The potential effects of short course of Statins on some platelets parameters in rats

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الخلاصة

خلفية البحث : الصفيحات الدموية تلعب دورا مهما في عملية تنظيم النزف وخصوصا في حالة نشوء تصلب الأوعية الدموية عندما تترسب البروتينات الدهنية الصغيرة الوزن على جدران الأوعية الدموية وتكوين السدادة والتي تصاحبها كثير من العمليات الالتهابية والتي واحدة منها هو زيادة فعالية الصفائح الدموية كنتيجة لالتصاق هذه الصفائح على جدار الأوعية نتيجة إفراز النواقل التي تقوم بتحفيز تجمع الصفيحات الدموية.هدف البحث : الستاتينات أدوية تلعب دور مهم في علاج زيادة الدهون ولها أكثر من فائدة علاجية منها أنها مضادة للالتهابات وتثبيت السدادة وكذلك منع زيادة في فعالية الصفيحات خلال تكوين تصلب الأوعية الدموية .طريقة البحث: لتقييم فعالية الصفائح الدموية هنالك عدد من المقاييس البسيطة والتي من الممكن عملها مثل تعداد الصفيحات ، التوزيع العرضي للصفيحات ،ومعدل حجم الصفيحات.في الوقت الحاضر هذه المقاييس تعتبر علامة عن حالة فعالية الصفيحات . تم انجاز البحث باستخدام واحد وعشرون جرذ ذكر وقد قسموا إلى ثلاثة مجاميع ، كل مجموعة تضم سبعة جرذان.المجموعة الأولى اعتبرت مجموعة سيطرة ، المجموعة الثانية أعطت دواء السمفاستاتين ، المجموعة الثالثة أعطت دواء الاتورفاستاتين. استمرت فترة العلاج لخمسة عشر يوما بعدها تم إجراء تحليل كل مقاييس الصفيحات الدموية ومن ثم قارنا النتائج التي حصلنا عليها بين مجموعتي السمفاستاتين الاتورفاستاتين مع مجموعة السيطرة.النتائج : لا يوجد فرق معنوي بين مجموعة السيطرة مع كل من مجموعة السيمفستاتين الاتورفاستاتين من حيث التأثير على تعداد الصفيحات ، معدل حجم الصفيحات أو التوزيع العرضي للصفيحات.

الاستنتاج : لم يسبب كلا من السيمفستاتين الاتورفاستاتين أي تأثير على تعداد الصفيحات ، معدل حجم الصفيحات أو التوزيع العرضي للصفيحات.

Abstract

Background : Platelets play an important role in the process of homeostasis, specifically in atherosclerosis formation when low molecular weight lipoprotein deposit in the wall of blood vessels and plaques formation ,this associated with many inflammatory response one of them is Platelet activation subsequent to the adhesion of platelets to the vascular wall results in the release of mediators that promote platelet aggregation. Aim : Statins as most drugs used for treatment hyperlipidemia have multiple effects including anti inflammatory effects , stabilization of plugs and inhibits platelets activation during atherosclerosis of the blood vessels.Materials and Methods : To evaluate the platelets activation there are many simple parameters can be made like platelets count , platelets distribution width, and mean platelets volume. Platelets parameter considered as marker about platelets activation state. Twenty one males rats were enrolled in our research , divided into three group , each group contain seven rats .First group considered as control group , second group considered was given simvastatin , third group was given atorvastatin. The drug dosing continued for 15 days after that blood was withdrawn to measure platelets count , platelets distribution width, and mean platelets volume. Results : There was no significant differences among control and treatment groups in regard to their effects on platelets count , platelets distribution width, and mean platelets volume ($P > 0.05$). Conclusion : Neither simvastatin nor atorvastatin affect platelets count , platelets distribution width, and mean platelets volume.

Key words: Atorvastatin , Simvastatin , Platelets count , Mean platelet volume , Platelet distribution width.

Introduction

Platelets, or thrombocytes , are 2–3 μm in diameter,[which are derived from fragmentation of precursor megakaryocyte ,the average lifespan of a platelet is normally just 5 to 9 days(1). Platelets are small a nucleated blood element of critical important role in aggregation to form blood clots in response to endothelial injury(2).so that platelets play a key and beneficial role for primary homeostasis on the disruption of the integrity of vessel wall , in which platelets adhere to exposed sub endothelial collagen by interaction of Von Willebrand factor and glycoprotein Ib –IX-V complex , a major platelets membrane receptor responsible for adhesion (3). Platelets represent an important linkage between inflammation , thrombosis and atherogenesis(4).In fact the atherosclerosis is an inflammatory processes in the endothelial cells of vessel wall in response to deposit low density lipoprotein molecules(5) .Initial damage to the endothelium results in inflammatory response when monocytes enter wall from blood stream with platelets adhering to the area (6).The treatment with statins drugs or called 3-hydroxy-3- methyl glutaryl –CO A reeducates inhibitor have been proven to be highly effective in the management of hyperlipidemia and the prevention of atherosclerotic vascular disease(7) . Recent studies demonstrates that statins drugs have inhibitory activity on platelets , this effect in part by lower blood levels of inflammatory mediators such as IL-6, IL- 8 , and on the other hand demonstrates that statins activate platelets receptors peroxisome proliferator-activated receptors (PPARs),PPAR γ and PPAR α, and that the damping activity of statins appears to be PPAR- dependent for attenuate platelets activation(8). Recent literature indicates that PPARs are present in platelets and their activation inhibit platelets function by non genomic mechanism(9). Satins exert many pleotropic effects on the vascular wall these include beneficial effects on endothelial function and blood flow , decreasing low density lipoprotein ,enhance stability of atherosclerotic plagues and inhibit platelets aggregation(10). Many platelet parameters can test the platelets activation like, mean platelets volume(MPV) and Platelets distribution width (PDW) are simple platelet indices, which increase during platelet activation. PDW is a more specific marker of platelet activation, since it does not increase during simple platelet swelling(11).

Material and Method

A total of 21 adult males albino rats weighing 180-200 grams , were available by animal house at college of veterinary – Kufa university. They were housed at room temperature at 25C and allowed to access to food and water for one week of an acclimatization after that they divided randomly into three groups ,each groups contains seven rats. First group was without treatment and considered as control group. Second group was treated with simvastatin orally, single daily dose (20mg /kg) , and considered as simvastatin group. Third group contains seven rats treated with atorvastatin , orally single daily dose (20mg /kg) for fifteen days, and considered as atorvastatin group. The treatment was continued for 15 days. A drop of blood was drawn for measurement of platelets count (PC) , platelets distribution width (PDW) , and mean platelets volume (MPV) by using hematology analyzer count 60. From Genex company USA , with kits which is supplied by Cyan company Belgium. The data were expressed as mean +/- standard deviation , multiple

comparisons were done using one ANOVA. The data were analyzed by using SPSS version 18 computer program.

Result

There was no significant difference among treatment groups in regard to their effects on platelets count , platelets distribution width and man platelets volume in comparison with control group(P >0.05) as showed in table(1).

Table (1) : Differences among treatment groups in regard to their effects on platelets count , platelets distribution width and mean platelets volume in comparison with control group.

ANOVA		Sum of Squares	df	Mean Square	F	Sig.
Platelets count	Between Groups	263040.179	2	131520.089	.745	.497
	Within Groups	1942386.750	11	176580.614		
	Total	2205426.929	13			
Mean platelet volume	Between Groups	1.373	2	.686	.952	.416
	Within Groups	7.927	11	.721		
	Total	9.300	13			
Platelets Distribution width	Between Groups	2.658	2	1.329	4.137	.046
	Within Groups	3.534	11	.321		
	Total	6.192	13			

Data expressed as mean +/_ SD.

Discussion

MPV and PDW are easily measured platelet indices, which increase during platelet activation. In order to obtain a larger surface platelets change in shape during activation. Their shape changes from discoid to spherical. Pseudopodia are formed as well(12). Our results not agree with the international researches , and this may due to short course treatment or sub- optimal animal dose of the used statins during this research. In addition to what was mentioned above , lack of induced an atherogenesis state in experimental animals, and so there in no inflammatory process induced in the study animals and so there is no platelets activation .PuccettiL ,et al (2002) wrote that the effect of statin is time – dependent on platelets function in hypercholesterolemia(13).

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