Are Iron Chelators Safe to Be Used in Hypoxia-induced Lung Injury?

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Commentary on:
Mousavi et al., Place of iron chelators like desferrioxamine and deferasirox in management of hypoxia-induced lung injury; a systematic review. Int. J. Pharmacol., 2010, 6(4): 397-408.

Although oxygen is essential to sustain life, hypoxia is a common cause of cellular oxidative stress. Too much oxygen is known to be toxic due to the production and accumulation of reactive oxygen species. These oxygen species, when released at the tissue or cell level, play a significant role in the pathogenesis of tissue injury and the pathogenesis of some common complicated diseases such as inflammatory bowel disease (Rezaie et al., 2007), diabetes (Rahimi et al., 2005), osteoporosis (Abdollahi et al., 2005), acute respiratory distress syndrome (Soltan-Sharifi et al., 2007) or toxicity-related chronic debilitating diseases (Abdollahi et al., 2004; Mohammadrad and Abdollahi, 2011). Antioxidant therapy is believed to be useful in such cases, particularly in patients with impaired oxidative defense mechanism (Hasani-Ranjbar et al., 2009, 2010).

Iron is the most abundant metal ion in the body and is responsible for oxidative injuries. Although iron is a vital source especially in erythrocytes, if it is not appropriately chelated by citrate, carboxylates, nucleotides and other ligands in biological tissues, it can form harmful free radicals such as hydroxyl radicals (Kakhlon and Cabantchik, 2002; Leonard et al., 2004). It has been suggested that iron chelators may have protective effect in the cardiovascular system and prevent the formation of superoxide radicals during reperfusion injury (Jenova and Valko, 2011). Iron chelators are found neuroprotective in patients with Alzheimer’s disease, in which oxidative stress play a significant role (Amit et al., 2008).

The systematic review conducted by Mousavi et al. (2010) has searched several broad-based databases and examined the usefulness and therapeutic effect of iron chelators in the management of hypoxia-induced lung injury within the constraint of the available research data. Although, many studies have been published on the advantages of iron chelators, such as Desferrioxamine, however, the clinical efficacy of these agents is inconclusive, especially in the management of oxidative-induced pulmonary injury. This review concludes that the clinical advantages of iron chelators should outweigh the disadvantages if they are to be considered a strong therapeutic agent and recommended by clinicians.

A major point to consider is that iron is involved in many important biological processes in the body, including cellular biosynthesis, cell division, gene regulation and signal transduction. Therefore, interference with iron can potentially cause widespread disruption to a range of cellular functions despite offering a beneficial therapeutic effect. Thus, the clinical role and therapeutic application of iron chelators deserve well-designed preclinical studies to evaluate the efficacy and safety of these agents in various medical conditions including oxidative-induced pulmonary injury. In that regard, this systematic review is an important step in examining the true beneficial effects of iron chelators, either alone or in combination with other drugs to improve the management of hypoxia-induced pulmonary injury.

REFERENCES