EXPERIMENTAL STUDY

Does infliximab attenuate oxidative stress following traumatic brain injury?

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ABSTRACT

BACKGROUND: Traumatic brain injury is a global health problem. Infliximab is used daily to treat a variety of inflammatory systemic disorders. The goal of this study was to compare the pathological and biochemical changes induced by dexamethasone and infliximab usage in rats with blunt head trauma.

METHODS: Thirty-two adult rats were used in our study. Groups of eight animals were used, and those with skin incision without any additional trauma were called sham (Group 1); those with skin incision and head trauma were called control (Group 2); those who received 1 mg/kg intraperitoneal dexamethasone immediately after head trauma were called steroid (Group 3); and those who received 5 mg/kg subcutaneous infliximab immediately after trauma were called infliximab (Group 4). The animals were euthanized seven days after the operation.

RESULTS: Brain tissue malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione peroxidase (GPx) values of the four groups were compared and a statistically significant difference was shown. However, no significant difference was observed between the infliximab and dexamethasone groups in terms of tissue MDA, SOD, and GPx concentrations. Pathological sections showed that trauma-induced cortical damage, interstitial edema, and perivascular edema were reduced in the infliximab group.

CONCLUSION: Infliximab demonstrates comparable neuroprotective effects to dexamethasone in oxidative stress markers, while providing superior efficacy in edema reduction.

Keywords: Infliximab; rat model; head injury; antioxidant.

INTRODUCTION

Traumatic brain injury is a global health problem as well as a growing socioeconomic problem. In the United States alone, more than 1.5 million people suffer from traumatic brain injury each year.[1] While traffic accidents are responsible for more than 50% of cases of acute trauma, falls are the second-most common cause.[2] In a study conducted in Southeastern Anatolia, Berber et al. observed a mean age of 7.7 years among patients with traumatic head injury and underscored the importance of causes of head trauma such as traffic accidents and falls. They additionally concluded that traumatic brain injury warrants attention as a problem for public health.[3]

Infliximab, developed by Merck & Co., Inc. (Whitehouse Station, NJ, USA) and approved by the U.S. Food and Drug Administration for managing various inflammatory systemic conditions, acts as an antagonist to tumor necrosis factor-alpha (TNF-α). As a chimeric monoclonal antibody, infliximab neutralizes elevated levels of TNF-α both within the bloodstream and at sites of inflammation. A review of the literature indicates that several types of anti-TNF-α therapy, including infliximab, are recommended for treating spinal cord injuries.[4]

However, infliximab's effect on head trauma has not been in-

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vestigated. Therefore, in our study, we investigated the effects of infliximab and dexamethasone on malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione peroxidase (GPx) in cases of blunt head injury in a rat model and compared their effects pathologically.

MATERIALS AND METHODS

Rat Model

The study was conducted in accordance with the Declaration of Helsinki. Ethical considerations concerning our study's experimental protocol were meticulously reviewed and subsequently approved by the Local Ethics Agency (No. 795, November 1, 2024). The animal subjects employed in our investigation were sourced from the Experimental Animal Breeding Laboratory affiliated with Health Sciences University, Ankara Training and Research Hospital and all experimental procedures were conducted within the Experimental Animal Research Laboratory at the same institution. The biochemical analyses associated with the study were performed by trained staff at the Medical Biochemistry Department at Ankara Bestepe Hospital.

Our experiment involved 32 male adult Wistar rats, each weighing 250–300 g, which were maintained under standardized laboratory conditions and provided unrestricted access to food and water.

Anesthesia and Surgical Procedure

Anesthesia was administered via the intramuscular injection of 45 mg/kg of ketamine hydrochloride in conjunction with 10 mg/kg of xylazine. After checking anesthetic depth by corneal reflex and tail pinch test, physiological values such as breathing, pulse, and rectal temperature of the animals were recorded preoperatively, postoperatively, and after one week (Table 1).

Prior to the surgical intervention, the frontoparietal regions of the rats' heads were shaved and disinfected using a 10% solution of polyvinylpyrrolidone–iodine. The surgical procedure involved inducing head trauma following the method outlined by Marmarou et al.[5] A midline incision spanning the coronal and lambdoid sutures was made in the scalp, after which a stainless-steel disc 1 cm in diameter was meticulously affixed to the central portion of the calvarium. Once the trauma device was prepared, the rat was positioned in a prone orientation to ensure that the disc was located beneath the lower end of the device. A weight was subsequently allowed to drop freely from a height of 1 m onto the disc (Fig. 1). None of the rats exhibited respiratory arrest or seizures shortly after trauma. Post-impaction, the calvarium was carefully analyzed for any resulting fractures, after which the scalp was sutured.

Definition of Groups

The rats were assigned to four groups with eight rats each:

Table 1. Distribution of physiological parameters of groups measured preoperatively, postoperatively, and after one week (values are presented as the median scores (25th and 75th percentiles))

	Sham	Control	Dexamethasone	Infliximab		
Weight						
Preoperatively	284.5 (279.5-293.25)	292.5 (276.5-295.5)	280.5 (275.5-291.5)	279 (276-290.75)	*	†
Postoperatively	289 (283.5-290.25)	283.5 (277.75-291.25)	288.5 (284.5-293.75)	280 (272-289.25)	*	
1 week after	285.5 (280-289)	288 (283.5-296.5)	288 (277.5-291.25)	290.5 (283.75-297.25)	*	
Rectal tempera-ture						
Preoperatively	36.55 (36.48-36.82)	36.3 (36.25-36.6)	36.6 (36.4-36.78)	36.75 (36.68-36.9)	*	†
Postoperatively	36.65 (36.38-36.82)	36.3 (36-36.4)	36.45 (36.4-36.53)	36.7 (36.5-36.82)	*	
1 week after	36.25 (36.18-36.85)	36.45 (36.35-36.85)	36.5 (36.35-36.85)	36.55 (36.4-36.7)	*	
Number of respirations						
Preoperatively	97.5 (94.5-99.75)	104.5 (93.5-112)	84.5 (77.75-89.75)	103 (94.25-106.75)	*	†
Postoperatively	97 (89.25-105.5)	100 (84-110.25)	88 (77.75-93.5)	91 (88.5-92.5)	*	
1 week after	91 (83.75-103)	92 (75.75-105.5)	93 (90-100.25)	82.5 (79.5-93.25)	*	
Hearth rate						
Preoperatively	354.5 (311.25-378)	359.5 (323-390.25)	347 (306.25-411)	344 (272.25-413.5)	*	†
Postoperatively	352 (324.75-405)	302 (280.5-334.5)	359 (305.25-420)	393 (326.75-412.5)	*	
1 week after	368 (338-390.25)	277.5 (268.5-322.75)	354 (295.75-412.5)	418 (296.5-429.75)	*	

*No significant differences among the groups (p>0.05). †No significant differences among all groups (p>0.05).

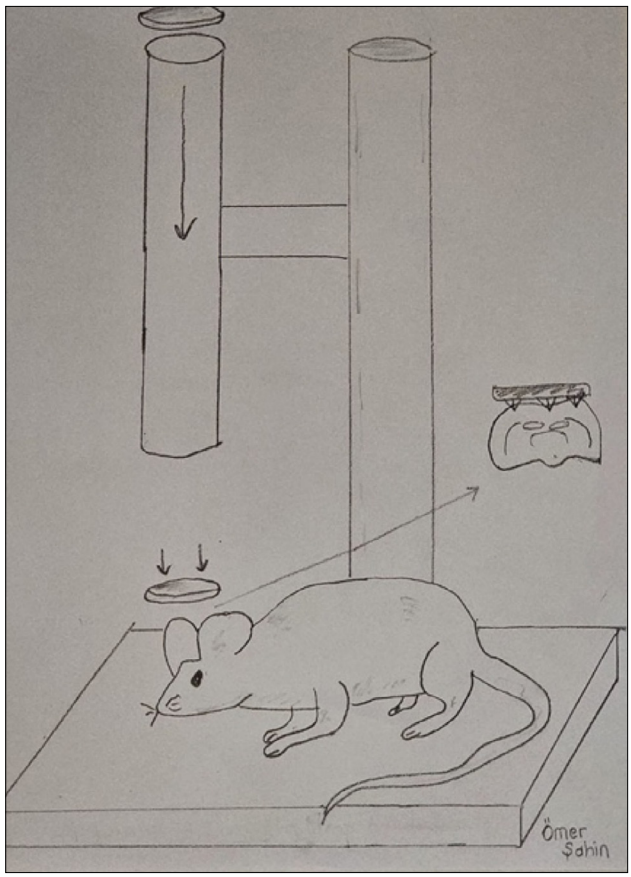

Figure 1. Schema presenting Marmarou weight drop model.

(1) a sham group that received a scalp incision without any additional trauma being inflicted; (2) a control group that received a scalp incision, underwent head trauma, but had no medical treatment administered; (3) a dexamethasone group that received 1 mg/kg intraperitoneal dexamethasone immediately following head trauma; and (4) an infliximab group that received 5 mg/kg subcutaneous infliximab immediately following trauma.[4]

The animals were euthanized seven days after the operation. The cranial bones, including the scalp, were extracted as a single unit. After dividing from the midline, one hemisphere was sent for pathological sections. The other side was used for biochemical evaluations.

Evaluation of Pathologic Sections

The samples were fixed in a 10% formaldehyde solution, after which standard processing procedures were conducted utilizing the LEICA ASP 300S apparatus. Subsequently, paraffin blocks were created, and 4-micron-thick cross-sections were obtained using the LEICA RM 2255 microtome. The sections underwent staining with hematoxylin and eosin. Following these steps, examinations were conducted with an OLYMPUS BX51 microscope. The examiner who evaluated the sections was unaware of the group information of the samples. Following the evaluation of sections for neuronal degeneration, perivascular edema, and interstitial edema, all parameters were quantified as a percentage of the affected area. The classification system employed was as follows: 0 (no edema), 1 (slight) 5%, 2 (minimal) 6–20%, 3 (moderate) 21–50%, 4 (severe) 51–75%, 5 (very severe) 76–100%.[6]

Measurement of MDA, GPx, and SOD Activity

Tissue samples were processed via homogenization using 1 mL of distilled water in an Ultra Turrax tissue homogenizer. The resulting homogenates served as the basis for quantifying the activities of MDA, GPx, and SOD. All experimental procedures were conducted at a temperature of 4°C to ensure enzymatic integrity. The protein content of the brain samples was analyzed according to Lowry's method,[7] while the level of lipid peroxidation in the samples was determined by measuring concentrations of MDA using the NWLSS NWKMDA01 assay, with results expressed in micromoles per gram of protein. Meanwhile, GPx activity was assessed using a colorimetric assay kit, based on methods established by Paglia and Valentine, and concentrations of GPx were recorded as milliunits per gram of protein.[8] Last, SOD activity was evaluated using a superoxide dismutase assay kit, with results expressed in units per gram of protein.

Statistical Analysis

As each group had a sample size of eight, we reported median values alongside the interquartile range (25th and 75th percentiles), and we used non-parametric tests as suggested in previous research.[9] For overall group comparisons, we applied the Kruskal-Wallis test. If significant differences were detected, we performed pairwise subgroup comparisons using the Mann-Whitney U test. The significance level (type I error) was set at 5%, and we adjusted p-values using the Bonferroni correction to account for multiple comparisons. All analyses were conducted using IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA).

RESULTS

Physiological parameters of groups are given in Table 1. No statistically significant difference was found between the groups ($p>0.05$).

Pathological Examination

Table 2 presents a summary of the pathological findings. Regarding neuronal degeneration, significant differences were observed among all groups ($p<0.05$). The sham group showed no neuronal degeneration, while the control group exhibited severe neuronal damage. Both treatment groups demonstrated reduced neuronal degeneration compared to the control group, with infliximab showing slightly better results than dexamethasone, although no significant difference was found between the two treatment groups ($p>0.05$). Significant differences in perivascular and interstitial edema were observed among all groups ($p<0.05$). The sham group exhibited no edema (Fig. 2a). Notably, there was a statisti-

Table 2. Injury grading scores in samples (values are presented as the median scores (25th and 75th percentiles))

Score	Sham	Control	Dexamethasone	Infliximab	
Neuronal degeneration	0 (0-0)	4 (4-5)	2.5 (1.75-3.25)	2 (1-3)	† *
Perivascular edema	0 (0-0)	4 (4-5)	2 (1.75-2.25)	1 (1-1.25)	† ‡
Interstitial edema	0 (0-0)	4.5 (4-5)	2 (1.75-3)	1 (0-1.25)	† ‡

† Significant differences among the groups ($p<0.05$). ‡ Significant difference between Dexamethasone and Infliximab groups ($p<0.05$). * No significant difference between Dexamethasone and Infliximab groups ($p>0.05$).

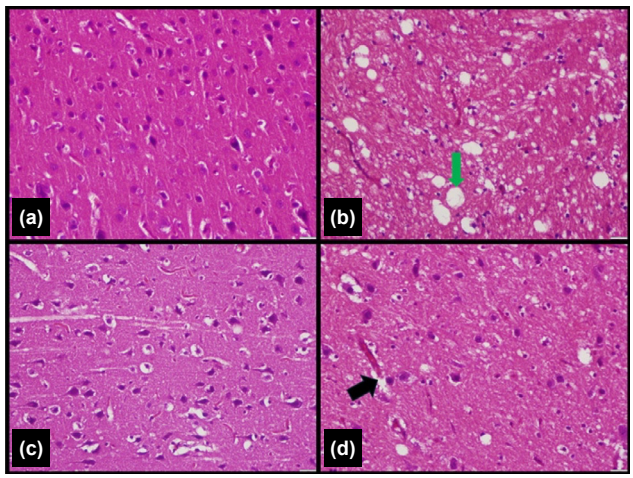

Figure 2. Hematoxylin and eosin-stained sections: **(a)** Sham group demonstrates normal brain tissue; **(b)** Trauma group shows severe perivascular and interstitial edema; **(c)** Dexamethasone group demon-strates moderate perivascular and interstitial edema; **(d)** Infliximab group shows mild perivascular and interstitial edema. (Black arrow: Perivascular edema; Green arrow: Interstitial edema).

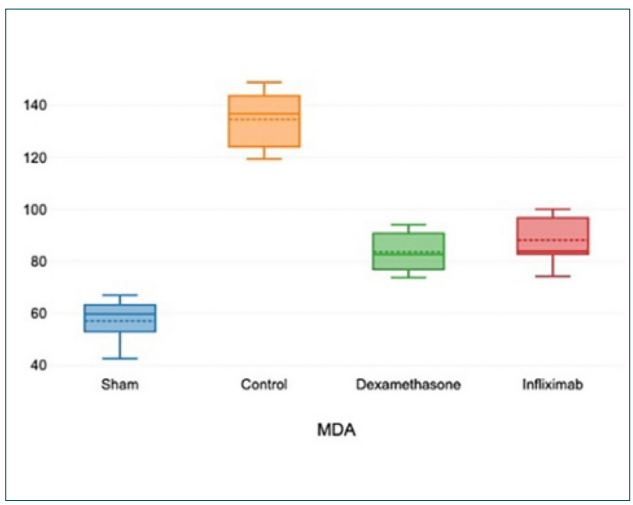

Figure 3. Box and whisker plots showing malondialdehyde (MDA) levels in brain tissue. Lipid peroxidation content is expressed as micromoles per gram protein.

cally significant distinction between the trauma and infliximab groups ($p<0.05$). Moreover, infliximab demonstrated statistically superior results compared to the dexamethasone group ($p<0.05$). The control group displayed severe edema (Fig. 2b). Examination of the study group sections revealed that both infliximab and dexamethasone groups showed reduced perivascular and interstitial edema, particularly when juxtaposed with the trauma group (Fig. 2c). This observation underscores the relative effectiveness of infliximab in reducing perivascular and interstitial edema in the subjects under investigation (Fig. 2d).

MDA Levels by Group

A statistically significant difference in MDA levels was detected between the control group and all the other groups ($p<0 .05$). The presence of trauma resulted in a marked elevation in MDA levels. Meanwhile, the infliximab group displayed a statistically significant difference in MDA concentrations compared with the control group ($p<0.05$); however, no such significant difference was observed when compared to the dexamethasone group ($p>0.05$). These findings are depicted in Figure 3.

GPx Levels by Group

Levels of GPx in the brain were notably lower in the control group than in all other groups ($p<0.05$). By contrast, the groups treated with infliximab and dexamethasone demonstrated elevated GPx levels that were not statistically significant ($p>0.05$) (Fig. 4).

SOD Levels by Group

The control group displayed a significant reduction in SOD activity compared with the sham and drug groups ($p<0.05$) (Fig. 5). The infliximab group demonstrated a notable difference in SOD activity relative to the control group ($p<0.05$), although it did not differ significantly from the dexamethasone group ($p>0.05$). These results underscore the varied effects of different treatments on SOD activity in the context of trauma and inflammation.

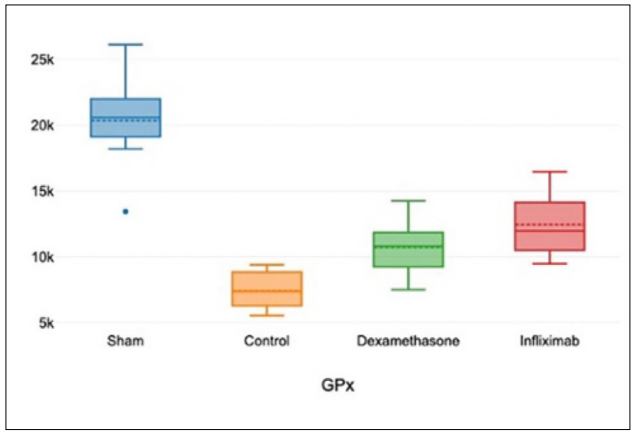

Figure 4. Box and whisker plots showing glutathione peroxidase (GPx) levels in brain tissue. GPx content of the brain is expressed as milliunits per gram of protein.

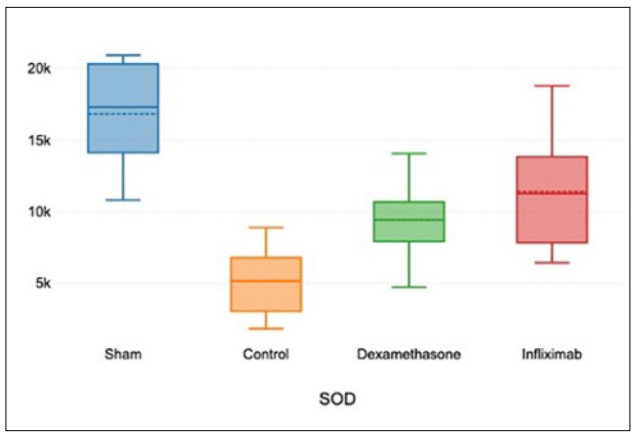

Figure 5. Box and whisker plots showing superoxide dismutase (SOD) levels in brain tissue. SOD content of the brain is expressed as units per gram of protein.

DISCUSSION

TNF-α, an important proinflammatory cytokine produced by many blood cells, interacts with two distinct receptors present on various types of cells: the type I TNF-α receptor, commonly called "p55," and the type 2 TNF-α receptor, commonly called "p75."[10] Cytokines, particularly TNF-α, play a crucial role in the injury of endothelial cells induced by activated leukocytes. Their effect occurs not only through the activation of neutrophils but also by enhancing the expression of adhesion molecules on endothelial cells, including E-selectin, which facilitates the adhesion of activated neutrophils to those cells.[11,12] Moreover, Zheng et al. have demonstrated that TNF-α can directly induce damage to endothelial cells independent of the involvement of neutrophils.[13] The effects of the cytokine on oxidative stress are mediated through the activation of multiple reactive oxygen species (ROS) generation pathways. This is primarily achieved by disrupting the efficiency of the mitochondrial electron transport chain, which normally results in 2–5% electron loss during oxidative phosphorylation. However, this increases significantly in the presence of TNF-α, causing mitochondrial dysfunction and decreased adenosine triphosphate (ATP) production[14] TNF-α also activates nicotinamide adenine dinucleotide phosphate (NADPH) oxidase isoforms (NOX2, NOX4, NOX1, and dual oxidase [DUOX]) and enhances other enzymes such as xanthine oxidase, lipoxygenases, and cyclooxygenases, thereby diversifying ROS production pathways.[15] This multi-pathway activation amplifies and perpetuates oxidative stress, which explains the dramatic increase in MDA levels observed following traumatic brain injury.[16]

Numerous researchers have explored the connection between TNF-α and neuronal injury. Wang et al. found that the concentration of TNF-α was elevated in the tissues of injured spinal cords,[17] while Yakovlev and Faden reported that spinal cord injuries in rats resulted in a significant rise in TNF-α messenger RNA at the injury site only 30 minutes post-trauma, with a direct correlation between the level of TNF-α and the intensity of the injury.[18] Furthermore, Taoka et al. observed that TNF-α levels in injured spinal cord tissue increased markedly following compressive trauma and peaked 4 hours after the initial injury.[19] The effects of TNF-α on antioxidant enzyme systems are paradoxical and significantly reduce cellular antioxidant capacity. TNF-α suppresses the expression of cytoplasmic Cu/Zn-SOD at the transcriptional level through nuclear factor kappa B (NF-κB)-independent pathways, thereby weakening the cell's defense against superoxide radicals, particularly in neurons.[20] Conversely, TNF-α increases mitochondrial Mn-SOD expression via NF-κB activation as a compensatory response; however, this is usually insufficient to counteract increased mitochondrial ROS production.[21] Furthermore, TNF-α reduces glutathione peroxidase (GPx) activity and disrupts glutathione homeostasis by suppressing glutathione synthesis and reducing glutathione reductase activity.[22] The loss of GPx7 expression promotes TNF-α-induced NF-κB activation, creating a positive feedback loop that sustains inflammatory responses and amplifies oxidative stress. This results in a net decrease in antioxidant capacity and increased susceptibility to oxidative damage.[23]

Infliximab, an innovative inhibitor of TNF-α, is widely used for a variety of therapeutic and research purposes. Its clinical applications include rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, Crohn's disease, ulcerative colitis, and psoriasis, all of which infliximab is officially sanctioned for.[24] Research conducted by Olmarker et al. has demonstrated that the targeted inhibition of TNF-α via the intraperitoneal administration of infliximab effectively mitigated both initial focal pain and subsequent widespread responses to pain triggered by experimental disc herniation in a rat model.[25] Furthermore, Demir et al. revealed that infliximab diminishes the production of interleukins IL-1, IL-6, IL-8, and TNF-α in a uveitis model.[26] In the present study, infliximab caused a statistically significant increase in the levels of GPx and SOD enzymes that protect against lipid peroxidation. The neuro-

protective effects of infliximab extend beyond the neutralization of TNF-α alone, operating through multiple complementary mechanisms. As a chimeric monoclonal antibody, it binds with high affinity to both soluble and membrane-bound TNF-α, thereby preventing interaction with TNF receptors and blocking downstream signaling cascades.[27] Its fragment crystallizable (Fc) domain activates both antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity, thereby eliminating inflammatory cells and activated macrophages.[28,29] By neutralizing TNF-α, infliximab blocks pathways that produce reactive oxygen species, including NADPH oxidase activation and mitochondrial dysfunction, while facilitating the restoration of antioxidant enzymes.[30] Furthermore, infliximab promotes a shift in the phenotype of microglia cells from M1 (pro-inflammatory) to M2 (anti-inflammatory) and preserves the integrity of the blood-brain barrier by reducing endothelial ROS production and protecting tight junction proteins. This contributes to superior neuroprotective outcomes compared to dexamethasone treatment.[31,32]

In our study, analysis of pathological sections revealed that trauma induced extensive perivascular and interstitial edema. Treatment with infliximab significantly reduced these trauma-related pathological changes. Notably, the infliximab-treated group showed statistically better outcomes compared to the dexamethasone-treated group. Following traumatic brain injury, TNF-α levels surge within hours, sustaining a pro-inflammatory state that exacerbates vascular hyperpermeability.[33,34] The role of TNF-α in disrupting vascular integrity is critical to edema formation. As Kunimura et al. demonstrated, TNF-α impairs endothelial cell junctions via the guanine nucleotide exchange factor-H1 (GEF-H1)/ Ras homolog family member A (RhoA)/ Ras-related C3 botulinum toxin substrate (Rac) signaling pathway, reducing membrane localization of tight junction proteins such as Claudin-5 and Occludin.[35] Infliximab's superior efficacy over dexamethasone in mitigating edema likely stems from its specific targeting of TNF-α. As shown by Zhou et al., infliximab binds with high affinity to both soluble and membrane-bound TNF-α, directly counteracting the primary driver of vascular permeability.[36] While dexamethasone exerts broad anti-inflammatory effects, infliximab's targeted mechanism may provide more precise control over edema development.

The use of synthetic glucocorticoids such as dexamethasone for the treatment of severe traumatic brain injury has been implemented in clinical and experimental settings to reduce inflammation and edema.[37] The target of our report was to compare the biochemical and pathological effects of infliximab, a TNF-α inhibitor, and dexamethasone on head trauma. The literature indicates that TNF-α inhibitors have been used in treating spinal cord injuries and contributed positively to recovery in such cases. However, the effect of TNF-α inhibitors in a head trauma model has not previously been examined. Chengke and Kurt have mentioned the protective effects of infliximab in an experimentally induced spinal cord injury model,[4,38] while Börcek et al. have reported that adalimumab, another TNF-α inhibitor, caused a statistically significant decrease in MDA levels similar to infliximab.[39] Although infliximab has been studied with different tissues other than the brain in previous publications, the data obtained in our study is seen as compatible with previous studies. We found that trauma initiated a statistically significant increase in MDA levels, while infliximab and dexamethasone triggered a statistically significant decrease in those same levels. By the same token, infliximab produced a statistically significant increase in the levels of GPx and SOD enzymes that protect against lipid peroxidation. These findings were also supported by the pathological assessment of the brain tissues. Trauma caused significant neuronal degeneration, perivascular edema, and interstitial edema; and infliximab treatment decreased it.

It is important to recognize several limitations in this research. First, the small sample size may affect the generalizability of the findings. Future studies should include larger cohorts and both male and female animals to account for potential sex differences in traumatic brain injury response. Second, the study tested only a single dose of infliximab, leaving questions about optimal dosing. Further research should explore dose-dependent effects and compare infliximab with other TNF-α inhibitors. Third, while the study measured oxidative stress markers and pathological changes, deeper mechanistic investigations would strengthen the findings. These should include more extensive biochemical analyses, immunostaining, and electron microscopy, such as cytokine profiling, apoptosis markers, and blood-brain barrier integrity assessments. Fourth, the seven-day observation period may not fully capture long-term recovery or delayed neurodegeneration; extended studies with behavioral tests are needed. Finally, while rat models are useful, differences in human traumatic brain injury pathophysiology necessitate caution when translating findings to humans. Future work should include non-human primates or human cell models to improve clinical relevance. Addressing these limitations will help refine infliximab's potential as a therapeutic option for traumatic brain injury.

CONCLUSION

In sum, infliximab exhibits antioxidant effects comparable to those of dexamethasone, but is superior in terms of edema control. This suggests that targeted blockade of TNF-α may be a more effective approach to the treatment of post-traumatic cerebral edema. Long-term results and additional studies are needed, however, before the observed neuroprotective activity of infliximab can be used, especially following head trauma in humans.

Ethics Committee Approval: This study was approved by the Health Sciences University, Ankara Training and Research Hospital Ethics Committee (Date: 01.11.2024, Decision No: 795).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: Ö.Ş.; Design: Ö.Ş.;

Supervision: Ö.Ş.; Resource: Ö.Ş.; Materials: F.K.K.; Data collection and/or processing: F.K.K.; Analysis and/or interpretation: F.K.K.; Literature review: F.K.K.; Writing: Ö.Ş.; Critical review: Ö.Ş.

Conflict of Interest: None declared.

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REFERENCES

1. Owens BD, Kragh JF Jr, Wenke JC, Macaitis J, Wade CE, Holcomb JB. Combat wounds in operation Iraqi Freedom and operation Enduring Freedom. J Trauma 2008;64:295–9.
2. Çökük A, Kozacı N, Oğuzhan M, Acikalin A. Evaluation of Head Trauma Cases Referred to the Emergency Department. Cukurova Univ Med J 2013;38:63–71.
3. Berber G, Arslan MM, Karanfil R, Çekin N. Child deaths in Diyarbakır due to head trauma. Turkiye Klinikleri J Foren Med 2008;5:19–23.
4. Kurt G, Ergün E, Cemil B, Börcek AO, Börcek P, Gülbahar O, et al. Neuroprotective effects of infliximab in experimental spinal cord injury. Surg Neurol 2009;71:332–6.
5. Marmarou A, Foda MA, van den Brink W, Campbell J, Kita H, Demetriadou K. A new model of diffuse brain injury in rats. Part I: Pathophysiology and biomechanics. J Neurosurg 1994;80:291–300.
6. Hickey RW, Ferimer H, Alexander HL, Garman RH, Callaway CW, Hicks S, et al. Delayed, spontaneous hypothermia reduces neuronal damage after asphyxial cardiac arrest in rats. Crit Care Med 2000;28:3511–6.
7. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. J Biol Chem 1951;193:265–75.
8. Paglia DE, Valentine WN. Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxidase. J Lab Clin Med 1967;70:158–69.
9. Krzywinski M, Altman N. Points of significance: Nonparametric tests. Nat Methods 2014;11:467–8.
10. Kapadia MK, Rubin PA. The emerging use of TNF-alpha inhibitors in orbital inflammatory disease. Int Ophthalmol Clin 2006;46:165–81.
11. Klebanoff SJ, Vadas MA, Harlan JM, Sparks LH, Gamble JR, Agosti JM, et al. Stimulation of neutrophils by tumor necrosis factor. J Immunol 1986;136:4220–5.
12. Mulligan MS, Varani J, Dame MK, Lane CL, Smith CW, Anderson DC, et al. Role of endothelial-leukocyte adhesion molecule 1 (ELAM-1) in neutrophil-mediated lung injury in rats. J Clin Invest 1991;88:1396–406.
13. Zheng H, Crowley JJ, Chan JC, Hoffmann H, Hatherill JR, Ishizaka A, et al. Attenuation of tumor necrosis factor-induced endothelial cell cytotoxicity and neutrophil chemiluminescence. Am Rev Respir Dis 1990;142:1073–8.
14. Morgan MJ, Liu ZG. Reactive oxygen species in TNFalpha-induced signaling and cell death. Mol Cells 2010;30:1–12.
15. Anilkumar N, Weber R, Zhang M, Brewer A, Shah AM. Nox4 and nox2 NADPH oxidases mediate distinct cellular redox signaling responses to agonist stimulation. Arterioscler Thromb Vasc Biol 2008;28:1347–54.
16. Ushio-Fukai M. Compartmentalization of redox signaling through NADPH oxidase-derived ROS. Antioxid Redox Signal 2009;11:1289–99.
17. Wang CX, Nuttin B, Heremans H, Dom R, Gybels J. Production of tumor necrosis factor in spinal cord following traumatic injury in rats. J Neuroimmunol 1996;69:151–6.
18. Yakovlev AG, Faden AI. Sequential expression of c-fos protooncogene, TNF-alpha, and dynorphin genes in spinal cord following experimental traumatic injury. Mol Chem Neuropathol 1994;23:179–90
19. Taoka Y, Okajima K, Uchiba M, Murakami K, Harada N, Johno M, et al. Activated protein C reduces the severity of compressioninduced spinal cord injury in rats by inhibiting activation of leukocytes. J Neurosci 1998;18:1393–8.
20. Kemp K, Gray E, Mallam E, Scolding N, Wilkins A. Inflammatory cytokine induced regulation of superoxide dismutase 3 expression by human mesenchymal stem cells. Stem Cell Rev Rep 2010;6:548–59.
21. Warner BB, Stuart L, Gebb S, Wispé JR. Redox regulation of manganese superoxide dismutase. Am J Physiol 1996;271:L150–8.
22. Rahman I, MacNee W. Regulation of redox glutathione levels and gene transcription in lung inflammation: therapeutic approaches. Free Radic Biol Med 2000;28:1405–20.
23. Peng DF, Hu TL, Soutto M, Belkhiri A, El-Rifai W. Loss of glutathione peroxidase 7 promotes TNF-α-induced NF-κB activation in Barrett's carcinogenesis. Carcinogenesis 2014;35:1620–8.
24. Kuek A, Hazleman BL, Ostor AJ. Immune-mediated inflammatory diseases (IMIDs) and biologic therapy: a medical revolution. Postgrad Med J 2007;83:251–60.
25. Olmarker K, Rydevik B. Selective inhibition of tumor necrosis factoralpha prevents nucleus pulposus-induced thrombus formation, intraneural edema, and reduction of nerve conduction velocity: possible implications for future pharmacologic treatment strategies of sciatica. Spine 2001;26:863–9.
26. Demir T, Godekmerdan A, Balbaba M, Turkcuoglu P, Ilhan F, Demir N. The effect of infliximab, cyclosporine A and recombinant IL-10 on vitreous cytokine levels in experimental autoimmune uveitis. Indian J Ophthalmol 2006;54:241–5.
27. Billmeier U, Dieterich W, Neurath MF, Atreya R. Molecular mechanism of action of anti-tumor necrosis factor antibodies in inflammatory bowel diseases. World J Gastroenterol 2016;22:9300-–13.
28. Kaymakcalan Z, Sakorafas P, Bose S, Scesney S, Xiong L, Hanzatian DK, Salfeld J, Sasso EH. Comparisons of affinities, avidities, and complement activation of adalimumab, infliximab, and etanercept in binding to soluble and membrane tumor necrosis factor. Clin Immunol 2009;131:308–16.
29. Scallon B, Cai A, Solowski N, Rosenberg A, Song XY, Shealy D, Wagner C. Binding and functional comparisons of two types of tumor necrosis factor antagonists. J Pharmacol Exp Ther 2002;301:418–26.
30. Szondy Z, Pallai A. Transmembrane TNF-alpha reverse signaling leading to TGF-beta production is selectively activated by TNF targeting molecules: Therapeutic implications. Pharmacol Res 2017;115:124–32.
31. Kuno R, Wang J, Kawanokuchi J, Takeuchi H, Mizuno T, Suzumura A. Autocrine activation of microglia by tumor necrosis factor-alpha. J Neuroimmunol 2005;162:89–96.
32. Sumbria RK, Boado RJ, Pardridge WM. Brain protection from stroke with intravenous TNFα decoy receptor-Trojan horse fusion protein. J Cereb Blood Flow Metab 2012;32:1933–8.
33. Worrall NK, Chang K, LeJeune WS, Misko TP, Sullivan PM, Ferguson TB Jr, Williamson JR. TNF-alpha causes reversible in vivo systemic vascular barrier dysfunction via NO-dependent and -independent mechanisms. Am J Physiol 1997;273:H2565–74.
34. Abdullah Z, Rakkar K, Bath PM, Bayraktutan U. Inhibition of TNF-α protects in vitro brain barrier from ischaemic damage. Mol Cell Neurosci 2015;69:65–79.
35. Kunimura K, Miki S, Takashima M, Suzuki JI. S-1-propenylcysteine improves TNF-α-induced vascular endothelial barrier dysfunction by suppressing the GEF-H1/RhoA/Rac pathway. Cell Commun Signal 2021;19:17.
36. Zhou Y, Fan R, Botchway BOA, Zhang Y, Liu X. Infliximab Can Improve Traumatic Brain Injury by Suppressing the Tumor Necrosis Factor Alpha Pathway. Mol Neurobiol 2021;58:2803–11.
37. Macks C, Jeong D, Bae S, Webb K, Lee JS. Dexamethasone-Loaded Hydrogels Improve Motor and Cognitive Functions in a Rat Mild Traumatic Brain Injury Model. Int J Mol Sci 2022;23:11153.
38. Chengke L, Weiwei L, Xiyang W, Ping W, Xiaoyang P, Zhengquan X, et al. Effect of infliximab combined with methylprednisolone on expressions of NF-κB, TRADD, and FADD in rat acute spinal cord injury. Spine (Phila Pa 1976) 2013;38:861–9.
39. Börcek AÖ, Çivi S, Öcal Ö, Gülbahar Ö. Effects of tumor necrosis factor alpha blocker adalimumab in experimental spinal cord injury. J Korean Neurosurg Soc 2015;57:73

DENEYSEL ÇALIŞMA - *ÖZ*

İnfliximab travmatik beyin hasarı sonrası oksidatif stresi azaltır mı?

AMAÇ: Travmatik beyin hasarı küresel bir sağlık sorunudur. İnfliximab çeşitli enflamatuvar sistemik durumların tedavisinde günlük olarak kullanılmaktadır. Çalışmamızın amacı künt kafa travmalı sıçanlarda deksametazon ve infliximab kullanımı sonucunda ortaya çıkan patolojik ve biyokimyasal değişiklikleri karşılaştırmaktır.

GEREÇ VE YÖNTEM: Bu çalışmada 32 yetişkin erkek Wistar sıçan kullanılmıştır. Sekiz hayvandan oluşan gruplar kullanıldı ve ek travma olmaksızın deri kesisi yapılanlar sham (grup 1); kafa deri kesisi ve kafa travması olanlar kontrol (grup 2); kafa deri kesisi ve kafa travmasından hemen sonra 1 mg/kg intraperitoneal deksametazon alanlar steroid (grup 3); kafa deri kesisi ve travmadan hemen sonra 5 mg/kg subkutan infliximab alanlar infliximab (grup 4) olarak adlandırılmıştır. Hayvanlar operasyondan 7 gün sonra ötanazi ile öldürüldü.

BULGULAR: Tüm grupların doku malondialdehit, süperoksit dismutaz ve glutatyon peroksidaz verileri göz önüne alındığında, bütünde istatistiki olarak pozitif bir fark vardı ($p<0.05$). Öte yandan, infliximab ve deksametazon grupları arasında doku malondialdehit, süperoksit dismutaz ve glutatyon peroksidaz konsantrasyonları açısından istatistiksel olarak anlamlı bir fark tespit edilmedi. Patolojik kesitler travmaya bağlı kortikal hasarın, intertisyel ödemin ve perivasküler ödemin infliximab grubunda daha az olduğunu göstermiştir.

SONUÇ: Infliximab, oksidatif stres belirteçlerinde deksametazon ile karşılaştırılabilir nöroprotektif etkiler gösterirken, ödemin azaltılmasında üstün etkinlik sağlar.

Anahtar sözcükler: Antioksidan; infliximab; kafa travması; sıçan modeli.

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