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Therapy with statins is effective in some patients with homozygous familial hypercholesterolemia

Patients with homozygous familial hypercholesterolemia have elevated markedly low-density lipoprotein (LDL) cholesterol levels that are refractory to commonly used doses of hypolipidemic drugs, including statin [1]. We read with great interest the recently published report by Raal et al. who showed that high doses of atorvastatin (80 mg/day) are effective in lowering LDL cholesterol by 28% in patients with homozygous FH through inhibition of VLDL (and possibly LDL) synthesis by the liver cell [2]. High doses of statins (simvaststin 80–160 mg/day or atorvastatin 80 mg/day) have been shown previously to be partially effective in lowering LDL cholesterol levels in these patients [3–5]. Interestingly, statins reduced LDL cholesterol, not only in patients with defective LDL receptors but also in patients with no functioning LDL receptors. However, there are no data concerning the effect of statins in patients with class V mutations of the LDL receptor. In class V mutation, the LDL receptor retains the ability to bind and internalise its ligand but fails to release it in the endosome and thus the receptor does not recycle to the cell surface [6]. It has been pointed out that individuals with such mutations have lower lipid levels and are more responsive to hypolipidemic drug therapy [6]. We have identified recently five patients who are homozygous for the G1775A mutation, which has been previously characterized as a class V mutation. These patients had relatively low serum total and LDL cholesterol levels (422 ± 80 and 354 ± 75 mg/dl, respectively) and they were treated with relatively high doses of statins (lovastatin 40 mg/day, pravastatin 40 mg/day, simvastatin 40 mg/day or fluvastatin 80 mg/day) before atorvastatin was available in our country. As shown in the Table 1, significant decreases in the LDL cholesterol levels (mean decrease by 23.5%) were achieved, comparable to those which were noticed after atorvastatin administration in previous studies [2,4,5]. When atorvastatin (80 mg/day) was administered in these patients, a more pronounced decrease in LDL cholesterol levels by 35% was observed. It is suggested that therapy with statins and especially with the most potent drugs of this class should be considered in patients with homozygous FH either as an adjuvant to apheresis or as monotherapy for those patients who do not have access to apheresis or other such treatment modalities.

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Table 1
The influence of statins on LDL cholesterol levels (mg/dl) in patients with homozygous familial hypercholesterolemia[a]

	First patient	Second patient	Third patient	Forth patient	Fifth patient
	LOVA 40[b]	FLUVA 80[b]	PRAVA 40[b]	SIMVA 40[b]	PRAVA 40[b]
Before treatment	472	435	420	420	390
After treatment	392	290	330	305	310
Change (%)	17.3	33	21.4	227.4	20.5

[a] LOVA, lovastatin; FLUVA, fluvastatin; PRAVA, pravastatin; SIMVA, simvastatin.
[b] The numbers represent the drugs' daily dose (mg).

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