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EDITORIAL

Statin: Hope for a New Agent to Treat Osteoporosis

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Statin is a drug used to lower cholesterol level. It was first approved by the US FDA in 1987 and has since become a very popular drug to prevent cardiovascular diseases related to high cholesterol levels. In 1999, Mundy and his co-researchers discovered another interesting property of statin. After screening thousands of compounds, statin was the only compound found to promote bone morphogenetic protein (BMP) gene expressions and enhanced new bone formation *in vitro* and in animal model. This has caused excitement among the scientific community since very few agents were approved to treat osteoporosis, even though the number of osteoporosis cases was on the rise with the ageing society. This was rather a special discovery since there are not many drugs which have dual therapeutic effects, as seen in the case of statins i.e. lowering cholesterol and treating osteoporosis. Both these indications may seem to be unrelated, but further studies have revealed that adipose tissues (fat cells) and osteoblasts (bone-forming cells) originated from the same precursor stem cell i.e. the mesenchymal stem cell. It was noted that reduction in the formation of adipose cells from the mesenchymal stem cell resulted in the increase in the formation of osteoblast. With regard to mechanism of action, statin works by inhibiting HMG-CoA reductase, the rate-limiting enzyme in the cholesterol biosynthetic pathway to reduce cholesterol synthesis. The inhibition of this enzyme may also increase the production of BMP, thus increasing bone formation and preventing bone loss and osteoporosis. Several animal studies reported that statins protected bone against osteoporosis and promoted fracture healing of osteoporotic bone. Human studies were conducted on patients taking statins by measuring their bone mineral densities and assessing their risks of fractures. There were mixed results on these human studies. According to a systematic review by Salari and Abdollahi (2011), more longitudinal studies in different ethnicities with large sample size are required before any conclusion can be drawn on statin use as anti-osteoporotic

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agent. The question arises on why the data from human studies on statin's anti-osteoporotic effects were not convincing. The answer may lie in the oral doses of statins used. In most subjects, statins were taken according to the doses recommended to lower cholesterol.

Statins are degraded by the liver, resulting in low bioavailability to reach the bone environment. Abdul-Majeed et al. (2012) commented that the anti-osteoporotic effects could only be seen with very high oral doses of statins as they are extensively degraded in the liver. This may not be practical as high doses of statin were associated with risks of liver failure and rhabdomyolysis. Therefore, a new approach of delivering statins to the bone is required. Recently, Ibrahim et al. (2014) reported that statin that was delivered directly to bone via targeted and controlled delivery system, promoted fracture healing in osteoporotic bone of post-menopausal model. By using this delivery system, a low dose of statin was combined with a polymer and injected directly to the fracture site. This has opened up a new area of research on statin as an anti-osteoporotic agent. Further studies on statins are advised to determine its potential as anti-osteoporotic agent.

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