## No effect of statins or ezetimibe on fat metabolism during aerobic exercise in dyslipidaemic individuals

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Hypercholesterolaemic individuals are encouraged by health professionals to supplement lipid-lowering medication with regular exercise. However, studies in healthy normolipidaemic subjects have found that some lipid-lowering agents inhibit fat metabolism during prolonged aerobic exercise, which may lead to an increased reliance on carbohydrate stores and earlier fatigue (Eagles *et al.*, 1996; Head *et al.*, 1993). The current study investigated the effect of statins or ezetimibe on fat metabolism in dyslipidaemic individuals.

**Method.** All subjects received written approval from their doctor to participate in the study. A total of 21 subjects, consisting of 16 males and females taking a statin, and 5 females taking ezetimibe, were recruited. Subjects made a total of three visits to the laboratory. All subjects ceased lipid-lowering medication for 3 weeks prior to visit 1, at which they performed a submaximal exercise test on a treadmill to predict maximal oxygen uptake ($VO_2$max). Visit 2 continued in the absence of lipid-lowering medication whereas visit 3 occurred after subjects had resumed medication for a minimum of 3 weeks. The protocol for visits 2 and 3 were identical whereby subjects came to the laboratory after an overnight fast, a forearm vein was cannulated, and subjects were given a low fat 1 MJ carbohydrate meal. After 75 minutes, subjects walked on the treadmill at an intensity of 50% of their calculated $VO_2$max, corresponding to a 'brisk walk', for a period of 45 min. Blood (6 ml) was collected into ethylenediaminetetraacetic acid (EDTA) vacutainers immediately before the meal, immediately before exercise, and at time 15, 30, and 45 min of exercise. $O_2$ uptake and $CO_2$ expiration were measured using the ParvoMedic metabolic cart to determine the proportion of carbohydrate and fat metabolism. Data are reported as mean ± SEM and were analysed with SPSS using the paired sample t-test and repeated measures ANOVA.

**Results.** Subjects were moderately healthy with the following profile: age: 57 ± 2 yr, SBP: 124 ± 2 mmHg, DBP: 80 ± 2 mmHg, body mass index (kg/m$^2$): 28 ± 1, body fat: 30 ± 2% and $VO_2$max 32 ± 2 ml.kg.min$^{-1}$. Lipid-lowering medication resulted in a significant reduction in total cholesterol (5.7 ± 0.3 versus 4.1 ± 0.1 mmol/l (without and with statin)), (6 ± 0.2 versus 5.6 ± 0.2 mmol/l (without and with ezetimibe); and low density lipoprotein (LDL) (3.77 ± 0.2 versus 2.3 ± 0.1 mmol/l (without and with statin)); 4 ± 0.14 versus 3.7 ± 0.2 (without and with ezetimibe) ($p < 0.05$). Whilst there was a significant overall increase in the proportion of fat metabolism and decrease in the proportion of carbohydrate (CHO) metabolism and respiratory exchange ratio (RER) during the exercise session, % fat and CHO contribution and RER at time 15, 30, and 45 min did not differ in the presence compared to in the absence of either drug tested (see Table).

| | time | + statin | - statin | *p* | + ezetimibe | - ezetimibe | *p* |
|---|---|---|---|---|---|---|---|
| % FAT | 15 min | 19 ± 2 | 19 ± 3 | .950 | 22 ± 4 | 23 ± 5 | .396 |
| | 30 min | 31 ± 2 | 28 ± 3 | .315 | 31 ± 5 | 29 ± 5 | .425 |
| | 45 min | 38 ± 2 | 37 ± 3 | .850 | 33 ± 5 | 34 ± 5 | .496 |
| % CHO | 15 min | 82 ± 3 | 82 ± 3 | .982 | 78 ± 4 | 77 ± 5 | .418 |
| | 30 min | 70 ± 2 | 74 ± 3 | .182 | 70 ± 5 | 72 ± 5 | .411 |
| | 45 min | 62 ± 2 | 63 ± 3 | .835 | 67 ± 5 | 66 ± 5 | .489 |
| RER | 15 min | .93 ± .01 | .93 ± .01 | 1.000 | .92 ± .01 | .92 ± .01 | .587 |
| | 30 min | .90 ± .01 | .91 ± .01 | .180 | .90 ± .01 | .91 ± .01 | .513 |
| | 45 min | .88 ± .01 | .88 ± .01 | .751 | .87 ± .01 | .89 ± .01 | .606 |

**Conclusion.** These data indicate that neither statins nor ezetimibe decrease fat availability during exercise and do not appear to place increased demands on carbohydrate to reduce exercise tolerance.

Eagles CJ, Kendall MJ, Maxwell S. (1996) *British Journal of Clinical Pharmacology* **41:** 381-7.
Head A, Jakeman PM, Kendall MJ, Cramb R, Maxwell S. (1993) *Postgraduate Medical Journal* **69:** 197-203.