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Olive oil normalizes the altered distribution of membrane cholesterol and Na^+-Li^+ countertransport activity in erythrocyte of hypertensive patients

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The effects of olive oil (OO)- and high-oleic sunflower oil (HOSO)-enriched diets on erythrocyte membrane cholesterol distribution (by means of cholesterol oxidation after continuous cholesterol oxidase treatment) and Na^+-Li^+ countertransport activity in control subjects and patients with untreated essential hypertension (with or without concomitant hypercholesterolemia) have been examined. The participants were 12 normotensive and sixteen hypertensive women who consumed in randomized order the two monosaturated fatty acid (MUFA) diets over 4-week periods separated by a 4-week washout period. The half-times for cholesterol oxidation were significantly higher in hypertensive women, ranging from an increase of 38 to 57% in the normo- (20.6 ± 2.8 min; $P < 0.001$) and hyper- (23.4 ± 4.2 min; $P < 0.001$) cholesterolemic groups. There was a general decrease by 75% in the half-time for cholesterol oxidation after HOSO diet. Interestingly, the oxidation rates were almost normalized after OO diet. The activity of Na^+-Li^+ countertransport was found to be significantly higher in hypertensive women, ranging the increase from 22 to 57% in the normo- (0.314 ± 0.043 mmol × [h × liter cell]$^{-1}$; $P < 0.01$) and hyper- (0.405 ± 0.086 mmol × [h × liter cell]$^{-1}$; $P < 0.01$) cholesterolemic groups. This transport system was further activated after HOSO diet, while almost restored after OO diet. These findings suggest that dietary OO, but not HOSO, is helpful for normalizing the impaired distribution of membrane cholesterol and reducing elevated activity of Na^+-Li^+ countertransport in erythrocyte of hypertensive patients. This action of OO also indicates that alterations in membrane cholesterol distribution may be relevants for the pathogenesis of hypertension. The effects, however, cannot be exclusively attributed to the content of MUFAs (mainly oleic acid) in the diet, as HOSO was unable to induce favorable changes. (J. Nutr. Biochem. 8: 205–210, 1997) © *Elsevier Science Inc. 1997*

Keywords: membrane cholesterol oxidation; membrane cholesterol distribution; cation transport; monounsaturated fatty acids; olive oil; high-oleic sunflower oil; dietary fat; hypertension

Introduction

The role for dietary monounsaturated fatty acids (MUFAs) in the reduction of blood pressure and plasma cholesterol levels is still controversial.[1–6] The major discrepancies are reflected in the continuous shift to different proportions of calories to be provided by MUFAs, while keeping the total fat intake at 30% energy.

It is well accepted that isocaloric substitution of saturated fatty acids (SFAs) for oleic acid leads to a low incidence of coronary heart disease (CHD),[7] especially when hypertension (HT) is coexistent.[1] This assertion is largely based on plasma lipid profile as a powerful risk indicator for premature CHD.[8] However, an increase of plasma total cholesterol (TC) and low-density lipoprotein (LDL) cholesterol, and/or a decrease of high-density lipoprotein (HDL) cholesterol, are important, but not unique prerequisites for vascular disease. Indeed, multiple structural and functional

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alterations of cell membrane are also associated to CHD risk, which include changes of receptor properties, signal transduction, ion transport, calcium handling, and membrane fluidity and permeability.[9,10]

In support of this, it has been recently indicated that membrane cholesterol distribution is modified in erythrocytes of normocholesterolemic and hypercholesterolemic hypertensive patients where the inner monolayer is enriched in free cholesterol with regard to erythrocyte lipid bilayer of healthy subjects.[11] There is also evidence that transbilayer distribution of membrane cholesterol is strongly correlated with Na^+-Li^+ countertransport,[12] which has been suggested as a marker of essential HT.[13] Moreover, normocholesterolemic and particularly hypercholesterolemic hypertensive patients have also shown a slower rate of erythrocyte cholesterol transbilayer movement than healthy subjects,[14] suggesting that the steady-state distribution of membrane cholesterol and cell cholesterol exchange could be intimately linked to the risk severity of CHD.

The benefits of MUFA-enriched diets on plasma lipids and lipoprotein profile have been extensively studied.[6] These favorable effects are attributed to oleic acid, the major fatty acid found in olive oil (OO) and other vegetable oils rich in MUFAs. Indeed, we recently found that intake of OO may further reduce diastolic and systolic blood pressures in healthy subjects and hypertensive patients,[15] raising the question whether changes in erythrocyte membrane by dietary manipulation are involved in the attenuation of blood pressure. Accordingly, recent studies shown that transmembrane fluxes of Na^+ and K^+, including Na^+-Li^+ countertransport, are particularly sensitive to the content of erythrocyte membrane lipids in healthy subjects.[16] However, there are virtually no dietary MUFAs data available on membrane cholesterol distribution, and to our knowledge, there is little data available regarding distribution of membrane cholesterol in patients with essential HT. Although the traditional source of dietary MUFAs has been OO, other sources are now becoming available, such as the oleic-rich variant of sunflower oil (HOSO).[17]

Therefore, the present study was undertaken to evaluate the effects of OO and HOSO, as natural sources of MUFAs, on erythrocyte membrane cholesterol distribution of women with untreated essential HT and (normo- or) hypercholesterolemia as major risk factors for CHD. The erythrocyte Na^+-Li^+ countertransport activity was also examined.

Patients and methods

Study design

The study consisted of two 4-week dietary intervention periods separated by a 4-week washout period during which participants reverted to their usual diet (baseline). In randomized order they started with one of the two different diets: containing OO or HOSO. Baseline diet was recorded using daily 24-hr recall and food frequency questionnaires. Participants were recruited from a closed religious communities in Seville (Spain), because of their regular lifestyle and dietary habits. They were free-living and given free food, but no payment. All dishes were prepared in the same kitchen and planned as a 1-week menu for each participant, who was told what food items should be eaten for breakfast, lunch, dinner, and in-between meals. No other food items except water, mineral water, coffee, and tea were allowed to be consumed during the study periods. All participants were asked to record in a diary any event that could affect the outcomes, and none of them developed physical problems or overreached in dietary regimens. On admission and during the last days of the treatment periods assessment of biochemical and clinical indices were performed. The washout period lasted 4-weeks, and was enough to ensure the re-establishment of initial conditions. The design of the present study was approved by the Institutional Committee on Investigation in Humans (Hospital Universitario Virgen del Rocío. Seville) and all participants gave informed consent.

Table 1 Characteristics of healthy subjects (Control), and normocholesterolemic (HT/NChol) and hypercholesterolemic (HT/HChol) hypertensive patients enrolled for this study

Parameter	Control (n = 12)	HT/NChol (n = 8)	HT/HChol (n = 8)
Age (y)	54.2 ± 3.7	55.3 ± 4.0	56.1 ± 3.3
Body mass index (kg/m^2)	25.7 ± 3.4	25.7 ± 3.8	24.5 ± 2.5
Blood pressure:			
Diastolic (mm Hg)	72.4 ± 5.3	94.9 ± 5.0***	92.0 ± 3.1***
Systolic (mm Hg)	122.3 ± 8.1	161.2 ± 14.4***	163.9 ± 9.6***
Plasma lipid levels:			
Cholesterol (mmol/L)	4.7 ± 0.6	5.1 ± 0.3	6.5 ± 0.3***
LDL (mmol/L)	3.3 ± 0.4	3.3 ± 0.1	4.7 ± 0.3***
HDL (mmol/L)	1.2 ± 0.2	1.3 ± 0.3	1.0 ± 0.2
Triacylglycerols (mmol/L)	0.9 ± 0.4	0.9 ± 0.3	1.9 ± 0.7**

Values are expressed as means ± SD.
**Significantly different ($P < 0.01$) from control group.
***Significantly different ($P < 0.001$) from control group.

Subjects

Sixteen hypertensive (8 with normocholesterolemia and 8 with hypercholesterolemia) and 12 age-matched control female volunteers were enrolled for this study (*Table 1*). Criteria for inclusion were that the participants should be reliable and have a regular meal pattern. The criterion for hypertension was a diastolic blood pressure (DBP) of ≥90 mm Hg recorded on at least three different occasions after resting for 10 min in the supine position. The criterion for hypercholesterolemia was a plasma total cholesterol (TC) concentration of ≥6.22 mmol/L and LDL of ≥4.14 mmol/L after a 12-hr fast. None of the patients had received any antihypertensive or antihypercholesterolemic treatment. They underwent a clinical and laboratory examination to rule out any secondary cause of hypertension and none of them had diabetes mellitus or hypothyroidism. No history of alcohol or smoking abuse was presented. The control group maintained a DBP of <90 mm Hg, TC of <5.18 mmol/L, LDL of <3.37 mmol/L, and was in excellent health as defined by laboratory tests.

Diets

Diets were based on ordinary foods and planned as 1-week menus. The only difference between the diets lay in the edible fats, which were in the form of oils (Virgin olive oil: *Olea europaea*; High-oleic sunflower oil: *Helianthus annuus*) for cooking and for salads and occasionally spread on bread slices. Fatty acid content of two diets (30% fat, 6% SFAs, 21% MUFAs, and 3% PUFAs) was characterized by a lower amount of SFAs (mainly palmitic and stearic acid) and higher amount of oleic acid (12 to 13% of total energy) with regard to baseline (30% fat, 11% SFAs, 16%

MUFAs, and 3% PUFAs). HOSO contained oleic acid (80.2%), linoleic acid (9.4%), stearic acid (4.7%), palmitic acid (4.3%), linolenic acid (0.06%), and others; whereas OO contained oleic acid (79.2%), palmitic acid (11.8%), linoleic acid (3.5%), stearic acid (2.8%), linolenic acid (0.6%), and others. The energy content and the amounts of protein and carbohydrate were the same in the diets. Dietary instructions were given by a dietitian before entry into the study. Three duplicate food portions corresponding to each weekday were collected and homogenized to be analyzed for their fat content and other nutrients. The energy consumption of participants was ~8.6 MJ (~2056 kcal). Two investigators were present twice a week in the kitchen during the preparation of the meals and remained blinded along with the subjects to changes in erythrocyte membrane cholesterol distribution and Na^+-Li^+ countertransport activity. The other investigators conducted most laboratory analyses and were blinded to the dietary assignments. Sodium intake was similar on the baseline and MUFA-enriched diets.

Preparation of erythrocytes

For membrane cholesterol distribution studies, fasting blood samples were collected in 0.38% citrate. Erythrocytes were washed three times in saline buffer (145 mmol/L NaCl, 5 mmol/L KCl, 5 mmol/L sodium phosphate, pH 7.4) and three times in assay buffer (310 mmol/L sucrose, 1 mmol/L $MgSO_4$, 5 mmol/L sodium phosphate, pH 7.4) at 4°C, and used immediately.

For sodium transport studies, fasting blood samples were collected in heparinized tubes. Erythrocytes were washed four times in a solution containing 115 mmol/L $MgCl_2$ and 10 mmol/L MOPS-Tris (pH 7.4) at 4°C, and used immediately.

Cholesterol oxidation kinetics

Kinetics of cholesterol oxidation in the erythrocyte membrane were carried out according to the cholesterol oxidase method.[11,18] Briefly, cells were suspended in assay buffer to a 3% hematocrit (*c.a.* 50 μg of erythrocyte cholesterol/mL cell suspension), preincubated at 37°C for 15 seconds, and then treated continuously (from 0 to 30 min) with cholesterol oxidase from *Brevibacterium sp.* (6 U/mL). Aliquots of the reaction mixture were extracted with chloroform-methanol (2:1, v/v). The organic phase was used for sterol mass analysis. The extracts were dried under nitrogen and used immediately. Mass determinations of cholesterol and cholestenone were made by gas chromatography using a Hewlett-Packard 5790A gas chromatograph equipped with a Hewlett-Packard 3390a Integrator (Hewlett-Packard Co., Avondale, Pennsylvania USA). The samples were redissolved in cold isopropylic ether, and injected into a Supelcoport 80/100 column (3% OV-17, Teknokroma 14280C), with nitrogen carrier gas (20 cm/min). The column temperature was 325°C, whereas the injection and detector temperatures were 350° and 360°C, respectively. The mass of each sterol was found by comparison of peak areas to known quantities of an internal standard, stigmasta-4,22-dienone.

Na^+-Li^+ countertransport kinetics

Kinetics of Na^+-Li^+ countertransport were determined according to the lithium-loaded cells procedure.[13] Briefly, cells were suspended in loading buffer (75 mmol/L Li_2CO_3, 10 mmol/L glucose, 10 mmol/L MOPS-Tris, pH 7.4) to a 10% hematocrit and incubated at 37°C for 60 min. Cells were then washed four times in magnesium washing solution (115 mmol/L $MgCl_2$, 10 mmol/L MOPS-Tris, pH 7.4). Li^+ efflux was measured by incubating the erythrocytes in sodium-enriched medium (150 mmol/L NaCl, 10 mmol/L glucose, 0.1 mmol/L ouabain, 10 mmol/L MOPS-Tris, pH 7.4), or sodium-free medium (75 mmol/L $MgCl_2$, 85 mmol/L sucrose, 10 mmol/L glucose, 0.1 mmol/L ouabain, 10 mmol/L MOPS-Tris, pH 7.4) at 37°C for 60 min. At the end of this loading period, cells were centrifuged and the supernatants were used for analysis of lithium by means of atomic absorption spectrophotometry (Model 460, Perkin-Elmer, Norwalk, Connecticut USA). Kinetics of Na^+-Li^+ countertransport in the erythrocyte were estimated as the difference between Li^+ efflux into sodium-rich and sodium-free media. The lithium efflux was computed from the linear regression of lithium loss as a function of time.

Stability of erythrocytes

Hemolysis of cholesterol oxidase-treated erythrocytes was determined by hemoglobin absorbance at 540 nm and 410 nm (Soret's band) and measurement of adenylate kinase and lactate dehydrogenase activities, as more sensitive marker enzymes.[14,19]

Statistical analyses

Data were evaluated by using a two-tailed paired *t*-test. The significance of the differences between the groups were assessed by analysis of variance (ANOVA) with Tukey's post-hoc comparison of the means. Correlations were determined by linear regression analysis using Pearson's correlation coefficient. The analyses were done with the GraphPAD InStat (GraphPAD Software, San Diego, CA USA) and CoStat (CoHort Software, Berkeley, CA USA) statistical packages.

Results

Diets

All participants responded in a similar manner to HOSO and OO diets and completed the study according to schedule. Compliance with the diets was estimated to be ~90% from the evaluation of daily food questionnaires and by analysis of fatty acid composition of plasma cholesterol ester fraction in each participant.[20] There was a significant increase of oleic acid during MUFA-enriched diets, suggesting good adherence to the diets. Body weight was maintained after both MUFA dietary periods.

Oxidation of erythrocyte membrane cholesterol

Cholesterol oxidase was used as a tool for oxidizing cholesterol at the 3β-hydroxyl position to form Δ^4-cholestenone in erythrocyte exofacial membrane of healthy subjects and patients with untreated essential HT. Upon this enzyme treatment, leakage of hemoglobin was not apparent and less than 5% of cellular lysis was found either by means of adenylate kinase or lactate dehydrogenase activities at the end of the longest incubation time. Under these conditions of cell integrity, it is assumed that the reactive cholesterol represents a sampling of cholesterol in the outer monolayer of the plasma membrane.[18]

The half-times for membrane cholesterol oxidation were significantly higher in patients with untreated essential HT than in healthy subjects (*Table 2*), ranging the increase from 38% in the hypertensive normocholesterolemic (HT/NChol) group to 57% in the hypertensive hypercholesterolemic (HT/HChol) group. After HOSO diet, erythrocyte membrane cholesterol was rapidly oxidized by enzyme treatment in all groups, whereas OO diet normalized membrane cholesterol oxidation in erythrocytes of hypertensive pa-

Table 2 Half-times for erythrocyte membrane cholesterol oxidation during the periods on the high-oleic sunflower oil-rich (HOSO) and olive oil-rich (OO) diets

Participant group	Baseline	HOSO	OO
Control (n = 12)	14.9 ± 2.6	4.2 ± 0.8[a]	15.0 ± 3.1[b]
HT/NChol (n = 8)	20.6 ± 2.8*	4.9 ± 1.7[a]	14.8 ± 2.5[a,b]
HT/HChol (n = 8)	23.4 ± 4.2*	5.5 ± 0.6[a]	15.6 ± 3.9[a,b]

Values are expressed as means (in minutes) ± SD.
*Significantly different ($P < 0.001$) from control group.
[a]Significantly different ($P < 0.001$) from baseline diet.
[b]Significantly different ($P < 0.001$) from HOSO diet.
HT/NChol, hypertensive, and normocholesterolemic patients.
HT/HChol, hypertensive, and hypercholesterolemic patients.

Table 3 Activities of Na^+-Li^+ countertransport in erythrocytes during the periods on the high-oleic sunflower oil-rich (HOSO) and olive oil-rich (OO) diets

Participant group	Baseline	HOSO	OO
Control (n = 12)	0.258 ± 0.076	0.299 ± 0.104	0.248 ± 0.037
HT/NChol (n = 8)	0.314 ± 0.043*	0.355 ± 0.086[a]	0.266 ± 0.032[a,b]
HT/HChol (n = 8)	0.405 ± 0.086*	0.540 ± 0.098[a]	0.334 ± 0.061[a,b]

Values are expressed as means (mmol × [h × liter cell]$^{-1}$) ± SD.
*Significantly different ($P < 0.01$) from control group.
[a]Significantly different ($P < 0.05$) from baseline diet.
[b]Significantly different ($P < 0.01$) from HOSO diet.
HT/NChol, hypertensive, and normocholesterolemic patients.
HT/HChol, hypertensive, and hypercholesterolemic patients.

tients (with or without concomitant hypercholesterolemia) (*Figure 1*). Furthermore, the average change in the slope for oxidation profiles of erythrocyte membrane cholesterol indicated that the negative values associated to the hypertensive status were only nullified after OO diet, but not after HOSO diet (*Figure 2*).

Erythrocyte Na^+-Li^+ countertransport

Activities of Na^+-Li^+ countertransport, as an ouabain-insensitive pathway of sodium movement in human erythrocyte, were significantly higher in hypertensive patients (*Table 3*), ranging from an increase of 22% in the HT/NChol group to 57% in the HT/HChol group. The activity of this transport system was further increased in all groups after HOSO diet and almost restored in hypertensive patients after OO diet. Interestingly, the average change in the maximal rates of erythrocyte Na^+-Li^+ countertransport indicated that the negative values associated to the hypertensive status were only nullified after OO diet, but not after HOSO diet (*Figure 2*). This effect was less pronounced for hypercholesterolemic patients.

Discussion

This study was undertaken to investigate the effects of two MUFA-enriched diets on membrane cholesterol distribution and Na^+-Li^+ countertransport in erythrocytes of healthy subjects, and patients with untreated essential HT either with or without concomitant hypercholesterolemia. MUFA derived mainly from HOSO and OO. The diets were based on ordinary foods and contained similar amounts of total fats, proteins, carbohydrates, and other nutrients.

By using the continuous oxidation model with cholesterol oxidase as a probe,[18] our results show that the half-times for membrane cholesterol oxidation are increased in erythrocyte of hypertensive patients. This is consistent with an enhanced size of cholesterol-rich domains in the inner monolayer of the membrane.[11] Cholesterol oxidase [EC 1.1.3.6] attacks cholesterol to yield Δ^4-cholestenone and promotes the passive permeability of the plasma membrane to small solutes.[21] We recently indicated that cholesterol oxidase-treated human erythrocytes are able to retain their integrity by different means, including hemolysis and leakage of intracellular marker enzymes, even when cells were arrested.[19] Therefore, no adverse effect of cholesterol oxidase treatment on membrane cholesterol distribution would be expected.

The transbilayer asymmetry of cholesterol distribution was impaired after HOSO dietary period in erythrocytes either of healthy subjects or hypertensive patients, because there was a suddenly increase in the rate of cholesterol oxidation. However, the half-times for membrane cholesterol oxidation were almost normalized after dietary OO in erythrocyte of hypertensive patients. In addition, OO (but not HOSO) had a further beneficial effect in reducing the abnormally increased activity of erythrocyte Na^+-Li^+ countertransport, which is the major exchanger protein associated to the variations of erythrocyte membrane composition and plasma lipids in hypertensive and normotensive hyperlipidemic patients.[4,22–24] More recently, it has also been demonstrated that there exists an association between transmembrane cationic fluxes (*i.e.*, Na^+-Li^+ countertransport and Na^+-H^+ exchange systems) and lipid composition and fluidity of the membrane in erythrocyte and lymphocyte from normolipidemic subjects.[16,25] Therefore, a causal relationship seems to exist between membrane cholesterol distribution and the regulation of cation flux mediated by Na^+-Li^+ countertransport, a well-known marker of essen-

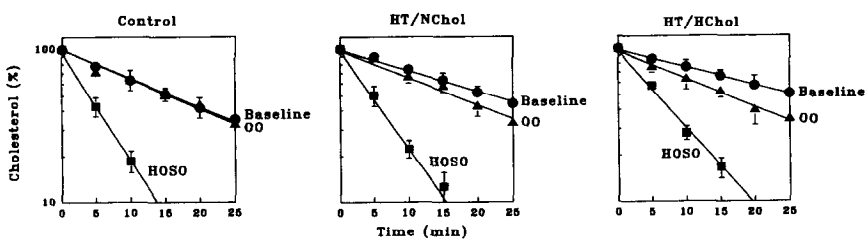

Figure 1 Oxidation of erythrocyte membrane cholesterol by cholesterol oxidase in control subjects, and (HT/NChol) normocholesterolemic and (HT/HChol) hypercholesterolemic hypertensive patients during the periods on the high-oleic sunflower oil-rich (HOSO) and olive oil-rich (OO) diets. The % oxidation was calculated by the ratio of the mass of cholestenone to total mass of free sterol (cholesterol and cholestenone). Values are expressed as means ± SD.

tial HT[13] and involved in the mode of operation of the Na^+-H^+ exchanger.[26]

Furthermore, our data indicate that changes in erythrocyte membrane cholesterol distribution may precede (or be primary) to changes in erythrocyte Na^+-Li^+ countertransport. We also observed a high activity of Na^+-Li^+ countertransport at low half-time for cholesterol oxidation (all groups after dietary HOSO), suggesting that the enrichment in cholesterol of the outer monolayer and/or an increase in the transbilayer movement of membrane cholesterol might play a major role in the regulation of erythrocyte sodium transport. Lipids in the cholesterol-rich domains will be more tightly packed and be less conductive to HDL interactions, protein translocation, and membrane assembly,[27,28] which reduces permeability and in turn compromises cell transmembrane cation flux. Indeed, erythrocytes with a highly cholesterol-rich environment (hypercholesterolemia, *i.e.*, HT/HChol group) elicited a more pronounced changes in the activity of Na^+-Li^+ countertransport. However, earlier studies demonstrated that the inner monolayer, rather than the outer monolayer of erythrocyte membrane from hypertensive patients is enriched in cholesterol,[11] in agreement with a decrease in the transbilayer movement of membrane cholesterol in erythrocytes of normo- or hypercholesterolemic patients with untreated essential HT.[14]

The mechanism(s) associated to the modulation of membrane cholesterol distribution and the significance of this asymmetry for nonreceptor mediated cholesterol transport are still unknown. It has been demonstrated that any alteration in transbilayer distribution of membrane cholesterol is not ascribable to modifications in the ratio of cholesterol to phospholipids.[29] However, when cells (mouse LM fibroblast and rat aortic smooth muscle cell lines) are cultured with unsaturated fatty acids in the medium, the transbilayer cholesterol gradient may be reversed[29,30] and the plasma membrane cholesterol efflux may be increased.[31] Our diets provided a similar content of oleic acid (18:1n-9), but HOSO had nearly 3 fold higher linoleic acid (18:2n-6), whereas OO had 10 fold higher linolenic acid (18:3n-3). It is difficult to establish the real efficiency of oleic and linoleic acids to change membrane choleterol distribution, because we recently found that both MUFA-enriched diets induced similar composition of these fatty acids in the erythrocyte membrane of hypertensive patients.[15] Interestingly, OO (but not HOSO) increased the content in long-chain n-3 PUFAs, by metabolic conversion of linolenic acid into eicosapentaenoic acid (20:5n-3) and docosahexaenoic acid (22:6n-3). These n-3 PUFAs can be selectively incorporated into phospholipid species (aminophospholipids) that are concentrated in the inner monolayer of human erythrocyte membrane.[32] Moreover, eicosapentaenoic and docosahexaenoic acids can adopt unique closely packed arrays in lipid bilayers, excluding cholesterol molecules from the inner to the outer monolayer of erythrocyte membrane.[31,33] It is therefore tentative to speculate that long-chain n-3 PUFAs yielded by dietary OO are responsible for changes in membrane cholesterol distribution, while this hypothesis remains to be corroborated.

In summary, we have demonstrated that dietary OO (but not HOSO) is helpful in restoring the impaired membrane cholesterol distribution and activity of Na^+-Li^+ countertransport in erythrocyte of patients with untreated essential HT. Differences between oils are not in the content of oleic acid, but in the content of other minor fatty acids, triacylglycerol composition, and non-fatty acid constituents[17,34] (our unpublished work). The present study is the first evidence for selective physiological effects on human erythrocyte membrane by two MUFA-enriched diets. In addition, it provides a basis for investigating the potential clinical utility of dietary OO.

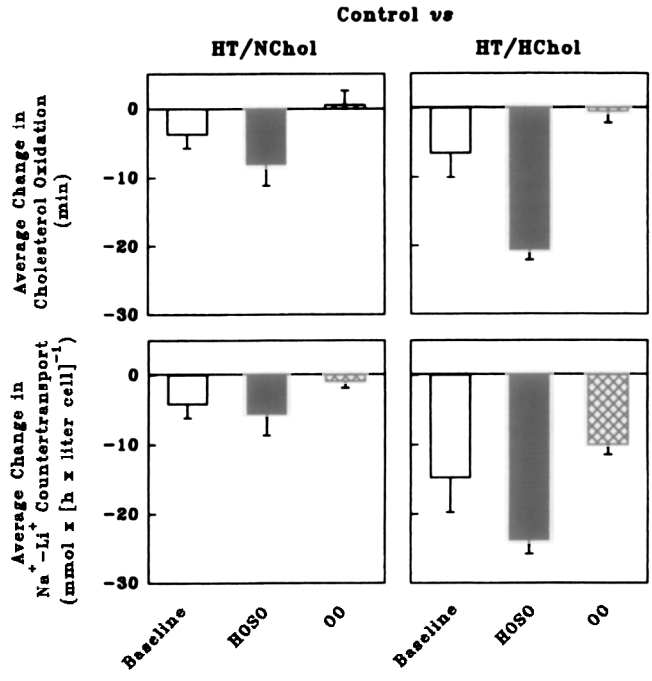

Figure 2 Average changes in the slope of membrane cholesterol oxidation and sodium transport kinetics in erythrocyte from baseline over the periods on the high-oleic sunflower oil-rich (HOSO) and olive oil-rich (OO) diets. Values are expressed as means ± SD. HT/NChol, hypertensive, and normocholesterolemic patients; HT/HChol, hypertensive, and hypercholesterolemic patients.

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