

Introduction to beta blockers biology essay



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The blockers are drugs which act by blocking the effect of mediators and agonists on the relevant receptors. The β -blockers show an antihypertensive effect, which is caused by reduced cardiac output, decreased release of renin, central decrease of sympathetic action. Also, they exhibit an antianginal effect, which is caused by slowing of the heart rate and thus decreased metabolic demand. The main side effects of general β -blockers are cardiac failure, such as cardiac depression, hypotension, sinus node dysfunction, atrioventricular block. The side effects depend on the properties of β -blockers. For instance, non-selective β -blockers show the unwanted effects caused by blocking β_2 -receptor. These show bronchoconstriction which is potentially life-threatening in asthmatic patients and clinically undesirable in patients with other respiratory problems. Lipophilic β -blockers may cause psychological symptoms, such as depression.

There are some important factors in the selection of β -blockers, which are ISA, MSA, β_1 -selectivity, lipophilicity, solubility, and the duration of effects. The β_2 -selective blockers are not used clinically, because of causing bronchoconstriction. Some β -blockers show the effect of not only blocking the

receptors, but also stimulating α -receptors. It depends on the situation whether ISA positive β -blockers stimulate or block α -receptors. For example, these act as α -blockers under the existence of α -agonists. On the other hand, these invigorate the receptors under the non-existence of α -agonists. Such an effect is termed ISA which is intrinsic sympathomimetic activity. The drugs which have ISA decrease the side effects caused by β -blockers. The non-selective blocks of β -receptors cause the increase in cardiac afterload and bronchoconstriction, because of β_2 -blocking. The β_1 -selective drugs slightly have the effect of β_2 -blocking, but the risk of causing cardiac afterload and bronchoconstriction is lower than that of non-selective β -blockers. The duration of effects depends on the disease. Long acting β -blockers are desirable for hypertension and heart failure, because of the low frequency of administration. In contrast, short acting β -blockers, propranolol, are ideal drugs for angina, because of the fast onset of action. As I stated above, lipophilic β -blockers have a risk of causing depression. The reason is such drugs are absorbed easily, so can penetrate BBB. MSA, membrane stabilising activity, is an activity which prevents sodium ions from entering inside of cells. Many β -blockers, such as propranolol, have the activity, so these are useful for arrhythmia.

The properties of propranolol

Propranolol is a non-selective β -blocker, which is clinically used as propranolol hydrochloride. The IUPAC name is (2RS)-1-(1-Methylethyl) amino-3-(naphthalen-1-yloxy) propan-2-ol monohydrochlorid. The molecular weight is 295. 80, and the melting point is around 165 degrees. It is white crystalline

powder, and it is easy to dissolve in water and methanol. Also, the methanol solution doesn't exhibit optical activity. Its structural formula is following.

Propranolol is absorbed from the gastrointestinal tract, its plasma level reach a peak, 42.9ng/ml, after 1.5 hours of administration. The half life is approximately 3.9 hours. The metabolism of propranolol is mainly conducted by the liver, so it is metabolised to naphthoxylactic acid, glucuronic acid conjugate, and 4-Hydroxypropranolol. It is mainly metabolised by CYP2D6, CYP1A2, and CYP2C19. As I discussed above, propranolol can penetrate BBB and transition to the brain, because of lipophilic. Its dosage amount is mostly excreted in urine within 48 hours, and the rest is excreted in faeces, which is just less than 4 percentages. Its pharmacological actions include an antihypertensive effect, an antianginal effect, and MSA. Propranolol doesn't show ISA in the experiment with using rats, so it is considered that propranolol doesn't show human ISA as well as rats. Some side effects have been reported, such as, bronchoconstriction, slowing of heart rate, and allergic. These days, a new side effect is becoming popular, which is mental symptoms, such as depression, nightmare, and insomnia. There is the drug-drug interaction in propranolol. For instance, propranolol can't use with thioridazine which is a psychotropic drug, especially for integration dysfunction symptom. The reason is the side effect of thioridazine is likely to happen, because of preventing propranolol from being metabolised thioridazine by enzymes in the liver. In the same way, propranolol can't use with rizatriptan which is a drug for migraine.

Combination use with propranolol and rizatriptan induce the extension of half life of and the increase of AUC, so increase the side effects. Also, it is

essential to avoid administering rizatriptan within 24 hours of administration of propranolol for the same reason. Its package leaflet approved by US Food and Drug Administration warns.

' There have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of propranolol therapy. Therefore, when discontinuance of propranolol is planned, the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If propranolol therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute propranolol therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.' (FDA 2010)

Therefore, its administration should not be stopped suddenly. Above statement is one of the most important warnings in the usage of propranolol.

Properties of atenolol

Atenolol is a 1-selective blocker without showing MSA and ISA, which is used for hypertension, angina, and cardiac dysrhythmias. It is sold as TENORMIN in the market. The IUPAC name is 2-(4-{(2RS)-2-Hydroxy-3-[(1-methylethyl) amino] propoxy} phenyl) acetamide. The molecular weight is 266.34, and the melting point is around 155 degrees. It is white or light yellow crystalline powder, and it is easy to dissolve in water and methanol as well as

propranolol. In addition, the methanol solution doesn't exhibit optical activity. Its structural formula is following.

Atenolol is almost half absorbed from gastrointestinal tract, and the rest enter systemic circulation without getting first pass effect on the liver. Its half life is approximately 7 hours. Atenolol is little metabolised in the liver, but some are metabolised to glucuronic acid conjugate. The data shows that atenolol is low distribution to brain compared to propranolol, because its drug is hydrophilic. Therefore, it has been reported that atenolol hardly have an influence on mental symptom unlike propranolol. The excretion of oral atenolol is approximately 50% in urine and faeces respectively, but 90% of them are not metabolised. As I stated above, atenolol is a β_1 -selective blocker, so it is little to affect bronchial tubes which is controlled by β_2 -receptor. However, the data have been reported atenolol inhibit β_2 -receptor at high dose. Its side effects are almost the same as propranolol. The main difference between atenolol and propranolol is the incidence of tracheal symptoms, such as bronchoconstriction and bronchial spasm. Propranolol blocks β -receptors non-selectively, so causes different tracheal symptoms. In contrast, atenolol inhibits β_1 -receptors selectively, so barely makes such symptoms happen. The sudden cessation of therapy with atenolol has a possibility of causing cardiac diseases for specific patients. Its leaflet approved by FDA cautions,

' Patients with coronary artery disease, who are being treated with TENORMIN, should be advised against abrupt discontinuation of therapy. Severe exacerbation of angina and the occurrence of myocardial infarction and ventricular arrhythmias have been reported in angina patients following <https://assignbuster.com/introduction-to-beta-blockers-biology-essay/>

the abrupt discontinuation of therapy with beta blockers. The last two complications may occur with or without preceding exacerbation of the angina pectoris. As with other beta blockers, when discontinuation of TENORMIN is planned, the patients should be carefully observed and advised to limit physical activity to a minimum. If the angina worsens or acute coronary insufficiency develops, it is recommended that TENORMIN be promptly reinstated, as least temporarily. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue TENORMIN therapy abruptly even in patients treated only for hypertension.' (FDA 2008)

The properties of -blockers in obese patients

These days, the number of obese people is increasing due to high calorie foods and the decrease of exercise. It is common for obese patients to take drug therapy in clinical practice, because obesity is connected with many diseases, such as diabetes and cardiovascular disease. Therefore, it is important to identify pharmacological and pharmacokinetic properties in obese patients. Jerzy Wojcickia studied the pharmacological and pharmacodynamic properties between propranolol and atenolol in obese patients. As a result, he concluded following.

' The results of our study suggest that obesity and concomitant lipid disorders have a minimal effect on the pharmacokinetics of -blockers. However, the observed differences in the pharmacokinetics did not result in any clinically significant differences in the pharmacodynamics of either drug between obese and non-obese subjects.' (Jerzy 2003)

Conclusion

In summary, there are some differences between propranolol and atenolol from the point of view of pharmacology, because of the difference of selectivity of β -receptor. In the same way, there are some pharmacokinetic differences as well, such as the duration of half life and the mechanism of metabolism and excretion. In contrast, their physicochemical properties are similar. In clinical use, there are some warnings respectively, and the common cautions are to avoid sudden discontinuation of administration. Its dosage should be progressively decreased over a few weeks in order to avoid such side effects. I studied the characters between these β -blockers in obese patients. In the study, it was not observed there are the obvious differences between obese patients and non-obese patients.