CODEN [USA]: IAJPBB **ISSN: 2349-7750**

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.2641173

Available online at: http://www.iajps.com ***Research Article***

AN EXPERIMENTAL RESEARCH TO DESIGN AND IDENTIFY THE EFFECTS OF LOW-DOSE UNITREXATE IN SECONDARY SPINAL CORD INJURIES

Dr. Maryam Suryya Zafar, Dr. Rauha Ahmad, Dr. Safina Babar
House Officer, Jinnah Hospital, Lahore.

Article Received: February 2019 **Accepted:** March 2019 **Published:** April 2019

Abstract:
Introduction: *Various inflammatory and biochemical reactions may develop because of the SSCI (Secondary Spinal Cord Injury) effects which also known as secondary cord damage and it also creates oedema in the course of an acute stage.*
Objective: *Keeping in view the facts, the aim of this research was to design and identify the therapeutic effects of low-dose unitrexate for neuropathological disorders.*
Material and methods: *The design of this research was experimental in nature which was carried out at Mayo Hospital, Lahore (October 2017 to July 2018). We considered all the ethical protocols of the hospital in this research. The research sample consisted of one hundred patients who were suffering due to any of the neurological disorder and also used such drugs. The research was carried out in fragments by dividing the population into different groups.*
Results: *The varying mean MPO level values were significant according to T-Test and ANOVA. Treated group and control group were significantly different. Outcomes reflect that combined therapy of MO and MTX present closer values to the control group; whereas, a separate effect reflects different values than the control group.*
Conclusion: *We conclude that low-dose unitrexate is more effective than methylprednisolone to treat patients of neurological disorders.*
Keywords: *Low-dose, Neurological, Injury, Disorder, Myeloperoxidase (MPO), MP, MTX, SCI (Spinal Cord Injury) and Unitrexate.*

Corresponding author:
Dr. Maryam Suryya Zafar,
House Officer, Jinnah Hospital, Lahore.

QR code

Please cite this article in press Maryam Suryya Zafar et al., ***An Experimental Research to Design and Identify the Effects of Low-Dose Unitrexate in Secondary Spinal Cord Injuries.,*** *Indo Am. J. P. Sci, 2019; 06(04).*

INTRODUCTION:

Various inflammatory and biochemical reactions may develop because of the SCI (Secondary Spinal Cord Injury) effects which also known as secondary cord damage and it also creates oedema in the course of an acute stage [1]. Such effect includes the release of aspartate and amino acid glutamate, arachidonic acid activation and glial cells activation. Microglial cells produce nitric oxide and superoxide in case of exposure to oxidative stress. Whereas, in the light of modern treatment the reduced cytokines production by the inflammatory cells blockage the secondary cord damage is also reduced [2]. At present, MP and low-dose unitrexate are used for the management of inflammatory diseases such as the damage of secondary spinal cord. Low-dose MTX inhibits lymphocytes proliferation for any of the response of inflammatory nature and reduces the leukocytes ability [3]. We still not know the exact mechanism of the drug but as per the available literature, it increases the accumulation of the adenosine at inflammatory sites. The interaction of Adenosine with receptors reduces the inflammatory cells [4].

The first standard drug for the management of SCI is MP for both human and animals [5]. A higher MP dose inhibits peroxidation of lipid. Present research efforts investigate the lipid peroxidation as it provides for the progressive tissue damage. MP also protects membrane against peroxidation of the lipid and it is a glucocorticoid steroid drug which also acts for other mechanisms along with peroxidation of the lipid [6]. Keeping in view the facts, the aim of this research was to design and identify the therapeutic effects of low-dose unitrexate for neuropathological disorders.

MATERIAL AND METHODS:

The design of this research was experimental in nature which was carried out at Mayo Hospital, Lahore (October 2017 to July 2018). We considered all the ethical protocols of the hospital in this research. The research sample consisted of one hundred patients who were suffering due to any of the neurological disorder and also used such drugs. The research was carried out in fragments by dividing the population in different groups respectively Group – A (Controls) and Group – B (MTX 30 mg/kg body weight) group.

Biochemical analysis was carried out through processing of blood sample through phosphate buffer saline with the help of homogenizer. Measurement of reactive substances was carried out through Mihara method [9, 10]. Suzuki method was employed to measure the blood sample MPO activity [12]. Blood homogenate centrifugation was carried out for ten minutes at a rate of (3000 rpm) followed by pallet suspension. Repeat the process of centrifugation for another five minutes at the same rpm rate. MPO activity was measured through separated resultant. Make a volume of one millilitre by combining phosphate buffer (50 mM), hexadecyltrimethylammonium bromide (0.5%) (HETAB), tetramethylbenzidine (1.6 mM) (TMB) and H^2O^2 (2 mM). Treat the reaction with H^2O^2 and measure the absorbance at (650 nm^7).

The researcher also made a statistical analysis through T-Test, SPSS, ANOVA and PostHoc. Every outcome was shown in Mean and SD (P-Value < 0.08).

RESULTS:

The varying mean MPO level values were significant according to T-Test and ANOVA. Treated group and control group were significantly different. Outcomes reflect that combined therapy of MO and MTX present closer values to the control group; whereas, a separate effect reflects different values than the control group. Detailed outcomes of control, MTX and MP groups are given in Table – I & II:

Table – I: Mean LPO & MPO Values

Groups		Maximum	Minimum	Mean	±SD
Control	LPO	35.330	30.350	30.000	7.320
	MPO	0.010	0.000	0.000	1.570
MTX	LPO	58.630	54.300	54.300	7.460
	MPO	14.530	11.3600	12.500	0.840
MP	LPO	44.140	40.000	42.000	9.220

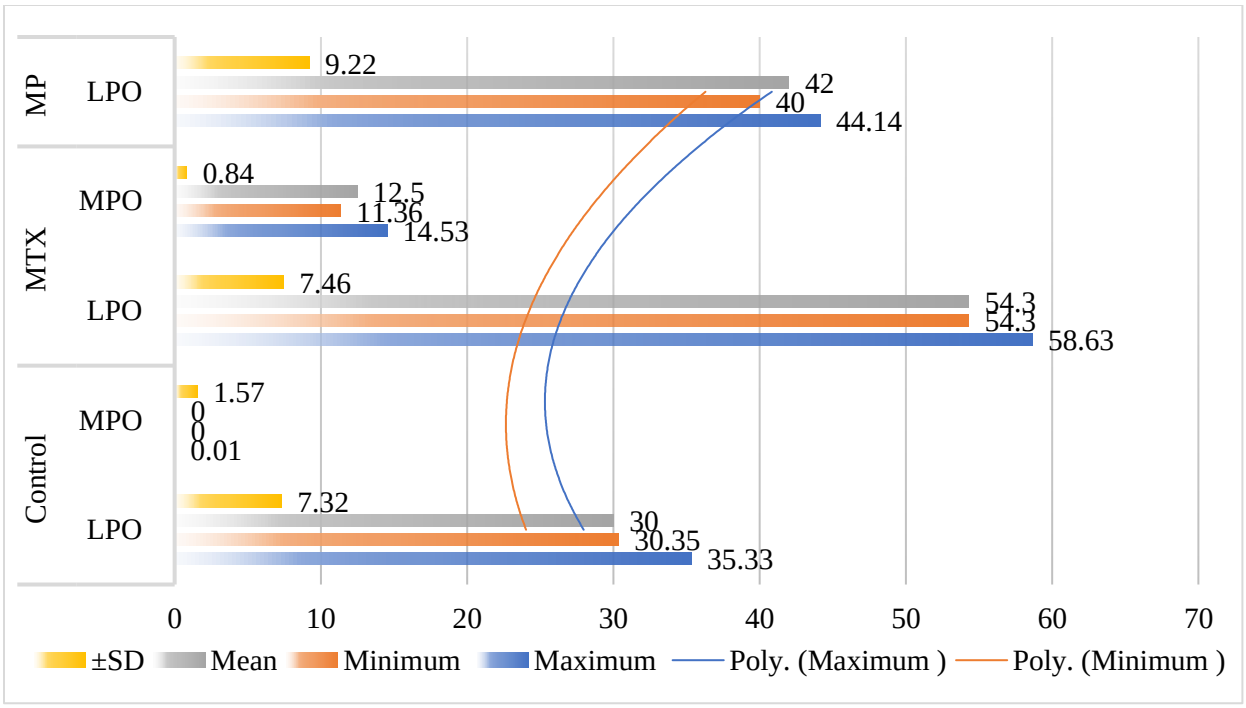
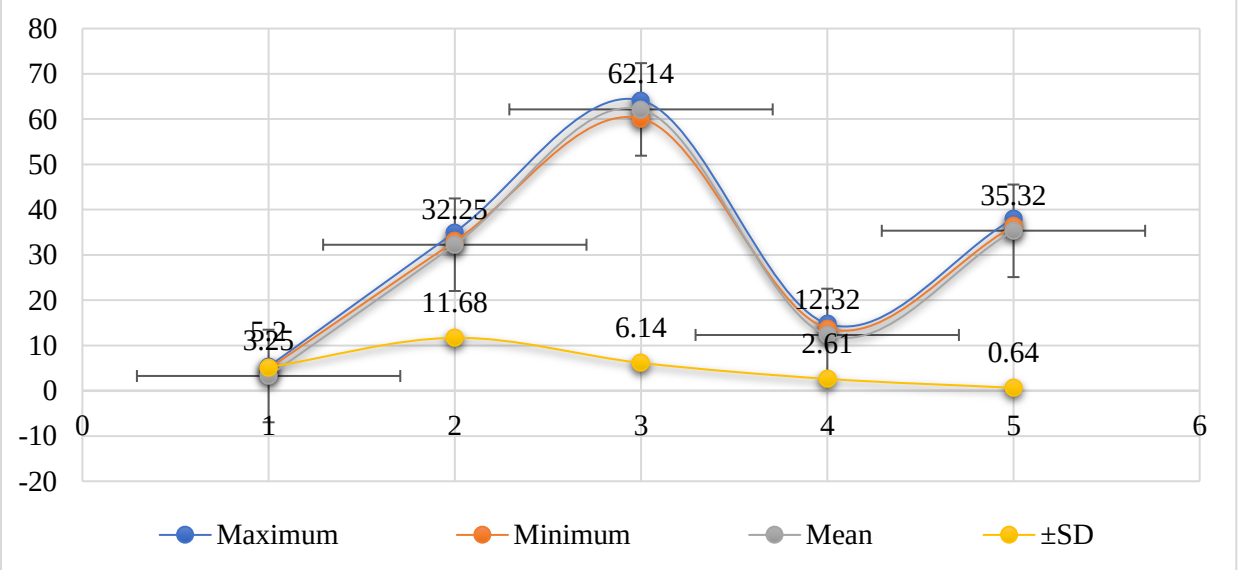


Table – II: Group-Wise Minimum, Maximum, Mean and SD values

Groups		Maximum	Minimum	Mean	±SD
MPO	MPO	5.320	4.850	3.250	5.200
High Dose MTX + MP	LPO	35.000	33.000	32.250	11.680
	MPO	64.140	60.140	62.140	6.140
MTX + High Dose MP	LPO	14.800	13.800	12.320	2.610
	MPO	38.000	36.330	35.320	0.640



DISCUSSION:

Various pharmacological agents describe protentional strong effects of the spinal cord injury. Another available treatment option is steroid therapy which is also accepted as the best available management for the spinal cord injuries. The effects are anti-inflammatory and antioxidant and they may favour while depending on dose and time [8]. They also carry activities like antiedema. We observed that every group presented degenerative actions except combined and control treatment groups. The inflammatory actions are also presented through histopathological grades along with cell degeneration in the specimen. These outcomes may also help in the explanation of MD and MTX response of inflammatory nature [9]. Furthermore, the MP group also presented a moderate inflammatory reaction due to neutrophils and inflammatory reaction of severe nature because of the macrophages in MTX specimen [10]. We may also say that MP is not capable to inhibit infiltration of the neutrophil into damaged tissue and low-dose of the MTX may increase histiocytic infiltration or macrophage into neural injured tissue in sub-acute SCI stage [11].

Macrophages and Neutrophils are best inflammatory reactions sources and they also free the radicals in any tissue. Moreover, SCI-induced ischemia faces the demands of the tissue energy and active ion channel functions after that it forces the neurons to shift from aerobic metabolism to anaerobic metabolism. This oxidative stress which is subsequent to SCI may also result in the production of free radicals that may initiate the activity of LPO in the neural damaged tissue [12].

Outcomes also reflect that low-dose MTX and MD also attribute in the free radical's formation and reduce oxidative stress as well [13]. When neutrophils and related phagocytes reach the spot of injured tissue of the spinal cord, they produce hypochlorite which is a strong oxidant enzyme synthesized MPO. MPO is an enzyme that is available in the neutrophils cells granules. The association of MPO activity is with the total neutrophils along with their activated state [14 – 15].

CONCLUSION:

We conclude that low-dose unitrexate is more effective than methylprednisolone to treat the patients of neurological disorders also known as secondary SCI (Spinal Cord Injury).

REFERENCES:

1. Means ED, Anderson DK, Waetrs TR, Kalaf. Effect of methylprednisolone in compression trauma to the feline spinal cord. J Neuro Surg 1981; 55: 200-8.
2. Braughler JM, Hall ED. Effects of multi-dose methylprednisolone sodium succinate administration on injured cat spinal cord neurofilament degradation and energy metabolism. J Neurosurg 1984; 61: 290-5.
3. Rivlin AS, Tator CH. Effect of duration of acute spinal cord compression in a new acute cord injury model in the rat. Surg Neurol1978; 10:38-43.
4. Demirpençe E, Köksoy C, Kuzu A, Kılınç K.A spectrophotometric assay for tissue associated myeloperoxidase activity and its application to intestinal ischemia-reperfusion. Turk J Med Sci 1997; 27:197-200.
5. Suzuki K, Ota H, Sasagawa S, Sakatani T, Fujikura T. Assay method for myeloperoxidase in human polymorphonuclear leukocytes. Anal Biochem 1983; 132:345-52.
6. Nie NH, Hull CH, Jenkins JG. SPSS: statistical package for social science. New York: McGraw Hill Inc.; 1975.
7. Leskovar A, Moriarty LJ, Turek JJ, Schoenlein IA, Borgens RB. The macrophage in acute neural injury: changes in cell numbers over time and levels of cytokine production in mammalian central and peripheral nervous systems. J Exp Biol 2000; 203:1783-95.
8. Brcken MB, Shepard MJ, Hellenbrand KG, methylprednisolone and neurological function 1 year after spinal cord injury. J Neurosurg 1985; 63:704-13.
9. Faden AI, Jacobs TP, Patrick DH, Smith MT. Megadose corticosteroid therapy following experimental traumatic spinal injury. J Neuro Surg 1984; 60: 712-7.
10. Hall ED. The neuroprotective pharmacology of methylprednisolone. J Neuro Surg 1992;76: 13-22.
11. Bao F, Chen Y, Dekaban GA, Weaver LC. Early anti-inflammatory treatment reduces lipid peroxidation and protein nitration after spinal cord injury in rats. J Neurochem 2004; 88:1335-44.
12. Kaynar MY, Hanci M, Kafadar A, Gümüştaş K, Belce A, Ciplak N. The effect of duration of compression on lipid peroxidation after experimental spinal cord injury. Neuro Surg Rev 1998; 21:117-20.
13. Cronstein BN, Naime D, Ostad E. The antiinflammatory mechanism of unitrexate. Increased adenosine release at inflamed sites diminishes leukocyte accumulation in an invivo

model of inflammation. J Clin Invest1993; 92:2675-82.
14. Katchamart W, Trudeau J, Phumethum V, Bombardier C. Efficacy and toxicity of methotrexate (MTX) monotherapy versus MTX combination therapy with nonbiological disease-modifying antirheumatic drugs in rheumatoid arthritis: a systematic review and meta-analysis. Ann Rheum Dis2009; 68:1105-12.
15. Chan ES, Cronstein BN. Molecular action of methotrexate in inflammatory diseases. Arthritis Res 2002; 4:266-73.