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Review Article

Review on the Role of Herbs in Schizophrenia

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ABSTRACT

Herbal supplements are used widely all over the world for prevention, delaying onset, decreasing overall severity, and potential reversal of mental illness. The main aimof the overview is to communicate the latest observations regarding the effectiveness of herbal and nutraceutical supplements in the prevention, treatment, and delaying onset of symptomology related to schizophrenia and other schizoaffective disorders, also to explore their laentrole in the future of psychiatry and related health practices. The supplements and their effectiveness studied in this literature overview are Omega-3 fatty acids, curcumin, folic acid, B_{12}, B_6, Vitamin D, N-acetylcysteine, SAM-e, *Bacopa monniera*, *Ginkgo biloba*, iron and glycine.

Key words: Schizophrenia, Herbs, Curcumin, Folic Acid, B_{12}, B_6, Vitamin D, N-acetylcysteine, SAM-e, *Bacopa monniera*, *Ginkgo biloba*, Iron and Glycine.

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INTRODUCTION

Several studies have reported the effects of herbal and nutraceutical supplements on the symptoms of mental illness. Fall in mental illness symptomology has been noticedby using particular phytochemical, adaptogenic herbs, essential fatty acids, and traditional medicines.[1] Out of 422,000 flowering plants that have been reported around the world, over 50,000 are used medicinally.[2] Specifically, schizophrenia and schizoaffective disorders have benefitted from the supplementation of herbs and nutraceuticals. Schizophrenia is a severe psychiatric disorder which adversely affects wide-range of cognitive functions like executive functioning, memory and attention.[3] It is characterized by negative symptoms (like emotional blunting and apathy), positive symptoms (hallucinations and delusions), and impairment of cognition. The standard treatment eradicatesthese negative, positive, and cognitive symptoms. Antipsychotic medications help in decreasing positive symptoms, but show almost no response in regard to negative symptoms and cognitive impairment. The etiology of schizophrenia is multifactorial, with a particular combination of environmental circumstances and biological predisposition that plays a major role.[4] Moreover, in individuals with schizophrenia, consumption of essential amino acids, vitamins, and nutritional building blocks to raise levels of neuroprotective chemicals such as endogenous glutathione can reduce cortical inflammation and help maximize the body's innate compensatory homeostatic healing mechanisms to deal more efficiently with states of psychosis have been reported.[5]

LITERATURE REVIEW

Omega-3 fatty acids, or PUFAs, have many possibilities for the treatment of psychotic disorders. Omega-3 PUFAs provide anextensive scope of neurochemical activities through modulation of the reuptake, degradation, synthesis and receptor binding actions of noradrenaline, dopamine and serotonin. Omega-3s also have anti-inflammatory and anti-apoptotic effects in addition to their substantial activity in increasing neurogenesis and cell membrane fluidity.[6] Omega-3 fatty acids may also decrease the risk of pathogenesis with psychotic disorders and reduced risk of psychiatric morbidity. Individuals treated with omega-3 group no longer showed severe functional impairment, and did not experience dramatic psychotic symptoms upon a 6.7 year follow-up of in a randomized, double-blind, placebo-controlled trial.[7] Those suffering from mental illness are often remarkably deficient in Omega-3 fatty acids.[8] Research also suggests the brains of schizophrenic persons have extreme abnormalities in myelin sheaths, oligodendrocytes, and implies that Omega-3 fatty acids are important for reparation and maintenance. The Omega-3 fatty acideicosapentaenoic acid (EPA) helps in the maintenance of a balanced mood and improving blood flow. It is proven to have major antidepressant properties in rodents and humans without any such adverse effects.[9] A 6 week placebo-controlled study has noted chronic supplementation of curcumin (1,000 mg daily) generatedmajor antidepressant behavioral responses in depressed patients.[10] Curcumin reduces levels of the inflammatory cytokines interleukin 1β and tumor necrosis factor α, and increases brain-derived neurotropic factor (BDNF) levels in plasma concentrations, while reducing concentrations of salivary cortisol as compared to placebo.[11] In patients with Alzheimer's disease (AD), it was discovered that curcumin eases the recovery of cognitive decline and psychological symptoms of dementia (BPSD). After 12 weeks of treatment, significant decreases in the acuity of symptoms and the burden on caregivers was seen. Within one year of treatment with curcumin, AD patients began to recognize their families once again. Curcumin shows antioxidant, anti-inflammatory, and anti-cancer properties. And is known to act as a neuroprotective agent in neurological disorders and can cross the blood-brain barrier with noteworthy bioavailability.[8] It is also effective in the amelioration of motor symptoms in Parkinson's disease. Furthermore, it modulates oxidative-stress induced apoptosis and neuro inflammation.[12] Curcumin extract was able to significantly restore depleted glutathione levels and recover oxidative damage after 72 hrs sleep deprivation in mice. Lastly, curcumin extract lessens some of the serious side effects associated with use of narcoleptics to schizophrenic patients. Curcumin was able to reverse oxidative damage induced by haloperidol. Curcumin helps in orofacial dyskinesia, a hyperkinetic disorder of high-incidence and unfortunate irreversibility during the treatment of schizophrenia with haloperidol.[13] High doses of glycineare effective at 30 grams per day to decrease social withdrawal, emotional flatness, and states of apathy in schizophrenia which are symptoms unresponsive to traditional antipsychotic medication.[9] Furthermore, clinical trials stated that glycine

given at 60 grams per day could be administered to schizophrenic patients with no adverse effects, as well as a twofold increase of glycine levels in the cerebrospinal fluid (CSF), as well as the B vitamins folic acid, B_{12}, and B_6 play a applicable role in neuronal function.[13] A deficiency causes increased risk of psychiatric disease and dementia. The most common of psychiatric symptoms of Vitamin B_{12} deficiencies are depression, mania, impaired cognition, dementia, delirium, psychotic symptoms, OCD, and states of confusion.[14] Vitamin B_{12} deficiency is causative of sub acute combined degeneration (SCD) where there is a demyelization of the lateral and dorsal spinal cord. Symptoms of SCD are psychosis, dementia, and severe depression which can be prevented by administering B_{12} supplements. Furthermore, deficiencies in B_{12} are related to proliferation of vascular risk factors and increase homocysteine and the load of cognitive decline in neuropsychiatric illnesses. B Vitamins and a broad-spectrum multivitamin extensively improve levels of stress and anxiety associated with natural disasters. Vitamin B_6 decrease extra pyramidal side-effects of typical antipsychotics. Same studies noted N-acetylcysteine (NAC) to be efficient against the negative symptoms of schizophrenia, in akathisia and abnormal movements in schizophrenia.[15]

N-ACETYLCYSTEINE (NAC)

NAC plays a considerable role to help in pathophysiological processes associated with psychiatric and neurological disorders. NAC supplementations are widely used for disorders such as autism, Alzheimer's disease, bipolar disorder, depression, OCD tendencies, and schizophrenia. Its action of lowering levels of glutamate is a key factor in its role of the amelioration of OCD and several grooming disorders.[16] In an another study, it was found that in individuals with chronic schizophrenia (SZ), adjunctive NAC-when compared to placebo-has therapeutic potential for overall functioning and a reduce in positive symptoms of schizophrenia.[17] Various researches havedirected that a large element of the pathogenesis of schizophrenia is deficit in brain glutathione (GSH) levels by result of impaired GSH synthesis. A study treated individuals suffering from schizophrenia with a GSH precursor, NAC, which suggestively decreased clinical severity and negative symptoms.[18] This same studyestablished that polyphenols, curcumin, and the flavonoid quercetin increase levels of GSH and decrease the overall clinical severity of schizoaffective disorders.[19]

VITAMIN D AND IRON

Supplementation of Vitamin D at levels of 2,000 IU per day in the first year of life resulted in a 77% decrease in the risk of developing schizophrenia in males, compared to those receiving less than 2,000 IU per day.[20] It was theorized that Vitamin D supplementation early in life is relevant in pro-differentiating signals in the critical periods of brain development, as well as recovery from brain damage after injury. There are many other vitamin and mineral deficiencies that play important role in the pathogenesis of schizophrenia.[21]

S-ADENOSYL METHIONINE (SAM-E)

SAM-E substantially decreases symptoms of psychosis including aggressive behavior.[22] It was stated that main function of SAM-E is as a methyl group donor for catecholamines, membrane phospholipids, fatty acids, choline carnitine, creatinine, nucleic acids, and porphyrins.[23] An important function of SAM-E is myelination of phospholipids to promote fluidity and micro viscosity of cell membranes.[24] The metabolism of SAM-E is crucial for the maintenance of myelin. SAM-E would affect catechol-O-methyltransferase (COMT) enzyme expression, in turn removing aggressive behavior in individuals with schizophrenia who have the low activity COMT polymorphism. SAM-E improves overall quality of life, improves depressive symptoms in females.[25]

BACOPA MONNIERA

This herbal extract has important neuroleptic effects with a reduction of dopamine concentration in the frontal cortex and conditioned avoidance response and reduction of amphetamine-induced stereotype.[26] Results show that *Bacopa monniera* may have substantial ability for the amelioration of the positive symptoms of schizophrenia. The herb *Ficus platyphylla (*FP) is said to have neuroleptic-like properties and reduces locomotor activity.[27] The study was able to reverse an apomorphine-induced prepulse inhibition deficit andhyperactivity by utilizing a co-administration of clozapine or FP. Furthermore, FP prevents the recovery of a conditioned avoidance reaction in individuals with schizophrenia.[28]

GINKGO BILOBA (GINKGO)

Ginkgo biloba (Ginkgo) extracts have anti-oxidant and anti-inflammatory mechanisms of action. They increase cerebral blood flow and possess antiplatelet effects that have been attributed to terpene and flavones lactones as well.[29] They are promising treatments for schizophrenia in combination with clozapine, as they significantly decrease the negative symptoms of individuals with schizophrenia.[30] This may be due to the antioxidant action of ginkgo or the effect it holds on the serotonergic pathway. Furthermore, it can standardize the levels of serotonin in the brain. Another study examining the adjunctive impact of ginkgo treatment with a prescription antipsychotic found a statistically significant moderate improvement with respect to the total and negative symptoms of schizophrenia.[31] Studies explored the role of antioxidants in schizophrenia's pathogenesis, indicating oxidative damage may hold a causative role in the progression of schizophrenia.[32]

DISCUSSION

Various ongoing studies have directed the clinical prospectiveof therapies with antipsychotics utilizing supplementation of antioxidants, B Vitamins, anti-inflammatory, neuro-protective nutrients, and dietary-restrictive practices. Notably, because of nonexistence of regulation by the FDA, using herbal and nutraceutical supplementation can have contraindications with any prior treatments. Moreover, using these supplements rather than the prescribed treatment without consulting the doctor can be dangerous and is not recommended.[33] While most of these researches regarding the above mentioned supplements implythere may be less risk with their use as compared to traditional antipsychotics, a doctor's consultation is necessary. Also, dosages of most of the herbal supplements have not been standardized.[34] Research signifies that schizophrenia and schizoaffective disorders are extensivelyrelated with nutritional and biochemical biomarkers as deficiencies in Vitamins D, B_6, and folate, and also oxidative stress. Disturbed amino acid metabolism is alsosaid to be involvedin the pathogenesis of schizophrenia. Herbs and nutraceuticals provides a wide range of noteworthydevelopmentsin those with schizophrenia, such as increased energy levels, enhanced overall perception of health, and reduced levels of pain. These supplements were beneficialin increasing emotional stability and alleviating anxiety, reducing social isolation and being causative of a perceived overall increase in sense of well-being.[35] As well as the herbs and nutraceuticalsempiricallyproposed to be therapeuticcontenders for schizophrenia and other psychiatric illness, there are still numerous potential herbal remedies that haven't been discovered yet or thoroughly researched. People of the Amazon use many psychoactive plants to ease the symptoms ofand even cure many psychiatric conditions. They acquire potential therapeutic CNS activity for the diminution of cognitive deficits related with schizophrenia and dementia by inhibiting and binding activity, instigating both antagonistic and agonistic functions with respect to muscarinic, adrenergic, and

serotonergic receptors *in vitro*.[36] This study is superficial regarding potentially clinically important herbal compounds. Morewide-ranging research with these compounds and other botanicals with promising CNS activity should be carried out to discover novel phytochemical properties with therapeutic and clinical potential.[37] We are blessed with rich biodiversity, including yet being explored lands. Much of these natural resources have been ignored by empirical research and should be preserved and explored in the hope that the untouched botanical species fill the gap of doable treatment.[38]

CONFLICT OF INTEREST

The authors declare no Conflict of interest.

ABBREVIATIONS

SAM-E: Adenosyl Methionine; **NAC:** N-Acetylcysteine.

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