The Effect of Nigella Sativa Supplementation on Il-6 Levels And Outcomes In Patients With Mild To Moderate Non-Operative Head Injury At Haji Adam Malik General Hospital, Medan

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ABSTRACT

Background: Head injury is a major cause of disability and death, with neuroinflammation playing a key role in long-term complications. Nigella sativa (black cumin) has shown neuroprotective and anti-inflammatory effects. This study evaluates its impact on IL-6 levels and clinical outcomes in non-operative mild to moderate traumatic brain injury (TBI) patients.
Methods: A randomized clinical trial (RCT) was conducted on 72 TBI patients divided into three groups: placebo, 500 mg/day Nigella sativa, and 1000 mg/day Nigella sativa. IL-6 levels were measured at baseline, day 3, and day 7. Data were analyzed using statistical tests with $p < 0.05$ considered significant.
Results: Patients receiving 1000 mg/day Nigella sativa showed the greatest reduction in IL-6 levels. All patients recovered well, with a Glasgow Coma Scale (GCS) score of 15 and no neurological deficits.
Discussion: Nigella sativa reduced IL-6 levels, suggesting its potential to manage neuroinflammation in TBI patients. The findings align with previous research on its anti-inflammatory and neuroprotective properties.
Conclusion: Nigella sativa, especially at 1000 mg/day, may help reduce inflammation in TBI patients without affecting recovery. Further studies are needed to confirm its benefits.

Keywords: Traumatic brain injury, Nigella sativa, IL-6, neuroprotection, inflammation.

INTRODUCTION

Head injury is a major cause of mortality and morbidity among individuals aged 18–45, with traffic accidents (62.5%) and falls (15.6%) being the most common causes. Despite improved awareness, structured management, and technological advancements reducing fatality rates, many survivors experience long-term disabilities, including cognitive decline, psychiatric disorders, and social dysfunction.[1,2]

Traumatic brain injuries (TBIs) are categorized as mild, moderate, or severe based on the Glasgow Coma Scale (GCS). Moderate to severe TBIs often require intensive medical care, with 40% of non-fatal cases resulting in long-term disability. Secondary brain injury, which occurs minutes to days after the primary trauma, involves inflammatory and molecular cascades that exacerbate neurological damage. Elevated interleukin-6 (IL-6) levels play a critical role in neuroinflammation and are associated with worse outcomes and systemic organ dysfunction.[2-4]

Nigella sativa (black cumin), a widely used traditional medicinal herb, has demonstrated neuroprotective and anti-inflammatory properties. Its active compound, thymoquinone, has shown potential in reducing infarct volume and improving motor function in experimental brain injury models. Despite advancements in preventive measures, surgical techniques, and diagnostic tools, there is still no effective pharmacological treatment targeting secondary brain injury.[5]

This study aims to evaluate the neuroprotective effects of Nigella sativa extract in moderate-to-severe TBI patients who do not undergo surgical intervention. By assessing IL-6 levels, this research seeks to determine the potential role of Nigella sativa in mitigating neuroinflammation and improving clinical outcomes.

METHODS

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This study utilizes a Randomized Clinical Trial (RCT) design, ensuring both subjects and data collectors remain blinded to treatment allocations, with group randomization performed using specialized software. The research aims to assess the effect of Nigella sativa supplementation on IL-6 levels and clinical outcomes in non-operative mild to moderate traumatic brain injury (TBI) patients at Haji Adam Malik Hospital, Medan. Ethical clearance and hospital approval are obtained before commencing the study, which is expected to last 2–3 months until the required sample size is reached.

Participants meeting the inclusion criteria aged 18–64 years, diagnosed with mild to moderate TBI, and providing informed consent are randomly assigned to one of three groups: Group A (placebo, 2 tablets), Group B (Nigella sativa 500 mg/day, 1 supplement + 1 placebo), and Group C (Nigella sativa 1000 mg/day, 2 supplements). The exclusion criteria include patients with contraindications to the study medications and those requiring surgical intervention. The intervention spans 7 days, with IL-6 levels and patient outcomes evaluated at baseline (T0), day 3 (T1), and day 7 (T2). Observations include recording supplement administration times and monitoring adverse effects. Patients may drop out if their condition worsens, necessitating surgery or ICU transfer, if they experience allergic reactions, or if they suffer cardiac arrest within 7 days.

Collected data is processed using Microsoft Excel 365 and analyzed with SPSS v.26, with statistical significance determined at $p < 0.05$ and a 95% confidence interval ensuring robust result interpretation.

RESULT

This study included 72 participants who met the inclusion and exclusion criteria**,** divided into three groups**:** Group A (placebo), Group B (Nigella sativa 500 mg), and Group C (Nigella sativa 1000 mg). The mean age of participants was 35.56 ± 16.86 years, with no significant difference between groups **(**Group A: 31.42 ± 13.78 years, Group B: 35.04 ± 16.39 years, Group C: 40.21 ± 19.44 years). Regarding gender distribution**,** 66.7% of participants were male and 33.3% were female, with no statistically significant differences between groups.

Table 1. Results of IL-6 Level Analysis

Time	Group				
	Total	A	B	C	P
T0	3,36	3,45	5,40	4,65	0,045
T1	3,16	3,52	5,18	4,19	0,170
T2	3,24	3,09	4,85	3,35	0,318

Table 2. Results of ΔIL-6 Analysis

Time	Group			
	A	B	C	P
T1 - T0	0,07	-0,22	-0,47	0,042
T2 - T1	-0,42	-0,33	-0,83	0,047
T2 – T0	-0,35	-0,55	-1,30	0,002

IL-6 levels were measured at T0 (baseline), T1 (day 3), and T2 (day 6). Since the normality test yielded $p < 0.05$, the Kruskal-Wallis test was applied for non-parametric analysis**.** At T0, a significant difference in IL-6 levels was observed, with Group A having the lowest levels, followed by Group C and Group B. However, at T1 and T2, the differences were no longer statistically significant. When analyzing ΔIL-6 (changes in IL-6 levels over time), Group C showed the highest IL-6 reduction, followed by Group B and Group A, with statistically significant differences. Multiple pairwise comparisons revealed significant differences between Group C and A (T1-T0, $p = 0.035$; T2-T1, $p = 0.050$; T2-T0, $p = 0.001$) and Group C and B (T2-T0, $p = 0.043$)**.**

Table 3. Further Analysis of ΔIL-6

Time	Group	P-value	Adj. P-value
T1 – T0	**C-B**	0.231	0.694
	C-A	0.012	0.035
	B-A	0.186	0.559
T2 – T1	**C-B**	0.085	0.254
	C-A	0.017	0.050
	B-A	0.503	1.000
T2 – T0	**C-B**	0.014	0.043
	C-A	P<0.001	0.001
	B-A	0.268	0.804

In terms of clinical outcomes, all patients had a GCS score of 15 with no neurological deficits**,** indicating a good recovery. This aligns with IL-6 measurements, as there was no significant difference at T2, despite the initial differences at T0. These findings

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suggest that Nigella sativa supplementation, particularly at 1000 mg/day, may contribute to IL-6 reduction without negatively impacting patient recovery.

DISCUSSION

Nigella sativa (NS) has been utilized since ancient Babylonian times for treating various conditions, including edema, hair loss, bruises, and digestive disorders. It possesses antioxidant, anti-inflammatory, and antifibrotic properties, making it a promising therapeutic agent for various diseases. Research has highlighted its significant benefits for the nervous system, including anti-inflammatory effects, antiepileptic activity, neuroprotection against oxidative stress, and antineurotoxic properties. Furthermore, NS has demonstrated hepatoprotective, antihypertensive, and antidiabetic effects.[6,7]

The neuroprotective properties of NS and its active compound, thymoquinone (TQ), have been shown to mitigate neural damage resulting from traumatic brain injury (TBI) and spinal cord trauma. Experimental studies indicate that NS reduces lipid peroxidation in the hippocampus following ischemia-reperfusion injury (IRI) and ameliorates neurodegenerative morphological changes in the frontal cortex and brainstem. Additionally, NS has been found to decrease mortality rates, enhance locomotor activity, and restore neurotransmitter levels—such as serotonin, dopamine, and gamma-aminobutyric acid (GABA)—in animal models of TBI, including rats and *Drosophila melanogaster*. The mechanism underlying NS and TQ's neuroprotective effects involves the activation of the Nrf2 and NF-κB pathways, which enhance antioxidant enzyme activity and suppress oxidative stress.[8-11]

This study revealed a significant reduction in IL-6 levels following NS administration, with the most pronounced effects observed at a dosage of 1000 mg. These findings align with previous research demonstrating NS and TQ's capacity to alleviate oxidative stress and apoptosis in secondary brain injury. Additionally, the study reported favorable clinical outcomes, as all patients who received NS exhibited a Glasgow Coma Scale (GCS) score of 15 without neurological deficits. This supports prior experimental findings that suggest NS exerts neuroprotective effects within 72 hours of administration. The results underscore NS's potential as a therapeutic intervention for managing neuroinflammation and oxidative damage in non-operative mild to moderate head injuries, highlighting its role in improving post-injury recovery and neurological outcomes.[9,12,13]

CONCLUSION

Nigella sativa demonstrates significant neuroprotective effects by reducing IL-6 levels, mitigating oxidative stress, and improving neurological outcomes, making it a promising therapeutic candidate for managing mild to moderate traumatic brain injuries.

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