The Effect of Methyl dopa on serum lipid profile in rat.

Laith Mohammed Abbass AL-Hussueni. **M.B. Ch. B, M. Sc. Pharmacology. AL-Qaddissia University. Medical College. Department of Pharmacology.*

الخلاصة

استهدفت هذه الدراسة معرفة تأثير دواء مثيل دوبا المستخدم في علاج ارتفاع ضغط الدم على مستوى الدهون في مصل الدم لدى الجرذان بسبب وجود ارتباط وثيق بين ارتفاع ضغط الدم وبين ارتفاع مستوى الدهون وبالتالي يتحتم علينا اختيار دواء لا يؤدي إلى زيادة الاضطراب في مستوى الدهون. عشرون جرذاً استخدمت في التجربة أعطيت غذاء عالي الكولسترول لمدة اثنا عشر أسبوعاً ومن ثم قسمت إلى مجموعتين الأولى: أُعطيت (33) ملغرام/ كغم/ اليوم من دواء مثيل دوبا عن طريق الفم مرتين في اليوم. والمجموعة الثانية: أعطيت ماء مقطر واعتبرت مجموعة سيطرة. العلاج استمر لمدة اثنا عشر أسبوع مع الغذاء عالي الكولسترول أيضاً. مستوى الدهون في مصل الدم تم قياسه قبل وبعد البدء بالعلاج وكانت النتائج كالأتي:

لم يكن لدواء مثيل دوبا تأثير على الكلسيريدات الثلاثية ولا على ولا على الكولسترول الكلي لكنه سبب نقصان ملحوظ في مستوى الكولسترول واطئ الكثافة وسبب زيادة في مستوى الكولسترول عالي الكثافة بالمقارنة مع مجموعة السيطرة الأمر الذي يظهر فائدة كبيرة في استخدام هذا الدواء للمرضى الذين يعانون من ارتفاع ضغط مع اضطراب مستوى الدهون لديهم.

Abstract:

Evidence liking hypertension and dyslipidemia are very important in deciding which antihypertensive drug is going to be describe to hypertensive patient who had or at risk to had dyslipidemia. Antihypertensive drugs which have neutral effect or preferably beneficial effect on lipid profile are the first choice in those patients. Drugs with harmful effect on serum lipid profile may add another problem to the patient and increase the risk of complications.

Purpose:

This study is carried on to evaluate the effect of methyl dopa on serum lipid profile.

Methods:

Twenty rats enrolled in the experiment given atherogenic diet for twelve weeks then randomly divided into two groups, first group received 33 mg /Kg /day P. O Methyl dopa dissolved in 2 ml distilled water given by nasogastric tube twice daily and serve as central group. The treatment continues with atherogenic diet for another twelve weeks. The serum lipid profile namely triglyceride, total cholesterol, LDL-cholesterol (low density lipoprotein cholesterol) HDL-cholesterol (high density lipoprotein cholesterol) and HDL-cholesterol / total cholesterol ratio were estimated before and after the treatment. The statistical analysis was done using ANOVA with level of significance $P<0.05$.

Result:

Methyl dopa was found to have no effect on serum triglyceride level and on total cholesterol serum level but it causes significant decrease in LDL-cholesterol serum level and significant increase in HDL- cholesterol serum level in comparison to control group.

Conclusion:

Methyl dopa has beneficial effect on serum lipid profile as it causes decrease in LDL-cholesterol level which is the atherogenic portion of cholesterol and causes increase in HDL-cholesterol level which is the protective portion of cholesterol. This effect justify it's use in patients who have or at risk to have dyslipidemia.

Key words:

Methyl dopa, hypertension, dyslipidemia.

Introduction:

Atherosclerotic cardiovascular diseases are the leading cause of death in the civilized population. Obesity, smoking, diabetes, high blood pressure and abnormal lipid levels are the recognized risk factors. Of these factors high lipid levels show the highest correlation with the development of coronary heart diseases [(1)] .

Dyslipidemia is characterized by raised serum triglyceride and low density lipoprotein cholesterol and lowered high density lipoprotein cholesterol [(2)]. Hypertension is supposed to accelerate atherosclerosis by increasing infiltration pressure across the intimal surface and thus carrying more lipoprotein to arterial wall [(3)]. Evidence linking hypertension and hyper cholesterolemia is strong and has fueled research into possible adverse effects of some antihypertensive agents on serum lipid profile [(4)].

Methyl dopa is one of the most early and most often drug used in treatment of hypertension. It works by relaxing the blood vessels so that blood can flow more easily through the body [(5)]. This effect is attributed to the inhibition of aromatic amino acid decarboxylase, an alternative false neurotransmitter hypothesis for the mechanism of antihypertensive action was proposed [(6)]. This study was designed to asses the effect of methyl dopa on serum lipid profile in rats fed atherogenic diet.

Materials and Methods:

Twenty male Sprague– Dawley rats were enrolled in the experiment. They were housed five per cage in a room with temperature maintained at 22 C° ± 2 C° and with a 12 hour light/ 12 hour dark cycle, all the animal had free access to food and water throughout the study and they left for one week for acclimatization. All the animal given atherogenic diet (4% cholesterol powder added to the standard rat chow pellet) [(7)] for twelve weeks and the ravage daily food intake was (20 gm/ rat).

After twelve weeks, the animals were randomly allocated into two groups:

First Group: received (33 mg/ kg/ day) [8] P. O methyl dopa (Aldomet 250 mg tablet SDI) dissolved in 2 ml distilled water twice daily through nasogastric tube.

The Second Group: received (2 ml) distilled water twice daily through nasogastric tube and serve as control group.

The treatment continued daily for another twelve weeks and the rats also continued on atherogenic diet. The serum lipid profile namely: triglyceride total cholesterol, LDL-cholesterol, HDL-cholesterol and HDL-cholesterol /total cholesterol ratio were estimated before and after treatment with drugs.

Statistical Analysis:

Results were expressed as mean ± standard deviation (SD), one way ANOVA was used for group comparisons. Statistical significance was accepted as $P<0.05$.

Results:

- ***Effect on Triglyceride:*** The effect of methyl dopa on serum triglyceride level is similar to that of control $P>0.05$.

	Before Treatment	***After Treatment***
Control	4 ± 140	**215 ± 4**
Methyl Dopa	**139 ± 3**	**212 ± 4**

Values expressed as mean ± SD

Table 1: Effect of methyl dopa vs control on triglyceride serum level (mg/ dl)

- ***Effect on Total Cholesterol:*** The of methyl dopa on total cholesterol serum level is similar to that at control group P > 0.05.

	Before Treatment	***After Treatment***
Control	124 ± 3	**194 ± 2**
Methyl Dopa	**126 ± 3**	**193 ± 3**

Values expressed as mean ± SD

Table 2: Effect of methyl dopa vs control on total cholesterol serum level (mg/ dl)

- ***Effect on LDL-cholesterol:*** Methyl dopa is found to cause a decrease in LDL-cholesterol serum level in comparison to control group P < 0.05.

	Before Treatment	***After Treatment***
Control	68 ± 2	**110 ± 2**
Methyl Dopa	**70 ± 2**	**100 ± 1**

Values expressed as mean ± SD

Table 3: Effect of methyl dopa vs control on LDL-cholesterol serum level (mg/ dl)

- ***Effect on HDL-cholesterol:*** Methyl dopa is found to cause an increase in HDL-cholesterol serum level in comparison to control group P < 0.05.

	Before Treatment	***After Treatment***
Control	28 ± 1	**45 ± 2**
Methyl Dopa	**29 ± 1**	**35 ± 2**

Values expressed as mean ± SD

Table 4: Effect of methyl dopa vs control on HDL- cholesterol serum level (mg/ dl)

- ***Effect on HDL-cholesterol / total cholesterol ratio:*** Methyl dopa is found to cause an increase in the ratio of HDL-cholesterol / total cholesterol in comparison to control group P <0.05.

	Before Treatment	*After Treatment*
Control	22.4 ± 0.5	**23 ± 0.5**
Methyl Dopa	**22.9 ± 0.6**	**26.3 ± 0.7**

Values expressed as mean ± SD

Table 5: Effect of methyl dopa vs control on HDL- cholesterol / total cholesterol ratio

Discussion:

Several antihypertensive agents have been found to influence serum lipid profile and a reasonable approach for managing the lipid problems often associated with hypertension is to select drugs that alone or in combination do not adversely affect lipid profile [(9)].

Ideally an antihypertensive agent should have a neutral effect or preferably, produce a favorable shift in the serum lipid profile, which is associated with a decrease in coronary hear disease risk [(10)]. The effectiveness of methyl dopa and many years of experience with the drug and with control of blood pressure in large number of patients constitute it's major advantages and justify it's continuous use in spite it's side effects. In this study, methyl dopa was found to cause significant increase in the HDL- cholesterol which is the protective portion of cholesterol and cause significant decrease in LDL- cholesterol which is the atherogenic protion of cholesterol.

These effects carry a significant importance in hypertensive patients who have dyslipidemic state as the drug in this condition does not aggravate the dyslipidemia as other classes of antihypertensive drugs did (like beta blockers) [(11)]. This beneficial effect is hidden for a long time by a long list of side effects which

limit methyl dopa use widely but this new connection between methyl dopa and effect on serum lipid level can justify it's use in hypertension associated with dyslipidemia a long with other list of antihypertensive drugs have such effects like doxazosin [12], valsartan[13] and amlodipine[14].

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