

Beneficial effect of colchicine in an animal model of atherosclerosis

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Background: Atherosclerosis is a chronic inflammatory disease and colchicine demonstrated clinical benefits in the treatment of stable coronary artery disease.

Purpose: Our aim was to assess the anti-inflammatory effects of colchicine on atherosclerotic vascular disease.

Methods: Atherosclerosis was induced in the abdominal aorta of 20 rabbits with high-cholesterol diet and balloon endothelial denudation. The study protocol lasted 36 weeks. After 18 weeks rabbits were randomized to receive either colchicine or placebo. Two animals died in each group. At randomization and at the end of the study, all animals underwent MRI and positron 18F-FDG PET/CT. In this post-hoc subgroup analyses, animals of each group in the first quartile of cholesterol levels were excluded. For MRI plaque volume values were expressed as Normalized Wall Index (NWI) and

for 18F-FDG PET/CT values were expressed as mean maximum standard uptake (meanSUVmax). Statistical comparisons were made by using the Mann-Whitney U test for unpaired data and Wilcoxon signed-rank test for paired data.

Results: Results are summarized in Table 1. Animals with higher levels of cholesterol (6 per group) showed significant differences in favor to colchicine group, both as NWI at the end of the protocol 0.47 (IQR 0.05) in the colchicine group versus 0.52 (IQR 0.03) in the placebo; $p=0.01$ and as relative increase in meanSUVmax $[-4.0\%$ (IQR 30.1) in the colchicine group versus 35.1 (IQR 59.0) in the placebo; $p 0.041$] (Figure 1).

Conclusions: Colchicine may stabilize atherosclerotic plaque by reducing inflammatory activity and plaque burden.

Table 1

	Placebo (6 rabbits) Median (IQR)	Colchicine (6 rabbits) Median (IQR)	Colchicine vs Placebo Difference of the medians (95% CI)	p
Wall volume in MR Imaging				
Pre NWI	0.43 (0.06)	0.42 (0.05)	-0.03 (-0.07 to 0.01)	0.13
Post NWI	0.52 (0.03)	0.47 (0.05)	-0.05 (-0.13 to 0.02)	0.01
Relative increase, %	16.7 (10.1)	9.0 (10.9)	-7.0 (-16.1 to 1.6)	0.07
¹⁸ F-FDG uptake in PET/CT Imaging				
Pre mean SUVmax	0.69 (0.26)	0.85 (0.40)	0.19 (0.09 to 0.47)	0.09
Post mean SUVmax	0.88 (0.22)	0.72 (0.14)	-0.13 (-0.22 to 0.06)	0.24
Relative increase, %	35.1 (59.0)	-4.0 (30.1)	-39.8 (-87.2 to -1.4)	0.04

IQR, Interquartile Range; NWI, Normalized Wall Index; meanSUVmax, mean maximum standard uptake; Pre, before randomization; Post, at end of the protocol; 95% CI, 95% Confidence Interval.

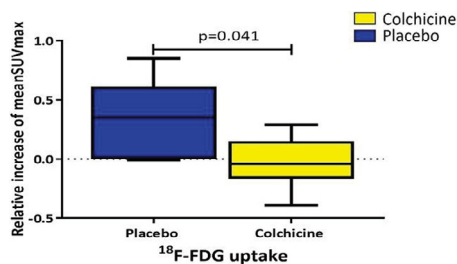


Figure 1