EXPERIMENTAL STUDY

Neuroprotective effects of pregabalin in experimental spinal cord injury: An investigation of oxidative stress and antioxidant enzymes in blood and neural tissue

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ABSTRACT

BACKGROUND: This study aimed to evaluate the neuroprotective potential of pregabalin (PB) and methylprednisolone (MP) in a rat model of spinal cord injury (SCI) by assessing serum and spinal cord levels of superoxide dismutase (SOD) and glutathione peroxidase (GPx), markers of oxidative stress, and neurological recovery outcomes.

METHODS: Forty-four rats were randomized into six groups: sham, PB control (40 mg/kg), SCI alone, MP-treated SCI (30 mg/kg), and PB-treated SCI (40 and 80 mg/kg). SCI was induced at the T10 level using the Allen weight-drop method. PB and MP were administered intraperitoneally for three days post-injury. Neurological recovery was assessed using the Tarlov scale and inclined plane test. Although 44 rats were initially allocated, mortality and technical loss resulted in a final cohort of 35 animals; however, post hoc power remained >90% for key biochemical outcomes.

RESULTS: SOD levels were significantly reduced in the MP+SCI group compared with the sham (p=0.006), SCI (p=0.015), 40 PB (p=0.004), and 80 PB+SCI (p=0.028) groups. Additionally, the SCI group exhibited lower SOD activity than the 40 PB group (p=0.007). Serum glutathione peroxidase levels were significantly lower in both the SCI (p=0.018) and 80 PB+SCI (p=0.009) groups compared with the sham group, whereas the 40 PB group showed higher GPx activity than the SCI (p=0.010) and 80 PB+SCI (p=0.006) groups. In spinal cord tissue, SOD activity in the 40 PB+SCI group was significantly lower than in the SCI group (p=0.007). Additionally, SOD activity in the SCI group was significantly higher than in the 40 PB group (p=0.007). Spinal cord GPx levels were significantly elevated in the SCI group compared with the sham (p=0.007), MP+SCI (p=0.010), 40 PB (p=0.003), 40 PB+SCI (p=0.003), and 80 PB+SCI (p=0.028) groups. Furthermore, the MP+SCI group demonstrated higher GPx activity than the sham group (p=0.045). Pregabalin improved inclined-plane performance but did not produce significant changes in Tarlov motor scores, indicating selective enhancement of postural stability rather than full locomotor recovery. Histopathological analysis revealed no significant differences between the trauma groups.

CONCLUSION: Pregabalin mitigated oxidative stress and partially improved functional stability in experimental spinal cord injury, suggesting possible clinical applicability pending further validation.

Keywords: Pregabalin; spinal cord injury; superoxide dismutase; glutathione peroxidase; antioxidant; methylprednisolone.

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INTRODUCTION

Spinal cord injury (SCI) is a devastating condition that can cause permanent motor, sensory, and autonomic dysfunctions.[1] SCI progresses in two phases: the primary phase, characterized by irreversible structural damage, and the secondary phase, driven by inflammation, oxidative stress, and excitotoxicity.[2,3] These secondary mechanisms exacerbate neuronal loss and drive long-term disability, making them critical therapeutic targets.

Reactive oxygen species (ROS) function as central mediators of secondary injury. ROS accumulation induces lipid peroxidation, protein and DNA damage, and mitochondrial dysfunction, ultimately triggering apoptosis and inflammation. Endogenous antioxidant enzymes, such as superoxide dismutase (SOD) and glutathione peroxidase (GPx), counteract these processes; however, this function is often insufficient in SCI.[4] Pregabalin (PB), an antiepileptic drug widely prescribed to treat neuropathic pain, binds to the α2-δ subunit of voltage-gated calcium channels, thereby reducing excitatory neurotransmitter release.[5-7] Beyond its analgesic properties, PB exerts neuroprotective effects by modulating oxidative stress and inflammatory responses.[5,8] In contrast, methylprednisolone (MP) is still used as a conventional treatment option, even though its efficacy and safety remain controversial.[9]

We hypothesized that PB would mitigate secondary injury after SCI by strengthening endogenous antioxidant defenses through modulation of SOD and GPx and by reducing excitotoxicity, thereby exerting neuroprotective effects equivalent or superior to those of MP. To test this hypothesis, the present study compared the effects of PB on antioxidant enzyme activity, histopathological alterations, and functional recovery with those of MP in an experimental SCI model in a dose-dependent manner.

MATERIALS AND METHODS

This study was conducted in accordance with the Guide for the Care and Use of Laboratory Animals (NIH publication no. 85-23, revised 1996). Ethical approval was obtained from the Experimental Animals Ethics Committee of İnönü University Faculty of Medicine (approval no. 2011 A-108).

Experimental Groups

Forty-four male Sprague–Dawley rats (250-400 g), all free of neurological deficits, were obtained from the İnönü University Experimental Animal Center. The study included six experimental groups: sham (laminectomy only, n=6), PB only (40 mg/kg, n=6), SCI (spinal cord injury and 0.5 cc saline, n=8), MP+SCI (30 mg/kg, n=8), PB+SCI (40 mg/kg, n=8), and PB+SCI (80 mg/kg, n=8). SCI was induced using the Allen weight-drop method in all groups except the sham and PB-only groups. Treatments were administered intraperitoneally at 30 minutes and 12, 24, 36, and 48 hours post-injury.

Anesthesia and Surgical Procedures

All rats were anesthetized with intraperitoneal xylazine (10 mg/kg) and ketamine (50 mg/kg). Following shaving and povidone–iodine disinfection, a midline incision was made at T9–L1. The paravertebral muscles were bluntly dissected, and T9–T11 laminectomies were performed. SCI was induced by exposing the intact dura and dropping a 5-g weight (2-mm tip) from a height of 10 cm onto the T10 level, according to the Allen weight-drop method (Fig. 1).

Drug Administration

PB (Lyrica®, 150-mg capsules) and MP (Sopharma) were administered intraperitoneally at 30 minutes and at 12, 24, 36, and 48 hours. PB powder was accurately weighed, suspended in sterile 0.9% saline, vortexed for homogeneity, and administered at doses of 40 or 80 mg/kg depending on group allocation.

Neurological Assessment

Motor function was evaluated on postoperative days 1–3 by a blinded neurosurgeon using the Tarlov scale and inclined plane test.[10,11] The Tarlov scale (0–5) was used to grade function as follows: 0=no movement (paraplegia), 1=minimal movement, 2=sitting with assistance, 3=sitting independently, 4=ambulation with abnormal gait, and 5=normal ambulation. Hind limb performance was further assessed using the inclined plane test, in which rats were positioned perpendicular to the platform, and the maximum angle maintained for ≥5 seconds without falling was recorded. Each rat was tested three times, and the mean value was used for analysis.

Sacrifice and Tissue Collection

At 72 hours, rats were anesthetized with intraperitoneal xylazine (10 mg/kg) and ketamine (50 mg/kg) and sacrificed by thoracotomy. Blood (2 mL) was drawn from the heart, centrifuged at 3000 rpm for 10 minutes, and the serum was collected and stored at −30°C. Spinal cords were harvested

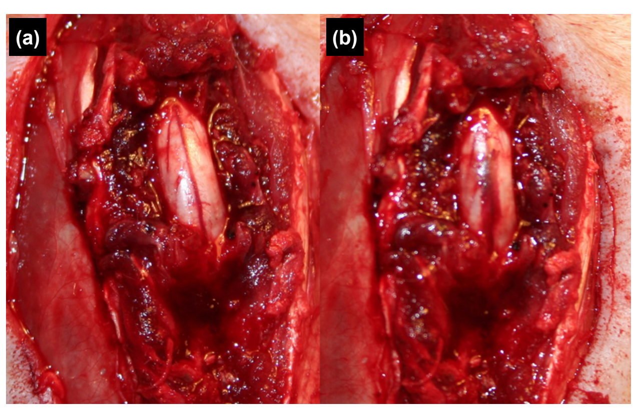

Figure 1. Postoperative laminectomy and induction of spinal cord injury at the T10 level. **(a)** Dorsal view following T9–T11 laminectomy, showing the intact dura mater. **(b)** Contusive spinal cord injury generated at the T10 level via the Allen weight-drop method, demonstrating traumatic disruption of neural tissue.

and divided into a 1-cm segment from the T10 lesion site for histopathology and a 2-cm caudal segment for biochemical analysis, both stored at −30°C.

Histopathological Evaluation

The T10 spinal cord segments were fixed in 10% formaldehyde, embedded in paraffin, and sectioned at 6 µm thickness. Hematoxylin–eosin–stained transverse sections were examined under a Leica DFC 280 microscope using image analysis software. The extent of hemorrhage, necrosis, and edema was graded semi-quantitatively based on the proportion of the affected area relative to the total cross-sectional area of the spinal cord as follows: 0, no damage; +, <25%; ++, 25–50%; +++, 50–75%; and ++++, >75%. This scoring system enabled standardized assessment of histopathological injury severity across experimental groups.

Biochemical Analysis

Superoxide dismutase and glutathione peroxidase activities were measured in spinal cord homogenates and serum. All samples were stored at −30°C until further analysis.

Preparation of Tissues for Biochemical Analysis

On the day of analysis, spinal cord tissues stored at −30°C were thawed, weighed, and homogenized (10% weight/volume [w/v]) in a phosphate buffer at 12,000 rpm for 1–2 minutes on ice. Homogenates were centrifuged at 5000 rpm for 30 minutes at 4°C, and the supernatants were collected for analysis.

Measurement of Enzyme Activities

SOD activity was determined using the method described by Sun et al.,[12] based on nitro blue tetrazolium (NBT) reduction. GPx activity was measured by monitoring the decrease in absorbance at 340 nm due to NADPH (nicotinamide adenine dinucleotide phosphate) oxidation during enzymatic activity, according to the method described by Paglia and George.[13]

Impact of Animal Losses on Statistical Power

Although the initial study design included 44 rats, losses reduced the final number to 35, creating some imbalance among groups. Nevertheless, post hoc power analysis demonstrated >90% power for key biochemical parameters, confirming the statistical robustness of our findings.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Due to small group sizes and non-normal data distributions, non-parametric tests were applied, including the Kruskal–Wallis test followed by Mann–Whitney U tests for pairwise comparisons. Effect sizes were reported as $\eta^2 H$ for Kruskal–Wallis tests and r for Mann–Whitney U tests, together with 95% confidence intervals. A two-tailed p-value <0.05 was considered statistically significant. Post hoc power analysis was conducted using G*Power (version 3.1; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) and demonstrated statistical power exceeding 90% for the primary biochemical outcomes.

RESULTS

Final Sample Size

Due to mortality, technical issues, or inadequate samples, the final group sizes were as follows: sham, n=5; PB 40 mg, n=6; SCI, n=7; MP+SCI, n=6; PB 40 mg+SCI, n=6; and PB 80+SCI, n=5.

Inclined Plane Test

Performance on the inclined plane test was significantly impaired in all trauma groups compared to controls on day 1 (p<0.01), confirming effective SCI induction. Both pregabalin-treated groups demonstrated superior motor recovery compared to the saline (SCI) and methylprednisolone (MP+SCI) groups. On days 1, 2, and 3, the 40 mg PB+SCI and 80 mg PB+SCI groups both showed significantly higher inclined plane angles than the SCI (p<0.004) and MP+SCI groups (p<0.006). Conversely, the 80 mg PB+SCI group showed no significant difference from the 40 mg PB+SCI group (p>0.05). A progressive, dose-dependent improvement was observed across three days, indicating enhanced motor recovery with pregabalin treatment compared to the MP and untreated trauma groups. The methylprednisolone (MP) group demonstrated statistically significant improvement in inclined-plane performance on post-injury days 2 and 3 compared with the saline-treated SCI group (p=0.008 and p=0.013, respectively) (Fig. 2).

Neurological Motor Function Results

Motor scores remained normal in the control and 40 mg PB-only groups (5.0±0.0). All trauma groups showed complete paralysis on day 1 (mean score of 0). By day 3, a dose-dependent trend of motor function improvement was observed in the pregabalin-treated groups, with the 80 mg PB+SCI group reaching the highest mean score (0.80±0.83), followed by the 40 mg PB+SCI group (0.5±0.83). However, these observed

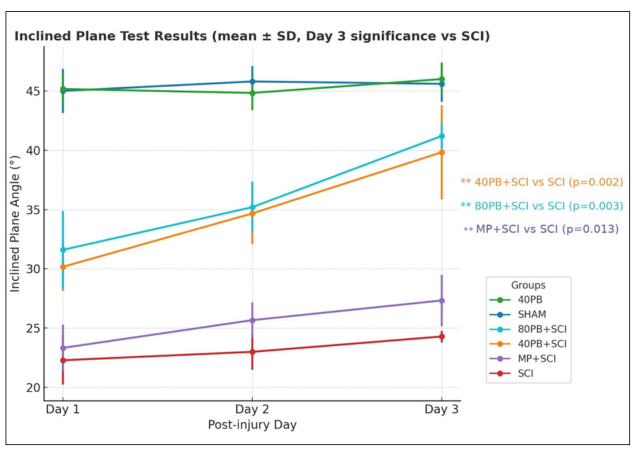

Figure 2. Inclined plane test outcomes (mean±SD) and corresponding p-values across experimental groups.

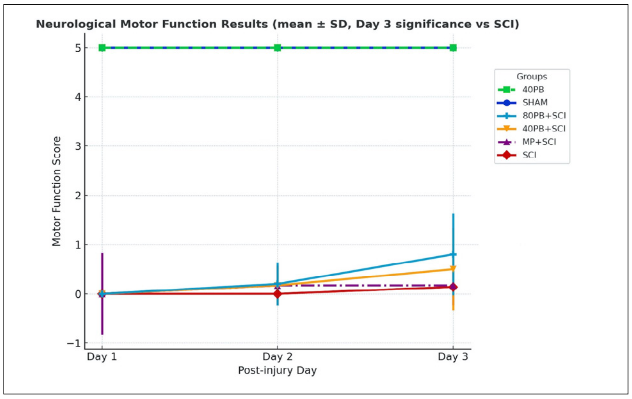

Figure 3. Neurological motor function outcomes (mean±SD) in experimental groups.

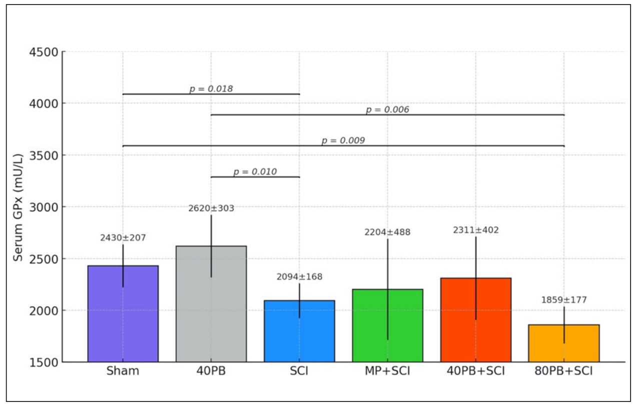

Figure 5. Serum glutathione peroxidase (GPx) levels (mean±SD) with corresponding p-values across experimental groups.

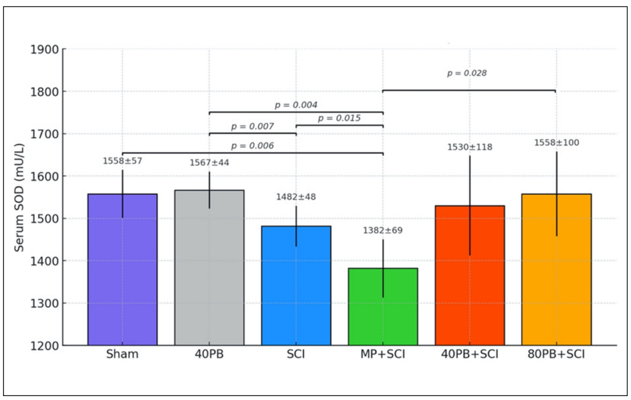

Figure 4. Serum superoxide dismutase (SOD) levels (mean±SD) with corresponding p-values across experimental groups.

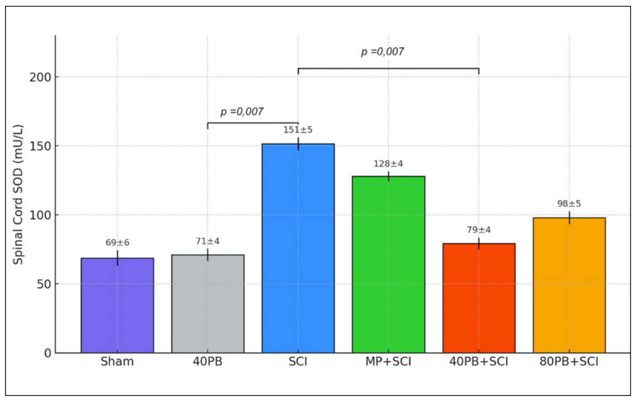

Figure 6. Spinal cord superoxide dismutase (SOD) levels (mean±SD) with corresponding p-values across experimental groups.

improvements did not reach statistical significance when compared to the SCI group (40 mg PB vs. SCI, p=0.383; 80 mg PB vs. SCI, p=0.097; MP vs. SCI, p=0.909 on day 3). Therefore, while a positive trend was noted, statistically significant locomotor recovery was not demonstrated within the 72-hour observation period (Fig. 3).

Serum SOD

Serum SOD levels differed significantly among the groups (Kruskal–Wallis H=15.40, p=0.009, η^2H=0.45, large effect). The MP+SCI group showed significantly lower values than the sham (p=0.006), SCI (p=0.015), and 40 mg PB (p=0.004) groups. The SCI group showed lower levels than the 40 mg PB group (p=0.007), and serum SOD levels were also significantly lower in the MP+SCI group compared with the 80 mg PB+SCI group (p=0.028). No other significant differences were observed (p>0.05). Post hoc power analysis confirmed high reliability (1–β=0.98) despite the reduced sample size (Fig. 4).

Serum GPx

Serum GPx levels also varied significantly (Kruskal–Wallis H=14.81, p=0.011, η^2H=0.44, large effect). Specifically, the SCI group showed significantly lower levels than the sham (p=0.018) and 40 mg PB (p=0.010) groups, whereas the 80 mg PB+SCI group showed significantly lower levels than the sham (p=0.009) and 40 mg PB (p=0.006) groups. No other significant differences were observed (p>0.05). Post hoc power analysis confirmed strong reliability (1–β=0.97) of the findings (Fig. 5).

Spinal Cord SOD

Spinal cord SOD levels differed significantly among the groups (Kruskal–Wallis H=13.06, p=0.023, η^2H=0.38, large effect). Spinal cord SOD levels in the SCI group were significantly higher than those in both the 40 mg PB+SCI group (p=0.007) and the 40 mg PB group (p=0.007). No other pairwise comparisons were statistically significant (p>0.05). Post hoc analysis indicated adequate statistical power (1–β=0.92) (Fig. 6).

Spinal Cord GPx

Spinal cord GPx levels differed significantly among the experimental groups (Kruskal–Wallis H=17.75, p=0.003, η^2H=0.52, large effect). Compared with the sham group, GPx levels

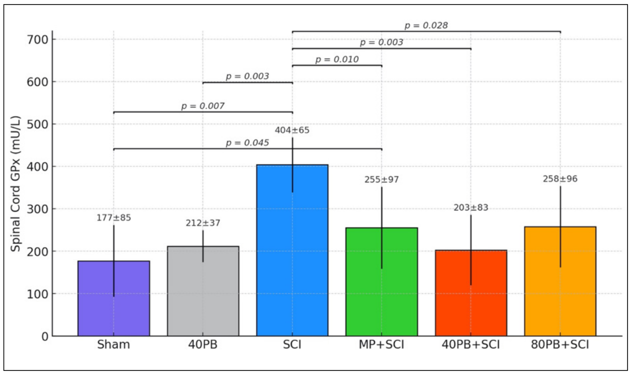

Figure 7. Spinal cord glutathione peroxidase (GPx) levels (mean±SD) with corresponding p-values across experimental groups.

were significantly elevated in the SCI (p=0.007) and MP+SCI (p=0.045) groups, indicating a trauma-induced oxidative response. Furthermore, GPx levels in the SCI group were significantly higher than those in the 40 mg PB (p=0.003) group, as well as the MP+SCI (p=0.010), 40 mg PB+SCI (p=0.003), and 80 mg PB+SCI (p=0.028) groups. These findings suggest that pregabalin and methylprednisolone mitigated spinal cord oxidative stress when administered after injury. MP+SCI animals showed slightly higher GPx activity than sham controls (p=0.045); however, this effect did not follow the overall trend of oxidative suppression and may reflect transient compensatory enzyme induction rather than true antioxidant improvement. Post hoc analysis confirmed excellent statistical power (1–β=0.997), reinforcing the robustness of these results (Fig. 7).

Histopathology

Histopathological evaluation revealed preserved spinal cord architecture in the control and 40 mg PB-only groups, with no evidence of hemorrhage, necrosis, or edema. In contrast, all trauma-induced groups (SCI, MP+SCI, 40 mg PB+SCI, and 80 mg PB+SCI) exhibited moderate-to-severe parenchymal damage, corresponding to histopathological scores of +++ (50–75%). These lesions were characterized by widespread hemorrhage, necrosis, and edema throughout the spinal cord. No statistically significant differences were observed among the treatment groups, indicating comparable structural injury patterns across all SCI models (Fig. 8).

DISCUSSION

Spinal cord injury leads to irreversible neuronal loss and paralysis, resulting in high morbidity and mortality.[3,14] Secondary injury mechanisms, including edema, ROS production, neuroinflammation, lipid peroxidation, calcium overload, and apoptosis, all play a central role in the progression of tissue damage.[2,3,15,16] Antioxidant enzymes such as SOD and GPx are critical for mitigating these processes; however, their activities can be suppressed under severe injury conditions.[17]

The present study evaluated the effects of PB and MP on

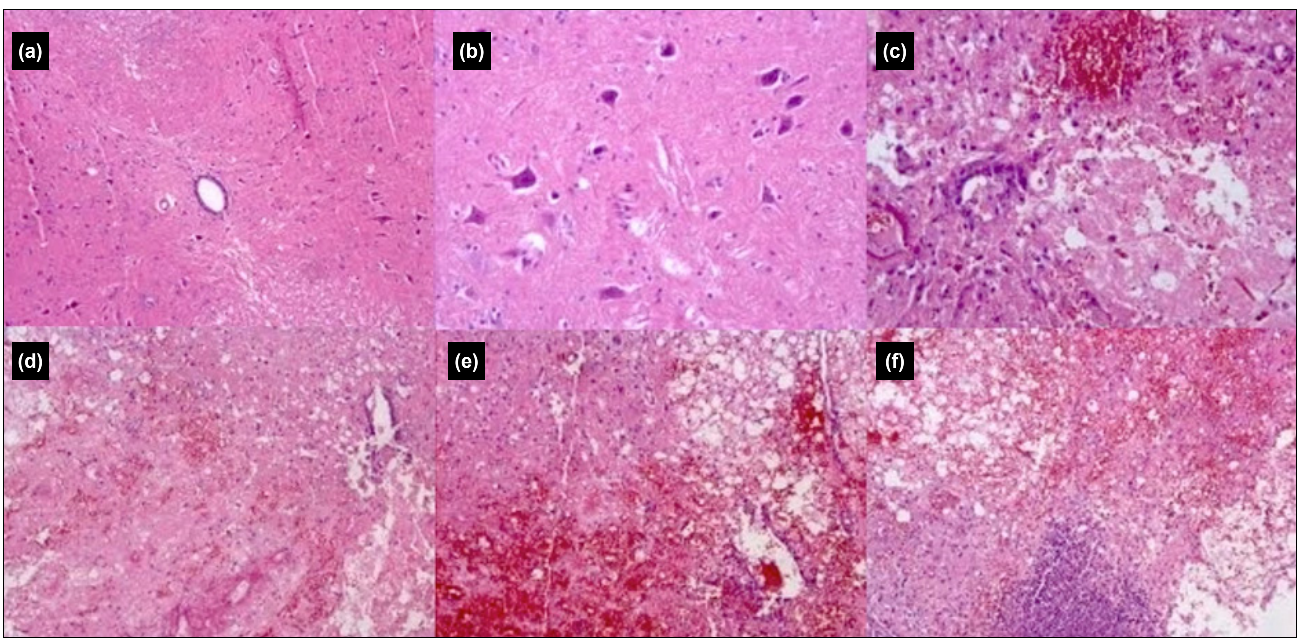

Figure 8. Histopathological abnormalities in hematoxylin and eosin-stained (H&E-stained) spinal cord sections from the study groups. Hematoxylin and eosin staining analyses of all groups: **(a)** Sham: Normal histoarchitecture with intact gray and white matter; **(b)** 40 PB: Preserved neuronal morphology in the substantia grisea. **(c)** SCI: Extensive hemorrhage and necrosis with disruption of central canal integrity; **(d)** MP+SCI: Diffuse hemorrhagic and necrotic areas accompanied by structural degeneration; **(e)** 40 PB+SCI: Widespread hemorrhage, necrosis, and edema with central canal disruption; **(f)** 80 PB+SCI: Severe hemorrhage and necrosis with prominent polymorphonuclear cell infiltration.

SOD and GPx activity in the serum and spinal cord tissue of SCI rats, as well as on their functional recovery. Pregabalin attenuated the SCI-induced elevation of spinal cord GPx activity at both doses while markedly suppressing SOD levels, particularly at 40 mg/kg. However, these changes were not evident in the serum, likely due to systemic dilution and pharmacokinetic factors. Although pregabalin showed partial modulation of serum antioxidant levels-particularly higher GPx activity in the 40 mg PB group compared to the SCI and 80 mg PB+SCI groups-these systemic effects were inconsistent relative to the localized spinal tissue response, likely due to dilution and pharmacokinetic variability. MP decreased serum SOD activity, indicating a distinct tissue-specific antioxidant profile. Although MP+SCI animals exhibited a marginal increase in spinal GPx compared with the sham group ($p=0.045$), this isolated fluctuation was inconsistent with the overall oxidative suppression trend and was therefore interpreted as a transient compensatory response rather than a genuine therapeutic effect. Overall, the antioxidant action of PB appears to be dose-dependent and predominantly localized to spinal tissue. Although the 80 mg PB+SCI group showed a paradoxical reduction in serum SOD compared with the MP+SCI group ($p=0.028$), this deviation from the expected dose-dependent trend may reflect pharmacokinetic saturation or a transient oxidative rebound at higher doses. Similar nonlinear antioxidant responses to pregabalin and other calcium channel modulators have been reported in previous neuroprotective models, suggesting that optimal dosing may require narrower therapeutic windows.

Methylprednisolone is a corticosteroid that reduces inflammation and limits tissue damage in SCI; however, its benefits for functional recovery remain controversial.[9,18,19] Although both PB and MP act through antioxidant and anti-inflammatory mechanisms, the clinical use of MP is limited by serious adverse effects, such as infection and gastrointestinal bleeding.[18]

Experimental models have highlighted the antioxidant potential of PB. In diabetic rats, PB increases brain SOD levels without affecting GPx, whereas nano-formulated PB increases SOD and glutathione levels in a fibromyalgia model.[8,20,21] Similarly, PB increases SOD and GPx activity in epilepsy and diabetic neuropathy models, thereby reducing oxidative stress.[8,20,22] In a spinal cord ischemia–reperfusion model, PB provided superior histopathological protection compared to MP.[7,23] These findings indicate that the antioxidant effects of PB vary depending on the experimental model and the specific parameters measured. In ischemia–reperfusion models, PB increases GPx activity.[24] Although its neuroprotective efficacy varies with dose and timing, several prior studies have confirmed its antioxidant effects.[23,25] Oxidative stress plays a central role in the pathogenesis of SCI.[8] Pregabalin administration has also been reported to significantly increase SOD and GPx activity and reduce MDA levels within 24 hours in an experimental traumatic brain injury model.[26] This finding indicates that pregabalin enhances antioxidant defense and mitigates oxidative stress during the early phase of traumatic injury, which is consistent with the GPx elevation observed in our spinal cord injury model. Pregabalin selectively strengthened postural resilience, improving inclined-plane resistance without restoring locomotor scores, indicating a partial rather than global neuromotor benefit. However, this functional gain did not translate into measurable histological protection, as no significant differences were detected in structural injury scores ($p>0.05$). This suggests that pregabalin exerts its early neuroprotective effects through metabolic and biochemical modulation rather than overt tissue preservation within the acute 72-hour period.

In the present study, PB partially improved GPx levels after SCI; however, its effects on antioxidant enzymes were less pronounced than those previously reported.[20,22,27] The marked increase in spinal cord GPx in the SCI group, together with the significant reduction of spinal SOD in the 40 mg PB+SCI group, confirms that oxidative stress is a major driver of secondary injury. Notably, these alterations were not consistently reflected in serum measurements, suggesting that systemic antioxidant levels may not accurately mirror local spinal cord redox status due to pharmacokinetic and compartmentalization differences. Differences between serum and spinal cord enzyme levels likely reflect pharmacokinetic and physiological factors, such as barrier permeability and local drug distribution.[28-30]

Our serum and spinal cord SOD/GPx findings alternately aligned with and diverged from those of previous reports, primarily owing to differences in experimental models, timing, and dosing. In previous studies using reversible SCI models, no significant changes in SOD or GPx levels were observed at 1, 4, or 24 hours, whereas in our study, marked increases were detected at 72 hours, suggesting that antioxidant responses may only be measurable after the acute phase.[31] Model-specific differences were also critical. Although GPx activity has been reported to decrease in ischemia–reperfusion models, the increase observed on day 3 in our contusion model likely reflects a compensatory response.[32] Differences in treatment protocols and dosing further contributed to these variations. For example, minocycline enhanced SOD/GPx activity, whereas the short-term, moderate-dose administration of PB and MP in our study produced limited systemic changes.[33] In summary, injury type, severity, timing, and treatment conditions collectively account for the variability observed in SOD/GPx outcomes across studies.

Discrepancies between histopathological findings and functional or biochemical improvements are expected in experimental models of acute SCI. Structural repair requires weeks to months to complete, whereas motor scores and biochemical markers may improve within a few days. This early recovery is attributed to reductions in edema, restoration of metabolic balance, and modulation of cellular signaling pathways.[34] Structural regeneration occurs during the subacute and chronic phases, and short follow-up periods are insufficient to demonstrate histological recovery. Routine hematoxylin–eosin (H&E) staining is limited in detecting early microstructural changes, whereas immunohistochemical markers, such as glial fibrillary acidic protein (GFAP), can reveal astrocytic activation and repair processes beginning on day 7.[35] Therefore, the absence of histopathological improvement in the acute phase should not be interpreted as treatment failure, but rather as a reflection of the delayed nature of structural repair. The fact that functional and biochemical recovery precedes histological changes indicates that acute-phase treatments primarily exert their effects through neuroprotective mechanisms.[34,35] Although this study was conducted in a rodent model, the results provide a mechanistic foundation for future translational studies. The established clinical use and safety of pregabalin in neuropathic pain management make it a promising candidate for repurposing in acute spinal cord injury. Nevertheless, interspecies differences in pharmacokinetics, metabolism, and dosing should be carefully addressed before clinical application.

Translation of experimental SCI models into clinical practice remains challenging due to interspecies biological, pharmacokinetic, and methodological discrepancies. Rodent models cannot fully reproduce the heterogeneous and chronic nature of human SCI, and drug doses proven safe in animals may yield different efficacy or adverse effects in humans. Therefore, preclinical benefits must be interpreted cautiously and validated through well-designed clinical trials.[36,37] To enhance translational value, large animal models with anatomical and physiological features closer to those of humans (e.g., pigs) have been recommended.[38] For PB, appropriate dose conversion, comprehensive safety analyses, and well-designed phase studies are all required to establish its clinical validity.

This study has certain limitations. The short follow-up period and small sample size may restrict the generalizability of the findings, and electron microscopy or confirmatory imaging (e.g., micro-computed tomography [micro-CT]) was not performed to validate structural injury. The rodent model cannot fully replicate human SCI, and interspecies pharmacokinetic differences may limit dose translation. Although sample size imbalance could increase the risk of type II errors, post hoc power analysis confirmed adequate statistical strength for key biochemical outcomes. Finally, the exclusive use of male rats and potential inter-observer variability should be considered when interpreting the results.

CONCLUSION

In the present study, PB demonstrated antioxidant activity in an experimental spinal cord injury model by normalizing spinal cord GPx levels and partially improving functional outcomes. Its neuroprotective effects appear to be mediated primarily by a reduction in oxidative stress. However, the precise mechanisms underlying these effects remain unclear, and further experimental studies are warranted to confirm them.

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Ethics Committee Approval: This study was approved by the Experimental Animals Ethics Committee of İnönü University Faculty of Medicine Ethics Committee (Date: 27.12.2011, Decision No: 2011/A-108).

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Authorship Contributions: Concept: B.O.G., M.E., M.G.; Design: B.O.G., M.E., Y.T.; Supervision: B.O.G., M.E., M.G., Y.T.; Resource: B.O.G., M.E., M.G., Y.T.; Materials: B.O.G., M.E., M.G., Y.T.; Data collection and/or processing: B.O.G., M.E., M.G.; Analysis and/or interpretation: B.O.G., M.E., Z.D.; Literature review: B.O.G., M.E., Y.T.; Writing: B.O.G., Z.D., M.E.; Critical review: Y.T., Z.D., M.E., B.O.G., M.G.

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DENEYSEL ÇALIŞMA - *ÖZ*

Deneysel spinal kord yaralanmasında pregabalinin nöroprotektif etkisi: Kanda ve nöral dokuda antioksidan enzimlerin oksidatif stres açısındandan incelenmesi

AMAÇ: Bu çalışma, oksidatif stres belirteçleri olan süperoksit dismutaz (SOD) ve glutatyon peroksidaz'ın (GPx) serum ve omurilik düzeylerini ile nörolojik iyileşme sonuçlarını değerlendirerek, sıçan omurilik yaralanması (SKY) modelinde pregabalin (PB) ve metilprednizolonun (MP) nöroprotektif potansiyelini araştırmayı amaçladı.

GEREÇ VE YÖNTEM: Kırk dört sıçan altı gruba randomize edildi: Sham, PB kontrol (40 mg/kg), yalnızca SKY, MP ile tedavi edilen SKY (30 mg/kg) ve PB ile tedavi edilen SKY (40 ve 80 mg/kg). SKY, Allen ağırlık düşürme yöntemi kullanılarak T10 seviyesinde oluşturuldu. PB ve MP, yaralanma sonrası üç gün boyunca intraperitoneal olarak uygulandı. Nörolojik iyileşme, Tarlov skoru ve eğik düzlem testi kullanılarak değerlendirildi. Başlangıçta 44 sıçan ayrılmış olsa da, mortalite ve teknik kayıplar nedeniyle nihai çalışma kohortu 35 hayvanla sınırlanmıştır; buna rağmen temel biyokimyasal sonuçlar için post-hoc güç analizi %90'ın üzerinde kalmıştır.

BULGULAR: MP+SKY grubunda SOD düzeyleri, sham (p=0.006), SKY (p=0.015), 40 PB (p=0.004) ve 80 PB+SKY (p=0.028) gruplarına kıyasla anlamlı derecede azalmıştı. Ayrıca SKY grubunda SOD aktivitesi, 40 PB grubuna göre daha düşüktü (p=0.007). Serum glutatyon peroksidaz (GPx) düzeyleri, hem SKY (p=0.018) hem de 80 PB+SKY (p = 0,009) gruplarında sham grubuna kıyasla anlamlı derecede daha düşüktü; buna karşın 40 PB grubunda GPx aktivitesi, SKY (p=0.010) ve 80 PB+SKY (p=0.006) gruplarına göre daha yüksekti. Omurilik dokusunda, 40 PB+SKY grubunda SOD aktivitesi SKY grubuna göre anlamlı derecede daha düşük bulundu (p=0.007). Ek olarak SKY grubundaki SOD aktivitesi, 40 PB grubuna kıyasla anlamlı derecede daha yüksekti (p=0.007). Omurilik GPx düzeyleri, SKY grubunda sham (p=0.007), MP+SKY (p=0.010), 40 PB (p=0.003), 40 PB+SKY (p=0.003) ve 80 PB+SKY (p=0.028) gruplarına kıyasla anlamlı derecede artmıştı. Ayrıca MP+SKY grubunda GPx aktivitesi sham grubuna göre daha yüksekti (p=0.045). Pregabalin, eğik düzlem performansını iyileştirdi ancak Tarlov motor skorlarında anlamlı bir değişiklik oluşturmadı; bu durum tam bir lokomotor iyileşmeden ziyade postüral stabilitenin seçici olarak arttığını düşündürdü. Histopatolojik analizde ise travma grupları arasında anlamlı bir fark saptanmadı.

SONUÇ: Pregabalin, deneysel omurilik yaralanmasında oksidatif stresi azalttı ve fonksiyonel stabiliteyi kısmen iyileştirdi; bu durum, ileri doğrulama çalışmalarının ardından klinik uygulamaya uygun olabileceğini düşündürmektedir.

Anahtar sözcükler: Antioksidan; glutatyon peroksidaz; metilprednizolon; omurilik yaralanması; pregabalin; süperoksit dismutaz.

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