Abstract

Statin drugs lower blood cholesterol by inhibiting hepatic 3-hydroxy-3-methylglutaryl-Coenzyme-A **reductase**. Statins are known to inhibit sterol production in the testis, but effect of statins on testosterone production has not been studied critically in vitro and clinical data are controversial. We measured 18-h testosterone production in vitro, using highly purified rat Leydig cells exposed to atorvastatin, mevastatin, or simvastatin and also determined if **statin**-induced inhibition of testosterone production could be bypassed with substrate distal to cholesterol. Statins had no effect on testosterone production during culture without LH. However, with 10ng/mL LH, testosterone production was ≥12-fold higher and **markedly** inhibited (-40%) by ≥0.3μM **statin**. Leydig cells provided sub-saturating pregnenolone or progesterone to bypass the site of **statin** action, maintained LH-stimulated testosterone production at or above amounts observed with LH stimulation and no **statin**. Pregnenolone resulted in greater testosterone production, but LH responsiveness was lost. With progesterone, LH responsiveness was maintained.