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ANALYSIS OF EFFECTS OF METHOTREXATE IN COMBINATION WITH METHYLPREDNISOLONE FOR SPINAL CORD INJURY IN PAKISTAN

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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.*

Objectives of the study: *The main objective of the study is to analyze the effects of methotrexate and methylprednisolone in spinal cord injury among local population of Pakistan.*

Material and methods: *This cross-sectional study was conducted in Bahawal Victoria Hospital, Bahawalpur during October 2018 to March 2019. The data was collected from 100 patients of spinal injury. The study was divided into two groups, one was control group and one who was treated with MTX. For biochemical analysis 5cc blood sample was taken from vein and sample were processed with phosphate buffer saline using homogenizer. Blood was centrifuged at 3000rpm for 10 minutes and after that pallet was suspended.*

Results: *The data was collected from 100 patients of SCI. There were significant difference between control groups and treated groups. The swing time in the MP group was significantly shorter than that of the SCI group ($P < 0.05$) from 2 to 8 weeks post-injury. At 8 weeks post-injury, improvement was significantly enhanced by combined MP and MTX compared with the use of MP alone ($P < 0.05$).*

Conclusion: *It is concluded that MTX therapy could improve the deficiency of MP treatment alone. MTX, with a flexible administration time, in combination with the traditional SCI treatment drug, MP.*

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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. Spinal cord injury (SCI) poses a serious threat to human health and typically results in incomplete or complete loss of motor and sensory function. The prevalence of SCI is relatively high. Notably, the prevalence among the elderly (aged >60 years old) and the younger (aged 16–45 years old) have been estimated to be ~24 and 49%, respectively, which are primarily due to traffic collisions. Although various methods of treating SCI are currently used, these treatments are not effective since SCIs still result in substantial permanent morbidity and mortality. Therefore, it is important to develop a novel effective method of treating patients with SCI [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]. 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 reactions. 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 [5].

OBJECTIVES OF THE STUDY:

The main objective of the study is to analyze the effects of methotrexate and methylprednisolone in spinal cord injury among local population of Pakistan.

MATERIAL AND METHODS:

This cross sectional study was conducted in Bahawal Victoria Hospital, Bahawalpur during October 2018 to March 2019. The data was collected from 100 patients of spinal injury. The study was divided into two groups, one was control group and one who was treated with MTX. For biochemical analysis 5cc blood sample was taken from vein and sample were processed with phosphate buffer saline using homogenizer. 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 MTX activity.

STATISTICAL ANALYSIS:

The data was collected and analyzed by using the SPSS software program (21.0). All results were expressed as the mean ± standard deviation (SD).

RESULTS:

The data was collected from 100 patients of SCI. There were significant difference between control groups and treated groups. The swing time in the MP group was significantly shorter than that of the SCI group ($P < 0.05$) from 2 to 8 weeks post-injury. At 8 weeks post-injury, improvement was significantly enhanced by combined MP and MTX compared with the use of MP alone ($P < 0.05$).

Table 1: Analysis of 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
MTX (High dose)	LPO	35.00	33.00	32.25±11.68
	MPO	64.14	60.14	62.14±6.14

DISCUSSION:

MTX is applied in clinical practice as an anti-inflammatory and antitumor drug. Previous studies have shown that low-dose MTX has a protective effect on nerves after SCI. The present study also found that MTX might play a neuroprotective role in SCI repair [5]. Our study illustrates that the restorative effects of this combination therapy may be through the anti-inflammatory reaction, inhibition of oxidative stress and apoptosis and other common gene regulation pathways [6]. 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 [7]. 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 [8].

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 [9]. 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 [10].

CONCLUSION:

It is concluded that MTX therapy could improve the deficiency of MP treatment alone. MTX, with a flexible administration time, in combination with the traditional SCI treatment drug, MP. The results showed that MP and MTX combination therapy could improve the deficiency of MP treatment alone, enhance the neuroprotective effect, inhibit the activities of inflammatory cytokines, strengthen the anti-oxidative and anti-apoptotic effects and increase the clinical therapeutic effect, which could provide new strategies for the control of S

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