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ANALYSIS OF THERAPEUTIC EFFECTS OF LOW DOSE UNITREXATE IN NEUROPATHOLOGICAL DISORDERS IN PAKISTAN

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Abstract:

Introduction: *There are many biochemical and inflammatory reactions which develop due to the effect of secondary spinal cord injury (SCI) are also called secondary cord damage creates the edema during acute stage.*

Objectives of the study: *Based on all facts this study was designed to investigate the comparison of effects of low-dose unitrexate in neuropathological disorders in Pakistan.*

Material and methods: *This cross sectional study was performed in CMH Lahore during January 2019 to July 2019. This study was done according to the ethical committee of university and hospitals and all the protocols were reviewed by the committee. A total of 100 patients were selected for study who was suffering from any neurological disorder and use these type of drugs. The study was further divided into further groups.*

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.*

Conclusion: *Low dose unitrexate is more effective as compared to methylprednisolone in neurological disorders.*

Key words: *Dose, Injury, Unitrexate*

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INTRODUCTION:

There are many biochemical and inflammatory reactions which develop due to the effect of secondary spinal cord injury (SCI) are also called secondary cord damage creates the edema during acute stage [1]. This effect includes the release of amino acid glutamate and aspartate, activation of arachidonic acid and activation of glial cells. 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 [2].

Now a days low dose unitrexate and methylprednisolone (MP) has been used for the treatment of some inflammatory diseases such as secondary spinal cord damage. Low dose MTX inhibits the proliferation of lymphocytes in any inflammatory response and also decreases the ability of leukocytes[3]. 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. 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 [6].

Objectives of the study:

Based on all facts this study was designed to investigate the comparison of effects of low-dose unitrexate in neuropathological disorders in Pakistan.

MATERIAL AND METHODS:

This cross sectional study was performed in CMH Lahore during January 2019 to July 2019. This study was done according to the ethical committee of university and hospitals and all the protocols were reviewed by the committee. A total of 100 patients were selected for study who was suffering from any neurological disorder and use these type of drugs. The study was further divided into further groups. The groups are as follows:

Group A: Control group
Group B: MTX- group (30mg/kg body weight)

Analysis of Specimen:

For biochemical analysis of blood sample were processed with phosphate buffer saline using homogenizer. Thiobarbituric acid reactive substances were measured according to the method of Mihara et al (9, 10). Myeloperoxidation (MPO) activity of the blood sample was measured according to the method of Suzuki et al [12].

Measurement of MPO activity:

Blood homogenate 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 [7].

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:

Biochemical analysis

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).

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

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

DISCUSSION:

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 [8]. They have also anti-edema activities. In our present study almost all groups show degenerative activities except control and combined treatment group. The histopathological grades show the inflammatory reactions in the specimen and it also shows the cell degeneration. These findings may explain the anti-inflammatory response of MTX and MD [9].

Furthermore moderate inflammatory reaction caused by neutrophils was observed in the MP group, and severe inflammatory reaction developed due to macrophages was observed in the specimens of the MTX group [10]. This may mean that MP could not block the neutrophil infiltration into the damaged tissue, and low-dose MTX may enhance the macrophage or histiocytic infiltration into the injured neural tissue in the sub-acute stage of SCI [11].

Neutrophils and macrophages are the best source of inflammatory reactions and free radicals in any tissue. Moreover, ischemia induced by SCI faces tissue energy demands and active ion channel functions, and then it may force the neurons to switch from aerobic to anaerobic metabolism. This oxidative stress subsequent SCI may also produce free radicals, which may initiate the LPO activity in the damaged neural tissue [12].

These results also indicated that low dose MTX and MD also contribute in the formation of free radicals and decrease the oxidative stress[13]. When the neutrophils and other phagocytes reach the injured spinal cord tissue, they produce hypochlorite, a strong oxidant synthesized by the enzyme MPO. MPO is the enzyme which is present in the granules of the neutrophils cells. MPO activity is associated with the total number of neutrophils and their activations[14-15].

CONCLUSION:

Low dose unitrexate is more effective as compared to methylprednisolone in secondary spinal cord injury

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