Mometasone furoate is more potent than methylprednisolone and dexamethasone in experimental spinal cord injury in mice

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Traumatic spinal cord injury (SCI) represents one of the most devastating injuries affecting the human body since it creates disability for the temporary or permanent impairment of sensory and/or motor system deficit, in particular hind limb locomotor function (McDonough A et al., 2015). Currently, therapy to treat acute SCI involves as first line choice steroidal anti-inflammatory drugs, in particular methylprednisolone sodium succinate (MPSS) administered at high doses within 3-8 hours from the trauma (Bracken et al., 1997). However, despite major progress in pharmacological, surgical and rehabilitative treatment approaches, SCI still remains a very complex medical and psychological challenge, with no curative therapy available.

The aim of the present study was to compare the efficacy of MPSS (6mg/Kg, daily i.p.) in respect to other GCs as dexamethasone (Dex, 1 mg/Kg, daily i.p.) and mometasone furoate (MF, 0.1 mg/Kg, daily i.p.) in mouse experimental SCI (compression model).

First we compared the effects of these GCs in an *in vitro* suitable model of inflammation a phenomenon that characterizes SCI. MPSS, Dex and MF inhibited in a significative and concentration-dependent manner nitrite production as well as inducible nitric oxide synthase (iNOS) and ciclooxygenase 2 expression in LPS-stimulated J774 cells. Surprisingly MF was more potent than Dex and MPSS. Similar results were observed also *in vivo* performing an experimental chronic model of SCI in mice (compression model).

In particular, after seven days from the induction of the trauma, SCI induced tissue damage, cellular infiltration, fibrosis, astrocyte activation (GFAP immunostaining), iNOS expression, extracellular signal regulated kinase 1/2 phosphorylation, PARP-1 activation as well as apoptosis (Bax and Bcl-2 expression) in injured tissue. All the three GCs have demonstrated the capability to modulate inflammatory, oxidative as well as apoptotic pathways, but MF has demonstrated the best efficacy, while Dex and MPSS have shown alternative potency with a different protection degree.

In conclusion we can suggest that MF is the best candidate for post-traumatic chronic treatment, since it ameliorates different molecular pathways involved in the damage's propagation to the surrounding areas of the injured spinal cord.

McDonough (2015). J Vis Exp 24
Bracken (1997). JAMA, 277, 1597.