Mechanisms of Action 6. Caffeine acts as a competitive inhibitor of the A1, A2a, and b receptors [63]. Caffeine competitively blocks these receptors as demonstrated in the experiment carried out by Sattin and Rall in [39], but this effect was reversed if more ATP adenosine precursor was added to the preparation. Paraxanthine, which is the main metabolite of caffeine, is an even more powerful blocker of these receptors than caffeine [2]. The action of adenosine depends on the type of receptor it stimulates and the type of tissue or cell in which it is found. The direct effects of adenosine on the different vascular systems are summarized in Table 2. The local vascular effects of adenosine are primarily vasodilation of the different beds. This effect depends mainly on the A2a receptors which are found in high concentrations in vascular tissue [57]. Vascular effects of adenosine. Caffeine, by competitively blocking the adenosine receptors, increases its plasmatic concentration [64] which increases its systemic effects. At a systemic level, adenosine stimulates the chemoreceptor distributed throughout the circulation, causing a generalized increase in sympathetic tone, with an increase in circulating catecholamines, peripheral vascular resistance, and renin secretion [44 , 65]. Several studies have documented an increase in systolic arterial pressure of 6 to 7. A meta-analysis carried out in [67] described an increase in the systolic and diastolic arterial pressure 2. When you abruptly stop the consumption of caffeine in a habitual consumer, there is a greater number of available adenosine receptors, which potentiates the vasodilation produced by adenosine, causing the symptoms [59 , 69 , 70]. In vitro studies do not evaluate the systemic response to caffeine, and therefore it is not clear yet which one of the mechanisms of action predominates in vivo, given that there are various factors that affect its metabolism and its effects. Caffeine in Relation to Migraine Type Headaches Migraines are irregular and episodic which is why there is no specific explanation for why a migraine occurs at any given time. In general it is supposed that exposure to certain environmental factors combined with individual internal factors causes migraine episodes. There are reports that certain dietary, physical, hormonal, emotional, and environmental factors trigger or cause migraine episodes. Those most frequently reported include stress, alcohol, foods, excess or lack of sleep, and weather conditions. Headaches migraine may be related to caffeine consumption due to its removal from the usual diet, causing an abstinence syndrome: The mechanism by which this occurs is a blocking of the adenosine receptors; when there is an excessive release of adenosine there is a response in which the release of neurotransmitter molecules, such as serotonin, noradrenaline, acetylcholine, and dopamine, is inhibited, causing an imbalance that can be seen in the symptoms associated with migraines [72] There is no clear conclusion that migraines can be caused by caffeine. Adenosine has opposite effects depending on its site of action; centrally, in the brain and spinal cord, adenosine acts as an analgesic, but peripherally it can cause pain. Adenosine dilates blood vessels in the head and neck.

Chapter 3 : Adenosine receptor - Wikipedia

Mechanism of action. When it is administered intravenously, adenosine causes transient heart block in the atrioventricular (AV) node. This is mediated via the A 1.

Adenosine, USP is a white crystalline powder. It is soluble in water and practically insoluble in alcohol. Solubility increases by warming and lowering the pH. Adenosine, USP is not chemically related to other antiarrhythmic drugs. Adenosine injection, USP is a sterile, nonpyrogenic solution for rapid bolus intravenous injection. The pH of the solution is between 4. Adenosine is antagonized competitively by methylxanthines such as caffeine and theophylline, and potentiated by blockers of nucleoside transport such as dipyridamole. Adenosine is not blocked by atropine. Hemodynamics The intravenous bolus dose of 6 or 12 mg Adenosine usually has no systemic hemodynamic effects. When larger doses are given by infusion, Adenosine decreases blood pressure by decreasing peripheral resistance. Pharmacokinetics Intravenously administered Adenosine is rapidly cleared from the circulation via cellular uptake, primarily by erythrocytes and vascular endothelial cells. This process involves a specific transmembrane nucleoside carrier system that is reversible, nonconcentrative, and bidirectionally symmetrical. Intracellular Adenosine is rapidly metabolized either via phosphorylation to Adenosine monophosphate by Adenosine kinase, or via deamination to inosine by Adenosine deaminase in the cytosol. Since Adenosine kinase has a lower Km and Vmax than Adenosine deaminase, deamination plays a significant role only when cytosolic Adenosine saturates the phosphorylation pathway. Inosine formed by deamination of Adenosine can leave the cell intact or can be degraded to hypoxanthine, xanthine, and ultimately uric acid. Adenosine monophosphate formed by phosphorylation of Adenosine is incorporated into the high-energy phosphate pool. While extracellular Adenosine is primarily cleared by cellular uptake with a half-life of less than 10 seconds in whole blood, excessive amounts may be deaminated by an ecto-form of Adenosine deaminase. As Adenosine requires no hepatic or renal function for its activation or inactivation, hepatic and renal failure would not be expected to alter its effectiveness or tolerability. Clinical Trial Results In controlled studies in the United States, bolus doses of 3, 6, 9, and 12 mg were studied. Seven to sixteen percent of patients converted after 1 to 4 placebo bolus injections. Similar responses were seen in a variety of patient subsets, including those using or not using digoxin, those with Wolff-Parkinson-White Syndrome, males, females, blacks, Caucasians, and Hispanics. Adenosine is not effective in converting rhythms other than PSVT, such as atrial flutter, atrial fibrillation, or ventricular tachycardia, to normal sinus rhythm. Conversion to sinus rhythm of paroxysmal supraventricular tachycardia PSVT , including that associated with accessory bypass tracts Wolff-Parkinson-White Syndrome. When clinically advisable, appropriate vagal maneuvers e. It is important to be sure the Adenosine injection solution actually reaches the systemic circulation see Dosage and Administration. Adenosine injection does not convert atrial flutter, atrial fibrillation, or ventricular tachycardia to normal sinus rhythm. In the presence of atrial flutter or atrial fibrillation, a transient modest slowing of ventricular response may occur immediately following Adenosine administration. Second- or third-degree A-V block except in patients with a functioning artificial pacemaker. Sinus node disease, such as sick sinus syndrome or symptomatic bradycardia except in patients with a functioning artificial pacemaker. Appropriate therapy should be instituted as needed. Patients who develop high-level block on one dose of Adenosine should not be given additional doses. Because of the very short half-life of Adenosine, these effects are generally self-limiting. Appropriate resuscitative measures should be available. Transient or prolonged episodes of asystole have been reported with fatal outcomes in some cases. Rarely, ventricular fibrillation has been reported following Adenosine administration, including both resuscitated and fatal events. In most instances, these cases were associated with the concomitant use of digoxin and, less frequently with digoxin and verapamil. Although no causal relationship or drug-drug interaction has been established, Adenosine should be used with caution in patients receiving digoxin or digoxin and verapamil in combination. Arrhythmias at Time of Conversion At the time of conversion to normal sinus rhythm, a variety of new rhythms may appear on the electrocardiogram. They generally last only a few seconds without intervention, and may take the form of premature ventricular contractions, atrial

premature contractions, atrial fibrillation, sinus bradycardia, sinus tachycardia, skipped beats, and varying degrees of A-V nodal block. Bronchoconstriction Adenosine injection is a respiratory stimulant probably through activation of carotid body chemoreceptors and intravenous administration in man has been shown to increase minute ventilation Ve and reduce arterial PCO2 causing respiratory alkalosis. Adenosine administered by inhalation has been reported to cause bronchoconstriction in asthmatic patients, presumably due to mast cell degranulation and histamine release. These effects have not been observed in normal subjects. Adenosine has been administered to a limited number of patients with asthma and mild to moderate exacerbation of their symptoms has been reported. Respiratory compromise has occurred during Adenosine infusion in patients with obstructive pulmonary disease. Adenosine should be used with caution in patients with obstructive lung disease not associated with bronchoconstriction e. Adenosine should be discontinued in any patient who develops severe respiratory difficulties. PRECAUTIONS Drug Interactions Intravenous Adenosine injection has been effectively 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. Digoxin and verapamil use may be rarely associated with ventricular fibrillation when combined with Adenosine see Warnings. Because of the potential for additive or synergistic depressant effects on the SA and AV nodes, however, Adenosine should be used with caution in the presence of these agents. The use of Adenosine in patients receiving digitalis may be rarely associated with ventricular fibrillation see Warnings. The effects of Adenosine are antagonized by methylxanthines such as caffeine and theophylline. In the presence of these methylxanthines, larger doses of Adenosine may be required or Adenosine may not be effective. Adenosine effects are potentiated by dipyridamole. Thus, smaller doses of Adenosine may be effective in the presence of dipyridamole. Carbamazepine has been reported to increase the degree of heart block produced by other agents. As the primary effect of Adenosine is to decrease conduction through the A-V node, higher degrees of heart block may be produced in the presence of carbamazepine. Carcinogenesis, Mutagenesis, Impairment of Fertility Studies in animals have not been performed to evaluate the carcinogenic potential of Adenosine injection. Adenosine, however, like other nucleosides at millimolar concentrations present for several doubling times of cells in culture, is known to produce a variety of chromosomal alterations. Fertility studies in animals have not been conducted with Adenosine. Pregnancy Category C Animal reproduction studies have not been conducted with Adenosine; nor have studies been performed in pregnant women. As Adenosine is a naturally occurring material, widely dispersed throughout the body, no fetal effects would be anticipated. However, since it is not known whether Adenosine can cause fetal harm when administered to pregnant women, Adenosine should be used during pregnancy only if clearly needed. Pediatric Use No controlled studies have been conducted in pediatric patients to establish the safety and efficacy of Adenosine for the conversion of paroxysmal supraventricular tachycardia PSVT. However, intravenous Adenosine has been used for the treatment of PSVT in neonates, infants, children and adolescents see Dosage and Administration. Geriatric Use Clinical studies of Adenosine did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, Adenosine in geriatric patients should be used with caution since this population may have a diminished cardiac function, nodal dysfunction, concomitant diseases or drug therapy that may alter hemodynamic function and produce severe bradycardia or AV block. Adverse Reactions The following reactions were reported with intravenous Adenosine injection used in controlled U. Post Marketing Experience see Warnings The following adverse events have been reported from marketing experience with Adenosine. Because these events are reported voluntarily from a population of uncertain size, are associated with concomitant diseases and multiple drug therapies and surgical procedures, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Decisions to include these events in labeling are typically based on one or more of the following factors: Cardiovascular Prolonged asystole, ventricular tachycardia, ventricular fibrillation, transient increase in blood pressure, bradycardia, atrial fibrillation, and Torsade de Pointes. Respiratory Central Nervous System Seizure activity, including tonic clonic grand mal seizures, and loss of consciousness. Thus, adverse effects are

generally rapidly self-limiting. Treatment of any prolonged adverse effects should be individualized and be directed toward the specific effect. Methylxanthines, such as caffeine and theophylline, are competitive antagonists of Adenosine. Adenosine injection should be given as a rapid bolus by the peripheral intravenous route. To be certain the solution reaches the systemic circulation, it should be administered either directly into a vein or, if given into an IV line, it should be given as close to the patient as possible and followed by a rapid saline flush. Adult Patients The dose recommendation is based on clinical studies with peripheral venous bolus dosing. Central venous CVP or other administration of Adenosine injection has not been systematically studied. The recommended intravenous doses for adults are as follows: If the first dose does not result in elimination of the supraventricular tachycardia within 1 to 2 minutes, 12 mg should be given as a rapid intravenous bolus. This 12 mg dose may be repeated a second time if required. Pediatric Patients The dosages used in neonates, infants, children and adolescents were equivalent to those administered to adults on a weight basis. A saline flush should follow. If conversion of PSVT does not occur within 1 to 2 minutes, additional bolus injections of Adenosine can be administered at incrementally higher doses, increasing the amount given by 0. Follow each bolus with a saline flush. This process should continue until sinus rhythm is established or a maximum single dose of 0. Administer the adult dose. Doses greater than 12 mg are not recommended for adult and pediatric patients. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. If crystallization has occurred, dissolve crystals by warming to room temperature. The solution must be clear at the time of use. The container closure is not made with natural rubber latex. Pediatric Cardiology ;

Chapter 4 : CV Pharmacology | Adenosine

Adenosine has a negative inotropic effect in cardiac atrial preparations ("direct" negative inotropic effect). This effect is probably due to an activation of a potassium outward current which shortens the action potential duration and hence reduces the force of contraction.

May repeat the 12 mg dose once if needed. Single doses greater than 12 mg are not recommended. The initial dose should be decreased to 3 mg in patients taking carbamazepine or dipyridamole, in those with a transplanted heart, or in those receiving the drug by central venous access. Infants, Children, and Adolescents weighing less than 50 kg 0. If conversion does not occur within 1 to 2 minutes, then administer 0. The manufacturer recommends an initial dose of 0. However, studies have shown that initial doses of 0. The median effective dose was approximately 0. If conversion does not occur within 1 to 2 minutes, additional boluses may be administered at incrementally higher doses increasing by 0. Studies have shown that initial doses of 0. For use as an adjunct to thallium myocardial perfusion imaging for coronary artery disease diagnosis in patients unable to exercise adequately. The adenosine infusion rate can be calculated from the following formula: The dose of thallium should be injected after the first 3 minutes of adenosine infusion. The thallium injection should be made as close as possible to the venous access to prevent an inadvertent increase in the dose of adenosine. Geriatric See adult dosage. In general, use adenosine with caution in the elderly since older patients may have cardiac dysfunction, nodal dysfunction, or concomitant diseases or drug therapy that may alter hemodynamic function and increase risk for severe bradycardia or AV block. Clinical practice guidelines suggest that patients with pulmonary arterial hypertension undergo acute vasoreactivity testing with a short-acting agent in the absence of contraindications, including low systemic blood pressure, low systemic cardiac output, or the presence of functional class FC IV symptoms. Acute vasoreactivity is defined as a fall in mean pulmonary artery pressure mPAP more than 10 mmHg, to an mPAP less than 40 mmHg, with an unchanged or increased cardiac output. Infants, Children, and Adolescents 0. If necessary, may administer a second dose of 0. When IV access is available, administer through IV access that is closest to the heart. Consider adenosine use only if the rhythm is regular and the QRS is monomorphic. Do not use adenosine in patients with Wolff-Parkinson-White syndrome and wide-complex tachycardia.

Chapter 5 : Caffeine's Vascular Mechanisms of Action

Mechanism of Action Adenocard (adenosine injection) slows conduction time through the A-V node, can interrupt the reentry pathways through the A-V node, and can restore normal sinus rhythm in patients with paroxysmal supraventricular tachycardia (PSVT), including PSVT associated with Wolff-Parkinson-White Syndrome.

Adenosine General Pharmacology Adenosine is a naturally occurring purine nucleoside that forms from the breakdown of adenosine triphosphate ATP. ATP is the primary energy source in cells for transport systems and many enzymes. Most ADP and AMP that form in the cell is rephosphorylated in the mitochondria by enzymatic reactions requiring oxygen. If there are large amounts of ATP hydrolyzed, and especially if there is insufficient oxygen available i. Adenosine can bind to purinergic receptors in different cell types where it can produce a number of different physiological actions. One important action is vascular smooth muscle relaxation, which leads to vasodilation. This is a particularly important mechanism for matching coronary blood flow to the metabolic needs of the heart. In coronary vascular smooth muscle, adenosine binds to adenosine type 2A A2A receptors, which are coupled to the Gs-protein. Activation of this G-protein stimulates adenylyl cyclase AC in figure , increases cAMP and causes protein kinase activation. This stimulates KATP channels, which hyperpolarizes the smooth muscle, causing relaxation. Increased cAMP also causes smooth muscle relaxation by inhibiting myosin light chain kinase , which leads to decreased myosin phosphorylation and a decrease in contractile force. There is also evidence that adenosine inhibits calcium entry into the cell through L-type calcium channels. Since calcium regulates smooth muscle contraction , reduced intracellular calcium causes relaxation. In some types of blood vessels, there is evidence that adenosine produces vasodilation through increases in cGMP , which leads to inhibition of calcium entry into the cells as well as opening of potassium channels. In cardiac tissue, adenosine binds to type 1 A1 receptors, which are coupled to Gi-proteins. Activation of this pathway opens potassium channels, which hyperpolarizes the cell. Activation of the Gi-protein also decreases cAMP, which inhibits L-type calcium channels and therefore calcium entry into the cell. In cardiac pacemaker cells located in the sinoatrial node, adenosine acting through A1 receptors inhibits the pacemaker current If , which decreases the slope of phase 4 of the pacemaker action potential thereby decreasing its spontaneous firing rate negative chronotropy. Inhibition of L-type calcium channels also decreases conduction velocity negative dromotropic effect particularly at the atrioventricular AV nodes. Finally, adenosine by acting on presynaptic purinergic receptors located on sympathetic nerve terminals inhibits the release of norepinephrine. In terms of its electrical effects in the heart, adenosine decreases heart rate and reduces conduction velocity, especially at the AV node, which can produce atrioventricular block. Note, however, that when adenosine is infused into humans, heart rate increases because of baroreceptor reflexes caused by systemic vasodilation and hypotension. Adenosine has a very short half-life. In human blood, its half-life is less than 10 seconds. There are two important metabolic fates for adenosine. Most importantly, adenosine is rapidly transported into red blood cells and other cell types where it is rapidly deaminated by adenosine deaminase to inosine, which is further broken down to hypoxanthine, xanthine and uric acid, which is excreted by the kidneys. Adenosine deamination also occurs in the plasma, but at a lower rate than that which occurs within cells. Dipyridamole is a vasodilator drug that blocks adenosine uptake by cells, thereby reducing the metabolism of adenosine. Therefore, one important mechanism for dipyridamole-induced vasodilation is its potentiation of extracellular adenosine. Adenosine can be acted on by adenosine kinase and rephosphorylated to AMP. This salvage pathway helps maintain the adenine nucleotide pool in cells. Therapeutic and Diagnostic Use and Rationale Although adenosine is a powerful vasodilator, especially in the coronary circulation, it is not used as a vasodilator for the treatment of coronary artery disease. The reason is that it is very short acting, limited to intravascular administration, and in the heart it can produce coronary vascular steal. When administered by intravenous infusion, it can produce hypotension and atrioventricular block. The major therapeutic use of adenosine is as an antiarrhythmic drug for the rapid treatment of supraventricular tachycardias. Its supression of atrioventricular conduction makes it very useful in treating paroxysmal supraventricular tachycardia in which the AV node is part of the reentry pathway as in

Wolff-Parkinson-White Syndrome. For these indications, adenosine is administered either as bolus intravenous injection or as an intravenous infusion. Adenosine is not effective for atrial flutter or fibrillation. Patients can experience flushing and headache, both of which are related to vasodilation. Adenosine can produce rapid arterial hypotension; however, this is reversed shortly after stopping the infusion of adenosine. Coronary vascular steal is of theoretical concern in some patients with coronary artery disease, although there is no clinical evidence supporting this adverse effect. Methylxanthines such as caffeine and theophylline competitively antagonize the binding of adenosine at its purinergic receptor. Finally, adenosine may produce undesirable AV block; however, this is usually rapidly corrected by stopping adenosine administration. Therefore, adenosine is contraindicated in patients with preexisting second or third degree AV block. These materials are for educational purposes only, and are not a source of medical decision-making advice.

Chapter 6 : What is the mechanism of action of Adenosine in AVNRT ? | calendrierdelascience.comesan M

Adenosine is a prescription drug that is administered by a medical professional. In this lesson, we will learn more about what adenosine is used for and how it works.

Chapter 7 : Adenosine - Wikipedia

At the beginning of phase 4 you have Na influx and K efflux slowly depolarize the cell till membrane potential reach , then the T type Ca channel open and the Ca influx create further depolarization.

Chapter 8 : Adenosine - FDA prescribing information, side effects and uses

Mechanism of Action PSVT: Slows conduction through AV node and interrupts AV reentry pathways, which restore normal sinus symptoms Stress testing: A2A adenosine receptor agonist; activation of the A2A adenosine receptor produces coronary vasodilation and increases coronary blood flow.

Chapter 9 : Adenocard (adenosine) dose, indications, adverse effects, interactions from calendrierdelascie

This video contains detailed description of Mechanism of action of Adenosine/ Pharmacology of Adenosine/ Adenosine pathway. Link 1: Mechanism of 'Contraction/ Relaxation' of Vascular Smooth Muscle.