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Salmeterol is part of a broader group of drugs known as adrenergic agonists; it works specifically by binding to β2 receptors of the adrenergic receptor family, which are activated by the binding of the endogenous neurotransmitters, norepinephrine and epinephrine. The adrenergic receptors are as well part of a broader group of receptors known as G-protein coupled receptors. The G-protein receptor family is composed of a single peptide with seven trans-membrane regions that are attached to a G protein, Gs, Gq, or GI (Harvey & Champe, 2008). The G protein has 3 subunits; the α, β, and γ subunits; the α subunit in the resting state is bound to GDP as well as the β and γ subunits. When the receptor is activated the α subunit replaces GDP for GTP and the α-GTP complex and dissociates from the entire complex and activates a second messenger system. In the case of Gs as well as other G proteins the α-GTP complex activate or inhibit adenylyl cyclase, which increases or decreases respectfully the concentration of cAMP, an important regulator of protein phosphorylation. Other G proteins, for example Gq activate phospholipase C which leads the formation of the second messengers inositol 1, 4, 5 triphosphate and diacylglycerol.   
The adrenergic neurons release norepinephrine and are found in the CNS, where it regulates brain activity as well as in the sympathetic nervous system, where it functions as the connection between the ganglia and the effector organs. α – receptors are found presynaptically and at the effector organ level. α1 receptors are found on smooth muscle and lead to its constriction. α2 receptors are found presynaptically and function to mediate and down regulate the release of norepinephrine (Harvey and Champe, 2008). β receptors are subdivided into β1 receptors are found predominantly in the heart and kidneys, and β2 receptors, which are found in the blood vessels, uterus, bronchioles, skeletal muscle, liver, and pancreas. It is the effect of β2 at the level of the bronchioles, leading to bronchiolar dilation, which leads to the beneficial action of salmeterol and its use in asthma and COPD patients (Lionel, 2011).   
Salmeterol is similar in chemical structure to albuterol but has a lipophilic side chain making it more selective for β2 receptors. It is a long acting bronchodilator that has lasting effects for up to 12 hours; due to its slow onset of action it is not used for quick relief of symptoms but is rather efficacious when used as adjunctive therapy with corticosteroids (Ohar & Donohue, 2010). Salmeterol is inhaled to provide the more beneficial effect of bronchodilation vs. the systemic effect of activating the sympathetic nervous system. However, even though inhaling salmeterol is the more beneficial and safe method of delivery it is not without its side effects. Side effects due to therapy include effects on the cardiovascular system such as palpitations, tachycardia, increased BP; other adverse effects include tremor, nervousness and headache (Ogbru, 2010). The use of salmeterol has also been associated with an increase in asthma related mortalitly (Cates & Cates, 2008).   
Propranolol, Metoprolol, and Acebutolol are all β-blocking drugs that work to decrease sympathetic activity towards the various effector organs. Propranolol is a nonselective β blocker, meaning it works on both β1 and β2 receptors. Metoprolol and Acebutolol are both selective for β1 receptors, so they have a more concentrated effect on the heart since the β1 receptors dominate in the heart. The elderly, who are the predominant patients on these drugs, have been reported to account for the variations in pharmacokinetic properties of these drugs.   
Propranolol is absorbed by the GI tract and undergoes first pass metabolism. Due to the extensive first pass metabolism and hepatic tissue binding, bioavailability for propranolol is relatively low at 30%. Plasma levels peak approximately 1 -2 hours after administration (Propranolol, 1999). Metoprolol is also completely absorbed from the GI tract and undergoes first pass metabolism much in the same way as propranolol. However, bioavailability of metoprolol is considerably higher at 50% (“ AFT – Metoprolol CR”, 2009) Acebutolol just like the previous two drugs is completely absorbed from the GI tract and goes extensive first pass metabolism. It has a bioavailability in between that of metoprolol and propranolol at 40% of the original drug (“ Acebutolol”, 2001). Therefore metoprolol has a much higher amount of the actual active drug that can reach the systemic circulation, and exert its effects. Protein binding affects how much drug can actually act at the tissue. If protein binding is extensive, usually to albumin, that means less drug is active because only free unbound drugs can exert their effects. Acebutolol has a protein binding capacity of 26% (“ Acebutolol”, 2001), propranolol is extensively bound to plasma proteins, nearly 90-95% (Tritsch et al, 1999) Metoprolol is only 5-10% bound to plasma proteins, this means that is the most active since it has the highest bioavailability and it is the drug that is the least bound to plasma proteins. Acebutolol has a half life of the 3-4 hrs but its active compound following first pass metabolism has lasting effects of 13 hours; propranolol has a similar half life of 3-6 hours and is effective for up to 12 hours; and metoprolol has a half life of 3. 5 hours. The liver extensively metabolizes propranolol, and the metabolite 4-hydroxypropranolol is the active component; propranolol is nearly completely eliminated by hepatic metabolism from the body within 48 hours after the original oral dose, less than 0. 5% is excreted unchanged in the urine (Fitzgerald & O’donnel, 1971). Propranolol is also found in the breast milk of mothers being treated with a concentration of 50% of that in blood. Propranolol is highly lipophilic and can cross the blood brain barrier and can cross the placenta to the fetus. Acebutolol can also cross the placenta and effect the fetus. Acebutolol and its metabolite diacetolol appear to undergo enterohepatic circulation, as it is excreted in the feces as well as the urine. They are excreted in the feces via elimination from the bile and through secretion into the GI tract. (Acebutolol, 2004) Metoprolol is metabolized primarily by the liver and is excreted by the kidneys. 95% of the drug is excreted as metabolites that have no beta-adrenergic blocking activity; the rest of the drug is excreted unchanged (Metoprolol, 2005).   
Since propranolol is a non-selective β blocker it can exert action on β1 receptors leading to bronchoconstriction a serious complication for COPD and asthma patients that can lead to death by asphyxia. Other adverse effects associated with the use of propranolol include risk of arrhythmia, especially if the drug is abruptly stopped, rather then tapered slowly, sexual dysfunction, disturbances in metabolism such as decreased glycogenolysis and decreased glucagon release. Drugs that effects liver enzymes can effect the metabolism of propranolol, for example cimetidine, fluoxetine, and paroxetine can increase propranolol’s effects because they decrease it’s effects, whereas drugs such as barbiturates, phenytoin, and rifampin can decrease its effects. Propranolol is effective against hypertension, glaucoma, migraine headaches, hyperthyroidism and angina pectoris, by decreasing the oxygen requirement of the heart (Harvey & Champe, 2008).   
Acebutolol and metoprolol are selective for β1 receptors, meaning that the risk of bronchoconstriction is eliminated; this makes these drugs “ cardio-selective.” Cardio-selectivity is more pronounced when these drugs are given at lower doses vs. higher doses where they start to work on all β receptors. These drugs are mainly used for the treatment of hypertension as they do not have an effect on peripheral vascular β2 receptors, pulmonary function, and carbohydrate metabolism (Harvey & Champe, 2008).   
Propranolol, metoprolol and acebutolol are affected by renal and liver impairment and dosage should reflect the patient’s kidney and/ or hepatic function. Nevertheless these drugs have shown to decrease oxygen demand of the heart and decrease mortality in patients post MI and should therefore be part of the drug regimen of any patient with ischemic heart disease (Harrisson’s, 2008).

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