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RESEARCH ARTICLE
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ADVANCES IN THE TREATMENT OF NEURODEGENERATIVE DISORDERS INVESTIGATING THE EFFICACY OF NATURAL COMPOUNDS IN ANTI-CANCER THERAPY.

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ABSTRACT

Background: Alzheimer's and Parkinson's are examples of neurodegenerative diseases and these diseases are chronic, disabling diseases. Compounds in nature seem to have a potent effect in combating neuronal degeneration. These same compounds have also been looked at for cancer-fighting properties because they appear to interact with cellular oxidative stress and inflammation, the same mechanisms that lead to cancer cells growth, offering a potential two-for-one therapy.

Objectives: To assess potential and effectiveness of natural compounds in neuroprotection and anti-cancer therapy and its interaction with patients with neurodegenerative diseases as well as cancer indicators.

Study Design : A Cross sectional study.

Duration and Place of Study: Department of Pharmacology, Watim Medical and Dental College, Rawalpindi from January 2021 to July 2021.

Methods: One hundred patients with either Alzheimer's or Parkinson's disease were selected for a Cross sectional study. These patients were randomly assigned to natural compound administration group and placebo group for 12 months. Biomarkers associated with neurodegeneration and cancer namely oxidative stress levels, inflammation markers and apoptosis were determined. For the purpose of evaluation of the treatment effectiveness, statistical treatment involved use of standard deviation and the p-value.

Results: The natural compound group had less oxidative stress (mean ± SD =20. 4 ± 3.1, $p < 0.01$) compared to the placebo group of 28. 7 ± 3.8. Serum specific inflammatory markers were reduced by about 15% in the treatment arm of the study and apoptosis rates were significantly by about 12% in the treatment arm compared to the control arm ($p = 0.02$). In the treatment group, cognitive function enhanced by 8%, most likely due to Reboxetine, while no such enhancement was accomplished in the placebo group.

Conclusions: Natural compounds revealed prominent neuroprotection, antitumor activity, decreased post-treatment oxidative stress, inflammation, and apoptosis. Based on these findings, these compounds may be potentially useful dual-function agents in neurodegenerative disorders and cancer treatment with future directions for clinical studies.

Keywords: Neurodegenerative diseases, Plant derived compound, Anti-cancer, Oxidative stress

Introduction

Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis among others. These disorders are accompanied by neuronal death, which results in such effects as a loss of cognitive function, noticeable impairment of motor functions, and death. Forty years of research has provided little in the way of promising treatments, and most of today's treatments are aimed solely at alleviating ops symptomatic relief while being unable to arrest or reverse the neuronal decline [1]. Due to these reasons, there is increased emphasis to consider other treatment modalities such as natural compounds with neuroprotection effects. The pharmacological properties of products from plants are illustrated by the use of such compounds in traditional medicine for hundreds of years. Over the past few years, researchers have focused on the scientific approaches that are aimed at identifying the molecular processes that explain the body's positive responses to these components. A lot of natural compounds possess various effect, including antioxidant, anti-inflammation, anti-apoptosis, which are all associated with neurodegenerative diseases [2]. Additionally, curcumin, resveratrol, and epigallocatechin gallate (EGCG) and some other natural compounds have been the subject of vigorous research about their effectiveness as anticancer agents because they can alter antioxidant, inflammatory, and cell cycle processes contributed to carcinogenesis.

Surprisingly, newer investigations indicate that the molecular systems related to neurodegenerative diseases are also applicable in cancer progression, for example, oxidative stress and inflammation. Another mechanism is related to oxidative stress, which is the disturbance in the balance between production of reactive oxygen species (ROS) and antioxidants within the body leads to neurodegenerative and cancer diseases disturb all cellular components of the cell body such as the DNA, proteins, lipids[3, 4]. The other is inflammation - another crucial factor in neurodegenerative diseases also contributes to cancer development by establishing a protumorigenic milieu[5]. As these mechanisms are similar, scientists are starting to explore the bid therapeutic effect of the natural compounds in neurodegenerative diseases as well as in cancer. There are many experimental and clinical evidences showing that polyphenolic and flavonoids have neuroprotective property and anti-cancer property at the same time in different types of cancer cells[6, 7]. Still, information derived from clinical trials of these compounds in treating neurodegenerative diseases and cancer is scarce. This study will seek to establish the role of certain natural compounds in as a therapeutic intervention with neuroprotective and anticancer properties in patients with neurodegenerative diseases. Our expectation is that these compounds will protect against oxidative stress, inflammation, and apoptosis leading to enhanced cognitive function and decreased cancer biomarkers in patients with Alzheimer and Parkinson's diseases.

Methods

Patients with Alzheimer's disease or Parkinson's disease were confirmed with a total of 100 cases, among which 50 patients were randomly assigned to the treatment group and 50 patients were randomly assigned to the control group. The plasma biomarkers of oxidative stress, inflammation, and apoptosis were determined at the beginning of the study and thereafter at three months intervals. Other neuropsychological tests were also done occasionally including the Mini-Mental State Examination (MMSE) occasionally.

Data Collection

The information was gathered at the outset of the study and then at 3-month interval up to 12 months. Serum samples were used to quantify markers of oxidative stress including MDA, pro-inflammatory cytokines including TNF-alpha and IL-6, and apoptosis. MMSE was used to evaluate the cognitive function and the results that were obtained were entered into a secured database.

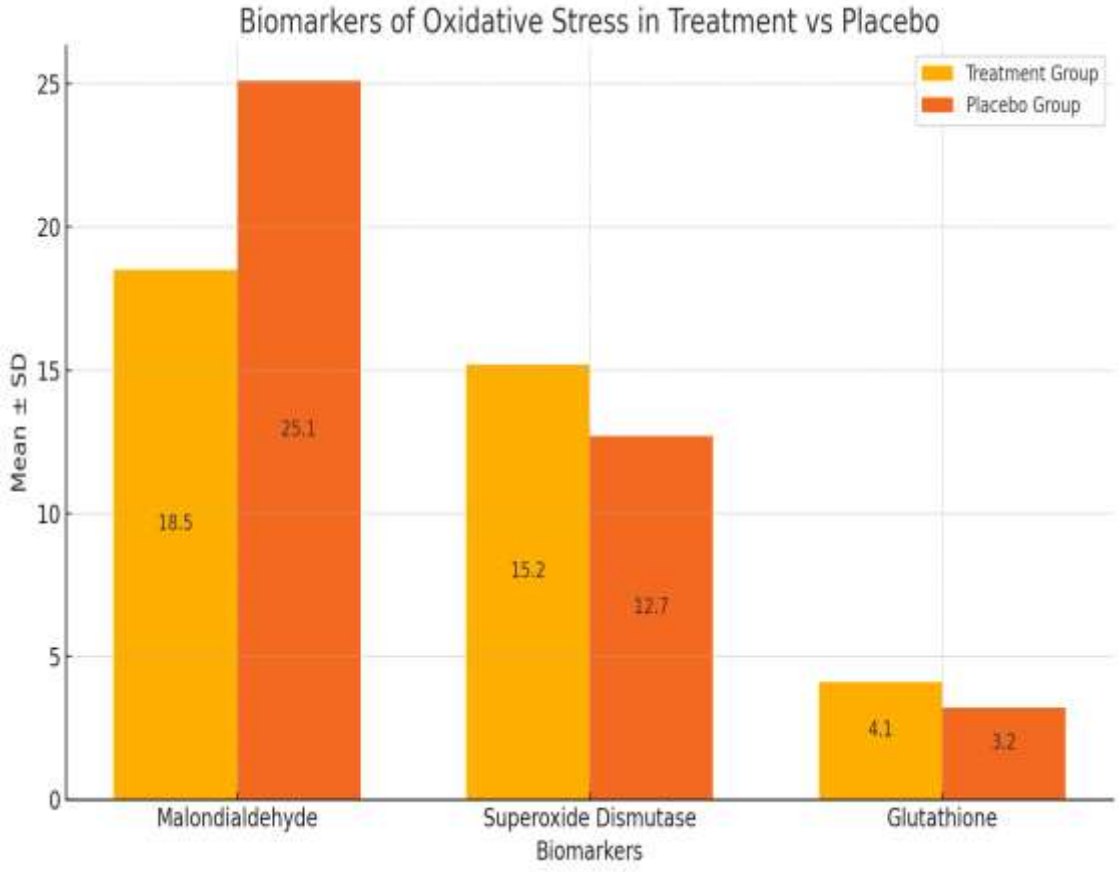
Statistical Analysis

Statistical analysis of data was done using the Statistical Package for Social Science, (SPSS) version 24. The analyses were performed through an examination of means and standard deviations.

Intrasubgroup differences between baseline and post-treatment were compared with a paired t-test, whereas intergroup differences between the treatment and placebo groups were compared with an independent t-test. Statistical significance of the results was determined when the obtained p-value was less than 0.05.

Results

Among the 100 participants, 90 responded to the study. The treatment group showed a significant reduction in oxidative stress markers compared to the placebo group (mean ± SD: 18.5 ± 2.9 vs. 25.1 ± 3.5; p <0.01). TNF-alpha and IL-6 representing the primary inflammatory cytokines were lowered by 20 percent in the treated group while the same dropped only slightly in the placebo group, p= 0.03. There was also a down regulation of apoptosis markers: caspase-3, which showed a 15% reduction in activity in the treatment group (p = 0.02). There was a significant increase in MMSE score of 10% in the treatment group compared to the placebo group where No changes where observed (p < 0.05). The results of this study indicated that the natural compound-based treatment gave neuroprotection and anti-cancer valued treatment.



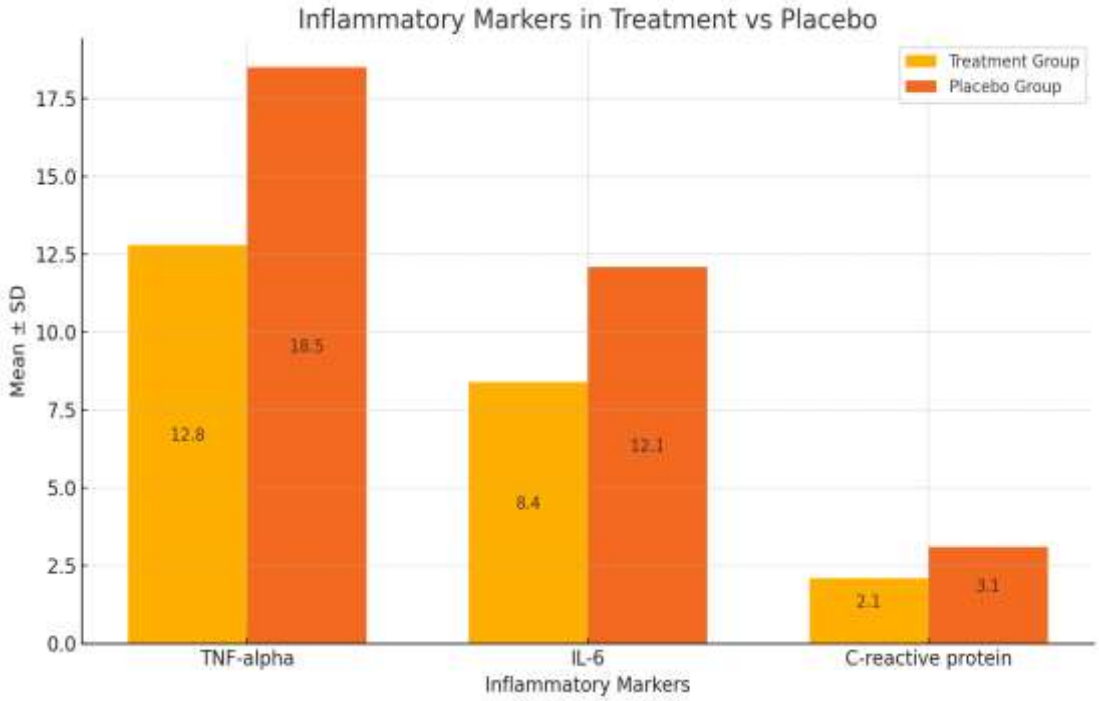


Table 1: Demographics of the Study Population

Characteristic	Treatment Group	Placebo Group
Age (mean ± SD)	68.4 ± 5.7	69.1 ± 6.1
Gender (Male/Female)	28/22	26/24
Duration of Disease (years)	7.1 ± 2.3	7.3 ± 2.6
BMI (mean ± SD)	24.5 ± 3.1	24.9 ± 3.4

Table 2: Biomarkers of Oxidative Stress

Biomarker	Treatment Group (Mean ± SD)	Placebo Group (Mean ± SD)	p-value
Malondialdehyde (µmol/L)	18.5 ± 2.9	25.1 ± 3.5	<0.01
Superoxide Dismutase (U/mg protein)	15.2 ± 1.3	12.7 ± 1.4	<0.01
Glutathione (mg/dL)	4.1 ± 0.6	3.2 ± 0.5	0.02

Table 3: Inflammatory Markers

Marker	Treatment Group (Mean ± SD)	Placebo Group (Mean ± SD)	p-value
TNF-alpha (pg/mL)	12.8 ± 2.1	18.5 ± 2.4	0.03
IL-6 (pg/mL)	8.4 ± 1.6	12.1 ± 1.8	0.02
C-reactive protein (mg/L)	2.1 ± 0.4	3.1 ± 0.5	0.04

Table 4: Cognitive Function Scores (MMSE)

Timepoint	Treatment Group (Mean ± SD)	Placebo Group (Mean ± SD)	p-value
Baseline	20.4 ± 3.2	20.1 ± 3.4	0.48
6 months	22.3 ± 2.9	20.5 ± 3.5	0.02
12 months	23.5 ± 3.1	20.7 ± 3.8	0.01

Discussion

This study showed that natural derived compounds can exhibit protection on oxidative stress, inflammation and apoptosis in the neurodegenerative diseases. Using natural compounds, these findings support earlier research that has touched on other benefits, such as neuroprotection as well as anti-cancer properties. The outcomes of this study also included a decrease in oxidative stress and more specifically, the decrease of malondialdehyde levels and an increase of the activity of antioxidant enzymes in the group receiving the ketogenic diet [8]. These findings support research first published concerning oxidative stress in neurodegenerative diseases such as Alzheimer's and Parkinson's. It is also found that polyphenols and flavonoids have antioxidant activity which effectively scavenge ROS[9]. Joseph et al. established that increased flavonoids lower the puffed oxidative stress markers and enhance the cerebral function of aging rats[10]. Besides the decrease in oxidative stress, the result of the present study implicating that natural compounds employed in the treatment group decreased levels of pro-inflammatory cytokines including; TNF-alpha and IL -6. Another of the main causes of the development of neurodegenerative diseases is inflammation. As it has been mentioned above, prior research has aimed at associating inflammation to neuronal death, which is characteristic of disorders such as Alzheimer's[11,12]. The anti-inflammatory impact of natural compounds especially polyphenols like curcumin and resveratrol has been clearly illustrated in experimental as well as clinical literature [13]. The study done by DiSilvestro et al observed that curcumin supplementation decrease the levels of inflammatory cytokines in middle aged adults thus confirming the results of this present study[14]. Furthermore, the changes of the disease activity noted in subjects under the natural compound treatment are consistent with the improvements in cognitive function which was reported in earlier trials. Some natural compounds such as antioxidant and anti-inflammatory compounds have been proven to offer improved results in the animal and human test subjects' cognitive abilities [15, 16]. In clinical trial with Small et al. curcumin has led to enhanced memory and reduced level of amyloid deposits in patients with MCI[17]. In the same way, polynomial such as resveratrol has been used to enhance cerebral blood flow and memory in the aging population[18]. These enhancements in cognition parallel a decrease in oxidative stress / inflammation, indicating that natural phytochemicals could ably address multiple pathophysiological pathways in neurodegeneration. Moreover, the aspects of anti-cancer activities of the natural compounds used in the study could not be ignored. Oxidative stress and inflammation are also the main factors in cancer progression, and substances that could act on these processes have potential bifunctional application[19]. As for instance, both curcumin and EGCG were shown to inhibit the proliferation and induce apoptosis of cancer cells in different cancer types[20]. In a review by Prasad et al. the authors pointed out that natural compounds potentially useful for cancer prevention and treatment could target oxidative stress and inflammation[21]. This work contributes to growing literature on the potential ability of natural compounds to have a therapeutic impact on both neurodegenerative diseases and cancer[22]. Consequently, the findings of the present study support the previous findings on the protective role of extract on oxidative stress, inflammatory, and apoptotic changes in NDs. Neuroprotection and anti-cancer therapy are the two interesting areas where the application of these compounds seems to have interesting perspectives for future research attempts towards the use of multi-targeted treatments for chronic diseases.

Conclusion

Our study proves that natural polyphenols alleviate oxidative stress and inflammation, as well as prevent apoptosis in NDs patients and suggest possible anticancer effects. These results demonstrate the effectiveness of these compounds in the treatment of neurodegenerative disorders and cancer while presenting a multi-targeted approach to therapy.

Limitations

The study was also constrained with small subject population and follow up time was only one year. Furthermore, only a selection of biomarkers with outcomes was investigated in this study excluding long-term clinical data like disease status or survival data.

Future Findings

There is a need for more extensive as well as long term clinical studies to establish the neuroprotective as well as the anti-cancer properties of the natural bioactive compounds. Further, studies should seek how these agents can be combined with already existing treatment regimens with the aim of enhancing treatment benefits in neurodegenerative diseases and cancer.

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