Minocycline May be Useful to Prevent or Treat Methamphetamine-Induced Neural Cell Death: Hypothetic Role of Autophagia and Apoptosis Signaling Pathway

Methamphetamine (METH) is a psychostimulant agent, and its neurotoxic and neurobehavioral consequences are serious.[1] Studies indicated that chronic abuse of METH can cause neural cell death in human and animal subjects.[1,2] Previous studies also showed that chronic abuse of METH can cause neurodegeneration, clear mechanism to these types of neurodegeneration remains unclear, but it seems that neuroinflammatory signaling pathways involved in this manner.[1] By induction of Bcl-2 phosphorylation after beginning an autophagy or apoptosis signal on the cell surface, in particular by activating tumor necrosis factor-alpha (TNF-α) receptor, c-Jun N-terminal kinase (JNK) causes phosphorylation of Bcl-2 which this phenomenon causes inactivation and dissociation of Bcl-2 from Beclin1 or Bax which cause initiation of autophagy or apoptosis respectively and therefore cell death was occurred[3,4] On the other way, during recent years, using new neuroprotective compounds with therapeutic probability for the treatment of drug abuses induced sequels has been amazingly increased.[5,6] Minocycline is a broad-spectrum and long-acting antibiotic and possesses anti-inflammatory, neuroprotective, and neural survival properties.[7,8] Pervious data suggested that minocycline has anti-inflammatory properties and can inhibit TNF-α receptor downstream signaling cascade in the neural cells.[9,10] Thus, according to the above evidence, we can suggest and have the theory that by inhibition of TNF-receptor activation and downstream JNK/Bcl-2-Beclin1 or Bcl-2/Bax signaling pathways, minocycline will likely inhibit METH-induced apoptosis and autophagia and probably by this mechanism can inhibit METH-induced neurodegeneration and neural cell loss [Figure 1].

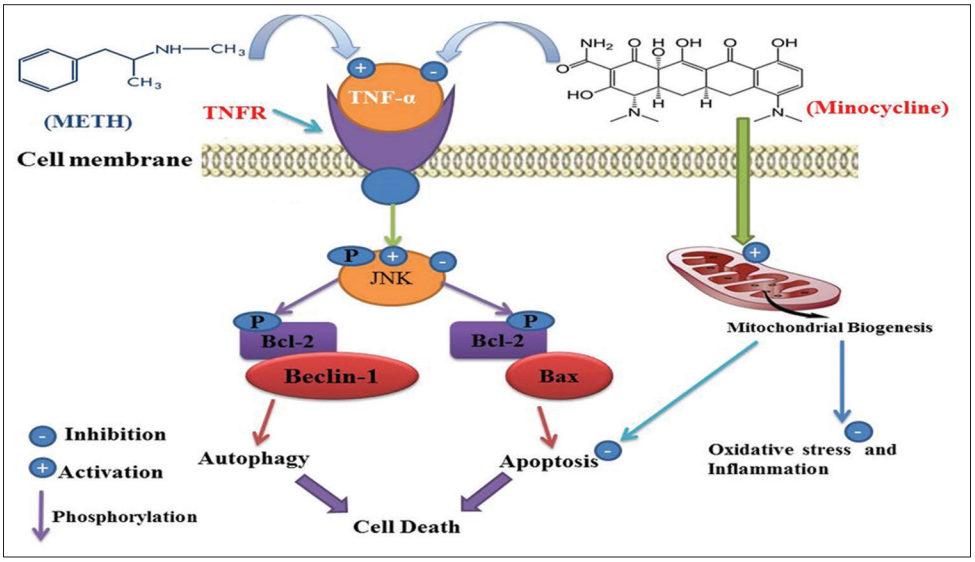

Figure 1: Minocycline can inhibit METH-induced TNFR activation and c-Jun N-terminal kinase/Bcl-2-Beclin1 or c-Jun N-terminal kinase/Bcl-2/Bax signaling pathway which may reduce METH-induced autophagia and apoptosis and consequences neurodegeneration. Further, minocycline directly activates mitochondrial biogenesis which leads to inhibition of METH-induced oxidative stress and inflammation. TNFR: TNF-α receptor, METJ: Methamphetamine

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