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ANALYSIS OF COMPARISON OF EFFECTS OF METHOTREXATE WITH THE COMBINATION OF METHYLPREDNISOLONE IN SPINAL CORD INJURY

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Abstract:

Introduction: *The incidence of spinal cord injury (SCI) caused by many events, including traffic accidents, mining and construction accidents, seismic and natural disasters, has tended to rise year on year. The pathology of SCI usually includes primary injury and secondary injury.*

Aims and objectives: *The basic aim of the study is to analyze the comparison of effects of methotrexate with the combination of methylprednisolone in spinal cord injury.*

Material and methods: *This cross sectional study was conducted in Fatima Memorial Hospital Lahore during March 2018 to November 2018. A total of 100 patients who were suffering from spinal injury due to any reason were included in this study. After analysis dose of drug according to schedule was given to the all patients. For biochemical analysis 5cc blood sample was taken from vein and sample were processed with phosphate buffer saline using homogenizer. Thiobarbituric acid reactive substances were measured according to the method of Mihara et al. Myeloperoxidation (MPO) activity of the tissue sample was measured according to the method of Suzuki et al.*

Results: *The variations between the mean values of MPO levels were significant according to the ANOVA and t-test. There were significant difference between control groups and treated groups. The data shows that the group of patients which was treated with both MTX and MP as a combine effect shows more close values to the control. But the separate effect shows somehow different values as compared to control*

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INTRODUCTION:

The incidence of spinal cord injury (SCI) caused by many events, including traffic accidents, mining and construction accidents, seismic and natural disasters, has tended to rise year on year. The pathology of SCI usually includes primary injury and secondary injury. Microglial cells produced superoxide and nitric oxide when they expose to oxidative stress. But according to modern treatment if we reduces the production of these cytokines by blocking these inflammatory cells, it will reduces the secondary cord damage (1). Primary injury often occurs in the spine, leading to SCI. The secondary damage includes inflammation, oxidative stress, neuronal apoptosis, intracellular and extracellular ion imbalance and a series of pathological reaction. Therefore, to avoid second injury and to promote the survival of axons and neurons, therapies aim to reduce or eliminate the destructive pathological response and to promote the regeneration, repair and functional reconstruction of nerve tissue in the chronic phase (2).

Now a days low dose methotrexate (MTX) and methylprednisolone (MP) has been used for the treatment of some inflammatory diseases such as secondary spinal cord damage (3). Low dose MTX inhibits the proliferation of lymphocytes in any inflammatory response and also decreases the ability of leukocytes. Exact mechanism of this drug is still unknown but according to some studies it increases the adenosine accumulation at the inflammatory sites. Adenosine interacts with the receptors and decreases the inflammatory cells (4).

MP is the first drug which is used for the treatment of spinal cord injury in animals and humans. This drug is considered to be the standard treatment method from whom which any other drugs will compare (5). High dose of MP inhibits the lipid peroxidation (6). Current studies investigated that lipid peroxidation is a major provider to the progressive damage of tissue injury. MP protects the membrane against lipid peroxidation and it must be remembered that MP is a glucocorticosteroid drug and it also act through another mechanism in addition to lipid peroxidation (7).

Aims and objectives

The basic aim of the study is to analyze the comparison of effects of methotrexate with the combination of methylprednisolone in spinal cord injury.

MATERIAL AND METHODS

This cross sectional study was conducted in Fatima Memorial Hospital Lahore during March 2018 to November 2018. A total of 100 patients who were suffering from spinal injury due to any reason were included in this study. The study was divided into following groups:

Group A: Control group
Group B: MTX- group
Group C: MP- group
Group D: MTX + MP

After analysis dose of drug according to schedule was given to the all patients. For biochemical analysis 5cc blood sample was taken from vein and sample were processed with phosphate buffer saline using homogenizer. Thiobarbituric acid reactive substances were measured according to the method of Mihara et al. Myeloperoxidation (MPO) activity of the tissue sample was measured according to the method of Suzuki et al. Blood was centrifuged at 3000rpm for 10 minutes and after that pallet was resuspended. Remove the pallet and again centrifuge at 3000rpm for 5 minutes. The resultant supernatant was separated and used for the measurement of MPO activity. Add 50mM phosphate buffer, 0.5% hexadecyltrimethyl ammonium bromide (HETAB), 1.6mM tetramethylbenzidine (TMB) and 2mM H_2O_2 and make the final volume of 1 ml. The reaction was started by the addition of H_2O_2 and absorbance was measured at 650 nm.

Statistical analysis

Statistical analysis (one way-Anova Test and Post Hoc) was performed using the SPSS software program (18.0). All results were expressed as the mean ± standard deviation (SD). As P value <0.08 was considered to be statistically significant (14).

RESULTS:

The variations between the mean values of MPO levels were significant according to the ANOVA and t-test. There were significant difference between control groups and treated groups. The data shows that the group of patients which was treated with both MTX and MP as a combine effect shows more close values to the control. But the separate effect shows somehow different values as compared to control (Table 1). The graph also illustrate that there is a significant relationship between control and treated groups. The p- values presented in the table 2 shows the clear significant relationship in the evaluation of LPO (table 2).

Table 1: Values of mean MPO and LPO in all groups

Groups	Variables	Maximum	Minimum	Mean±SD
Control	LPO	35.33	30.35	30.00±7.32
	MPO	0.01	0.00	0.00±1.57
MTX	LPO	58.63	54.30	54.30±7.46
	MPO	14.53	11.36	12.50±0.84
MP	LPO	44.14	40.00	42.00±9.22
	MPO	5.32	4.85	3.25±5.20
MTX (High dose)+MP	LPO	35.00	33.00	32.25±11.68
	MPO	64.14	60.14	62.14±6.14
MTX+MP (High dose)	LPO	14.80	13.80	12.32±2.61
	MPO	38.00	36.33	35.32±0.64

Table 2: Post-Hoc test values for all groups

No. Of observations	Study groups	df	P-value
1	Control	3	0.018*
2	MTX	1	0.019*
3	MP	1	0.017*
4	MTX (High dose)+MP	2	0.500
5	MTX+MP (High dose)	1	0.222

***p≤ 0.05 as significant value, df= degree of freedom**

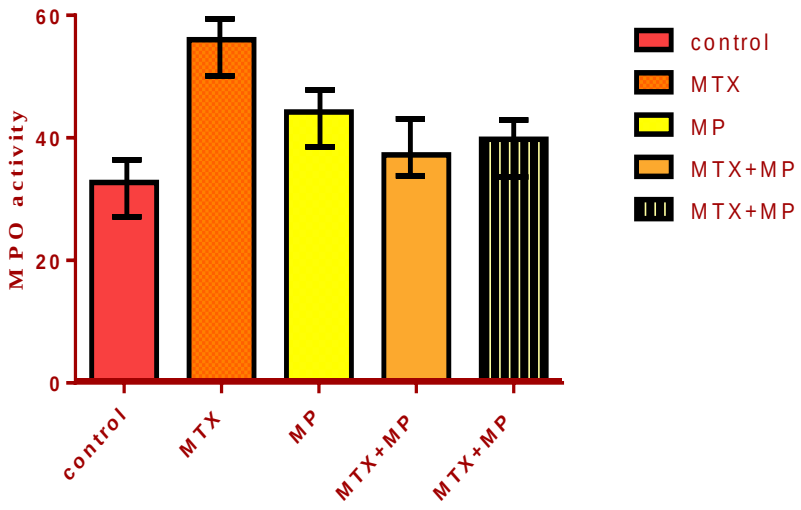

Figure 01: activity of MPO in all groups

DISCUSSION:

Our results indicated that the dose of 30mg/kg body weight of MTX and MD shows a significant effect but as compared to this combine treatment show synergistic effect. Due to this synergistic effect recovery is more close to the control group. MD has no effect on overall weight and any other level but MTX shows some notable effects (7). The inflammatory response in SCI is biphasic. In first phase lysosomal degradation and formation of free radicals occurred and in the next phase tissues damaged (8).

There are many pharmacological agents which described or considered as a potentially strong therapeutic effects for SCI. Steroids are also accepted as a best possible option for the treatment of SCI. They have antioxidant and anti-inflammatory and may be favorable in a time- and dose-dependent manner (9). They have also anti-edema activities. Methylprednisolone (MP) acts through a variety of mechanisms to prevent the occurrence of secondary SCI and is currently the only food and drug administration-approved drug for the treatment of acute SCI. However, high doses of MP lead to many side effects, including glucocorticoid-induced infection, diabetic complications, and impaired wound healing, and can endanger the lives of patients. Therefore, many experts suggest that high-dose MP shock therapy should not be used as a conventional treatment, although it can be used as a selective treatment strategy (10).

Methotrexate (MTX) is a common anti-rheumatic drug that can improve the disease state and has anti-inflammatory and immunosuppressive effects. MTX is generally used to compensate for the poor efficacy of glucocorticoid or other anti-rheumatic drugs. MTX can also be combined with hormones in early rheumatoid arthritis, so as to reduce hormone doses, thereby alleviating hormone side effects. MTX can be taken long-term because of low cost, various routes of administration, steady long-term efficacy and high safety; namely, it can be taken as an anchor drug (11).

CONCLUSION:

It is concluded that low dose methotrexate is more effective as compared to methylprednisolone in secondary spinal cord injury in patients.

REFERENCES:

1. Bao F, Chen Y, Dekaban GA, Weaver LC. Early anti-inflammatory treatment reduces lipid peroxidation and protein nitration after spinal cord injury in patients. J Neurochem 2004; 88:1335-44.
2. 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. Neurosurg Rev 1998; 21:117-20.
3. Cronstein BN, Naime D, Ostad E. The anti-inflammatory mechanism of methotrexate. Increased adenosine release at inflamed sites diminishes leukocyte accumulation in an in vivo model of inflammation. J Clin Invest 1993; 92:2675-82.
4. Katchamart W, Trudeau J, Phumethum V, Bombardier C. Efficacy and toxicity of methotrexate (MTX) monotherapy versus MTX combination therapy with non-biological disease-modifying antirheumatic drugs in rheumatoid arthritis: a systematic review and meta-analysis. Ann Rheum Dis 2009; 68:1105-12.
5. Chan ES, Cronstein BN. Molecular action of methotrexate in inflammatory diseases. Arthritis Res 2002; 4:266-73.
6. Brcken MB, Shepard MJ, Hellenbrand KG, methylprednisolone and neurological function 1 year after spinal cord injury. J Neurosurg 1985; 63:704-13.
7. Faden AI, Jacobs TP, Patrick DH, Smith MT. Megadose corticosteroid therapy following experimental traumatic spinal injury. J Neuerosurg 1984; 60: 712-7.
8. Hall ED. The neuroprotective pharmacology of methylprednisolone. J Neurosurg 1992; 76: 13-22.
9. Means ED, Anderson DK, Waetrs TR, Kalaf L. Effect of methylprednisolone in compression trauma to the feline spinal cord. J Neuerosurg 1981; 55: 200-8.
10. Braughler JM, Hall ED. Effects of multi-dose methylprednisolone sodium succinate administration on injured cat spinal cord neurofilament degradation and energy metabolism. J Nerosurg 1984; 61: 290-5.
11. Rivlin AS, Tator CH. Effect of duration of acute spinal cord compression in a new acute cord injury model in the rat. Surg Neurol 1978; 10:38-43.