STATINS RISE CYTOPLASMIC CALCIUM LEVEL $[\text{Ca}^{2+}]_i$ IN CULTURED ENDOTHELIAL CELLS

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Recently, we have shown that some HMG-CoA reductase inhibitors (statins) induce immediate pleiotropic effects in vascular endothelium both in vivo and in vitro, to mention only PGI$_2$-mediated thrombolysis in rats and NO-mediated endothelium-dependent vasodilation in guinea pig coronary circulation. Here we look whether immediate endothelial effect of statins is associated with mobilization of intracellular calcium ions $[\text{Ca}^{2+}]_i$ in cultured bovine aortic endothelial cells (BAEC). We analyzed the effects of various statins (atorvastatin, cerivastatin, simvastatin, lovastatin and pravastatin at concentration of 10–30 µM) on $[\text{Ca}^{2+}]_i$ in BAEC in comparison to responses induced by bradykinin (Bk) (10 nM), adenosine diphosphate (10µM), acetylcholine (100 nM), adrenaline (10 µM), serotonin (10 µM) or calcium ionophore A 23187 (0.1 µM) using FURA-2 according to fluorimetric method of Grynkiewicz et al. Basal $[\text{Ca}^{2+}]_i$ level in BAEC was between 60 and 100 nM. Bk was the most potent to induce $[\text{Ca}^{2+}]_i$ response. $\Delta[\text{Ca}^{2+}]_i$, induced by Bk was 331.9 ± 19.49 nM (n = 36). $\Delta[\text{Ca}^{2+}]_i$, induced by statins (30 µM), i.e. atorvastatin, cerivastatin, simvastatin, lovastatin and pravastatin were 66.4 ± 7.38% (n = 6), 54.8 ± 10.12% (n = 5), 58.8 ± 13.9% (n = 8), 27.7 ± 7.19% (n = 5) and 0% (n = 5) of the response induced by Bk (10 nM), respectively. In summary, all statins tested, except pravastatin, induce immediate increase in $[\text{Ca}^{2+}]_i$ in endothelium. This pleiotropic activity of statins in endothelium, mostly likely not related to the inhibition of HMG-CoA reductase, may represent an intracellular correlate for the immediate release of NO and PGI$_2$ by these drugs that was reported by us previously.

Key words: statins, pleiotropic effect, endothelium, intracellular calcium

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