Review Article

HERBAL AND DIETARY SUPPLEMENTS IN TREATMENT OF SCHIZOPHRENIA: AN APPROACH TO IMPROVE THERAPEUTICS

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ABSTRACT

Schizophrenia is a debilitating, hereditary, disorder of the brain, resulting from abnormalities that arises early in life and disrupt normal development of the brain and has a lifetime risk of 1% and affects at all age groups, approximately 10% die from suicide. Although antipsychotic drugs are the mainstay of treatment of schizophrenia, but they are associated with serious adverse effects such as tardive dyskinesia, oxidative stress, EPS. In addition, about 20% of people do not respond adequately to the treatment. Growing evidences supporting the dysregulation of antioxidant defense mechanism and a parallel increase in oxidantive load has been reported by several studies in schizophrenia. Although oxidative stress was produced by long term use of conventional antipsychotic medication, Ayurvedic herbal medicines and some dietary supplements score positively on this aspect, since they can be used long-term without any serious side effects and also possess antioxidant potential. Several herbal and dietary combinations are now available which can be used independently in patients with mild to moderate symptoms of schizophrenia. For Schizophrenic patients with severe symptoms, the Ayurvedic medicines and dietary supplements can be added to a modern medicine as adjuvant therapy, so that the therapeutic effect is optimized, without increasing the side-effect load.

Keywords: Schizophrenia, Herbal drug, Glycine, Oxidative stress, Dietary supplements, Antioxidants.

1. INTRODUCTION

Mental illness is any disease or condition affecting the brain that influences the way a person thinks, feels, behaves and/or relates to others and to his or her surroundings. Although the symptoms of mental illness can range from mild to severe and are different depending on the type of mental illness, a person with an untreated mental illness often is unable to cope with life's daily routines and demands.

Schizophrenia is a chronic, severe, and disabling brain disorder that has affected people throughout history. People with the disorder may hear voices other people don't hear. They may believe other people are reading their minds, controlling their thoughts, or plotting to harm them. This can terrify people with the illness and make them withdrawn or extremely agitated. People with schizophrenia may not make sense when they talk. They may sit for hours without moving or talking. Sometimes people with schizophrenia seem perfectly fine until they talk about what they are really thinking.

2. NEED OF HERBAL AND DIETARY SUPPLEMENTS

Families and society are affected by schizophrenia too. Many people with schizophrenia have difficulty holding a job or caring for themselves, so they rely on others for help. Treatment helps relieve many symptoms of schizophrenia, but most people who have the disorder cope with symptoms throughout their lives. However, many people with schizophrenia can lead rewarding and meaningful lives in their communities. Researchers are developing more effective medications and using new research tools to understand the causes of schizophrenia. In the years to come, this work may help prevent and better treat the illness. Antipsychotic medication is the mainstay of treatment for people with schizophrenia, and although effective, still leaves some people with distressing symptoms and/or disabling adverse effects. Therefore, safer and more effective health care interventions are needed. There is currently no complete cure for Schizophrenia, but many patients can be successfully managed with consistent long term medications and professional counseling. Many patients discontinue medicines because of unpleasant or intolerable side-effects of modern medicines. Ayurvedic herbal medicines and some dietary supplements score positively on this aspect, since they can be used long-term without any serious side effects. Several herbal and dietary combinations are now available which can be used independently in patients with mild to moderate symptoms. For Schizophrenic patients with severe symptoms, the Ayurvedic medicines and dietary supplements can be added to a modern medicine as adjuvant therapy, so that the therapeutic effect is optimized, without increasing the side-effect load. There is no 'cure', in traditional medicine, for Psychosis; and a prescription for one or more 'antipsychotics' with names like Haldolperidol and Risperidone, along with a cocktail of other drugs often prescribed for anxiety, depression and sleep are frequently on the menu. But what these people are rarely, if ever, told about are the long term side effects of these drugs. While doctors are ever prescribing anticholesterol 'statins', aspirin and blood pressure medications in order to achieve a 1 - 2% reduction in heart disease, they are knowingly giving schizophrenic individuals, who generally get their first

psychotic break as a teenager or young adult, a shortened lifespan from the medications that they are prescribing

3. HERBAL MEDICINE

Herbal medicine are also called botanical medicine or phytomedicine - refers to using a plant's seeds, berries, roots, leaves, bark, or flowers for medicinal purposes. Herbalism has a long tradition of use outside of conventional medicine. It is becoming more main stream as improvements in analysis and quality control along with advances in clinical research show the value of herbal medicine in the treating and preventing disease. Often, herbs may be used together because the combination is more effective and may have fewer side effects. Health care providers must take many factors into account when recommending herbs, including the species and variety of the plant, the plant's habitat, how it was stored and processed, and whether or not there are contaminants (including heavy metals and pesticides). Although antipsychotic drugs are the mainstay of treatment of schizophrenia, but they are associated with serious adverse effects such as tardive dyskinesia and tremor. In addition, about 20% of people do not respond adequately to treatment[1]. Some earlier reports have suggested that Chinese herbal medicine is effective for psychosis and that combination treatments (drugs plus herbs) are useful to enhance antipsychotic efficacy or reduce the period of recovery and adverse effects[2-3]. Since schizophrenia may not be a single condition and its causes are not yet known, current treatment methods are based on both clinical research and experience. These approaches are chosen on the basis of their ability to reduce the symptoms of schizophrenia and to lessen the chances that symptoms will return.

4. HERBAL SUPPLEMENTS

The use of herbal supplements has increased dramatically over the past 30 years. Herbal supplements are classified as dietary supplements by the U.S. Dietary Supplement Health and Education Act (DSHEA) of 1994. That means herbal supplements -- unlike prescription drugs -- can be sold without being tested to prove that they are safe and effective. However, herbal supplements must be made according to good manufacturing practices. Plants had been used for medicinal purposes long before recorded history. Ancient Chinese and Egyptian papyrus writings describe medicinal uses for plants. Indigenous cultures (such as African and Native American) used herbs in their healing rituals, while others developed traditional medical systems (such as Ayurveda and Traditional Chinese Medicine) in which herbal therapies were used. Researchers found that people in different parts of the world tended to use the same or similar plants for the same purposes.

4.1 List of herbal plants effective in mental illness

Hypericum perforatum

Is an aromatic perennial that is native to Europe but now grows wild in parts of Asia, North America, and South America. Its use can be traced back to the texts of the ancient Greek physicians Hippocrates and Galen. In the past decade it has become the second most commonly used herbal remedy in Germany[4] and is currently used in that country for the treatment of depression four times more often than the most commonly used prescription antidepressant[5]. The components of *hypericum* extracts that may be responsible for any antidepressant actions are unknown. Extracts of St. John's wort contain a large number of compounds[4-6] and although it is often assumed that hypericin is the active ingredient, it has not been proved. The mechanism of action is also unclear. Early studies suggested that extracts of St. John's wort inhibited monoamine oxidase[7] but more recent studies have failed to find such inhibition at the tissue concentrations that occur following typical dosages[8-9]. Instead, it appears that the extract may block the reuptake of norepinephrine and serotonin and down-regulate serotonin receptors[10]. This mechanism of action might be possible reason for antidepressant activity, since in depression MAO activity get enhanced which increases metabolism of neurotransmitter and decreases their level. In schizophrenia hyperactivity of serotonergic system was correlated to positive symptoms and many have now theorized that increased levels of serotonin in the prefrontal cortex will result in lower dopamine levels in this area. These reduced dopamine levels, which may be responsible for the negative symptoms of schizophrenias and cognitive deficits. Since this plant also down regulate serotonin receptors, whose activity was found to be enhanced in schizophrenia, it can be used in schizophrenia to alleviate some positive and negative and cognitive symptoms. Side effects of *hypericum* extracts are mild and uncommon. In a study of more than 3,000 patients taking *hypericum*, only 2.4 percent reported side effects, primarily allergic reactions and gastrointestinal upset[11]. Other reported side effects include dry mouth, sedation, and headache[12]. Photosensitivity appears to be a risk at dosages higher than those typically used to treat depression[13]. There do not appear to be significant adverse effects on cardiac conduction[14]. The use of *hypericum* extracts is contraindicated in pregnancy and lactation due to inadequate safety data[15]. Because the mechanism of *hypericum* extracts may involve serotonin reuptake blockade, extracts should not be combined with monoamine oxidase inhibitors or selective serotonin reuptake inhibitors, as the combination could cause a serotonin syndrome[16]. In addition, an interaction between *hypericum* extracts and olanzapine has been reported, with a patient having a 300 percent increase in olanzapine levels after starting St. John's wort[17]. The latter interaction may have been due to an effect of some component of the extract inhibiting CYP 1A2 and thus interfering with the metabolism of olanzapine.

Kava

Kava is one of the few herbal remedies in which the pharmacologically active ingredient is known. Meyer[18] proved that the effects of kava are due to the

kavapyrones, which in animal models act as muscle relaxants and anticonvulsants, protect against strychnine poisoning, and reduce limbic system excitability. Exactly how the kavapyrones produce these effects is unclear, as they have a variety of actions involving inhibition of voltage-dependent sodium channels, increasing $GABA_A$ (γ-amino-butyric acid) receptor densities, blocking norepinephrine reuptake, and suppressing the release of glutamate[19-21]. The fact that NMDA-receptor (N-methyl-D-aspartate) abnormalities may produce psychotic symptoms is due to their effects on striatal and limbic dopaminergic neurotransmission. NMDA receptor hypofunction reduces stimulation of cortical dopamine release, which produces negative and cognitive symptoms of schizophrenia. Simultaneously it reduces stimulation of GABA release, which is responsible for disinhibition of mesolimbic dopamine release and produces positive symptoms. Since Kava act by increasing $GABA_A$ receptor densities and suppressing the release of glutamate, this mechanism might explain its usefulness in schizophrenia. When kava has been taken in dosages ranging from 100 to 210 mg of kavapyrones daily, it has been associated with few adverse effects. In studies comparing kava and oxazepam, kava appears not to adversely affect cognitive function, mental acuity, or coordination[22-23] although slight morning tiredness and reduced reactivity while driving have been reported, as has ataxia[24]. In rare cases, kava may lead to allergic reactions, yellowing or scaling of the skin, gastrointestinal complaints, pupil dilation, and blurred vision[22].

Ginkgo

Ginkgo trees *(Ginkgo biloba)* are native to East Asia and are grown ornamentally in Europe and North America. Used in China for more than 2,000 years as a tea for treatment of asthma, ginkgo is now the most commonly sold herbal product in Germany and one of the top three herbals in the United States, where it is taken primarily to prevent or treat memory problems[24]. U.S. sales increased markedly after a report in *JAMA* of a clinical trial of the use of kava for patients with dementia[26]. Ginkgo extracts contain a large number of substances that have been found to have a variety of pharmacological effects[27]. The ginkgo flavonoids are thought to be antioxidants, and the ginkgolides, especially ginkgolide B, inhibit platelet-activating factor. There is also evidence that ginkgo extracts can improve vascular perfusion by modulating vessel wall tone. Side effects from ginkgo are relatively uncommon but include headache, gastrointestinal upset, and allergic skin reactions. Rarely, ginkgo preparations have been associated with cerebral hemorrhage[28]. The safety of ginkgo in pregnancy or lactation has not been established.

Valerian

Approximately 250 different species of valerian exist. The one used most commonly for medicinal purposes *(Valeriana officinalis)* is a perennial that is native to Europe and Asia. Valerian extracts contain more than 100 different constituents. Which of them are responsible for the pharmacological actions is not known with certainty, as the whole valerian extract has been demonstrated to have central nervous system actions not attributable to valeric acids, valepotriates, or volatile oils. In laboratory animals, valerenic acids have sedative and anticonvulsant effects, and valerian extracts have been demonstrated to have a variety of effects on GABA-ergic neurons, including increased release of GABA, decreased GABA reuptake, and decreased GABA degradation[4].

A second neurochemical that appears to have effects on dopamine levels is gamma-aminobutyric acid (GABA), an inhibitor amino acid. It is synthesized by the action of glutamic acid decarboxylase (GAD), which removes the alpha-carboxyl group of glutamate in an irreversible reaction. Dopamine production in dopaminergic cells is under the direct control of GABAergic neurons that produce GABA. An abnormally low amount of GAD, which by that lowers the effective GABA concentrations, promotes dopamine production[29]. So if there is any abnormalities in GAD action or synthesis of GABA, valerian can improve GABA action by decreasing GABA reuptake and degradation and simultaneously increasing GABA synthesis. Adverse effects of valerian preparations are rare but may include gastrointestinal upset, contact allergies, headache, restless sleep, and mydriasis. Valerian appears to be relatively safe in overdose[30], with the major effect being central nervous system depression[31]. Currently, little is known about its safety in pregnancy and lactation. The major drug interactions of valerian are with other sedative-hypnotics. The sedative effects of valerian may potentiate the effects of other central nervous system depressants.

Rhodiola rosea

(Golden Root, Roseroot, Aaron's Rod) is a plant in the Crassulaceae family that grows in cold regions of the world. These include much of the Arctic, the mountains of Central Asia, the Rocky Mountains, and mountainous parts of Europe, such as the Alps, Scandinavia, Iceland, Great Britain, Ireland. *Rhodiola rosea* contains a variety of compounds that may contribute to its effects[32] including the class of *rosavins* which include rosavin, rosarin, and rosin. Several studies have suggested that the most active components are likely to be rhodioloside and tyrosol[33] with other components being inactive when administered alone, but showing synergistic effects when a fixed combination of rhodioloside, rosavin, rosarin and rosin was used.[34] *Rhodiola Rosea* Root is now considered an adaptogen. This defines how it has an overall stabilizing effect on the body without disrupting other functions. Its ability to normalize hormones in the body suggested it may be effective for treating depression and anxiety.

Studies of the amazinly versitile *Rhodiola Rosea* demonstrate that it enhances neurotransmitters and adds to their effects on the brain. This includes the ability for the brain to process serotonin which helps the body to adapt to stress. *Rhodiola rosea*'s effects are potentially mediated by changes in serotonin and dopamine levels

due to monoamine oxidase inhibition and its influence on opioid peptides such as beta-endorphin[35] although these specific neurochemical mechanisms have not been clearly documented with scientific studies. A favourable study was commisioned to demonstrate the effects of *Rhodiola Rosea* when students are under stress is caused by intense mental work (such as final exams). Such studies concluded that using *Rhodiola Rosea* improved the amount and quality of work, increasing mental clarity and reducing the effects of fatigue. The effects of *Rhodiola Rosea* have also been demonstrated on stress and anxiety from both physical and emotional sources. A report by the American Botanical Council concluded that "Many users find that it (Rhodiola) improves both their mood, energy level, and mental clarity." They also reported on a study that indicated *Rhodiola Rosea* could increase stress tolerance while at the same time protecting the brain and heart from the physical effects of stress. This herb may be helpful in certain cases of dementia since it inhibits MAO B. Several compounds in this herb have potent antioxidant abilities. Administration of single dose of R. imbricata root aqueous extract significantly restricted rise in blood MDA, increased blood reduced glutathione (GSH) and superoxide dismutase (SOD) activity with restricted rise in blood, liver and muscle LDH; improved liver and muscle SOD on attaining, liver catalase (CAT) and liver GST (glutathione transferase) during recovery. Multiple doses treatment of the extract further increased blood, liver and muscle GSH and GST levels; restricted increase in LDH, increased CAT. Oxidative is one the major reason of neurodegerative disorder and it was also found that antipsychotic medications side effects are due to oxidative stress produced by them e.g. tardative dyskinesia. So this herbal supplements along with antipsychotics medication can reduces the risk of side effects and improve therapeutic value of drug.

Ziziphus jujube

Ziziphus zizyphus commonly called jujube (sometimes jujuba), red date, or Chinese date, is a species of *Ziziphus* in the buckthorn family Rhamnaceae, used primarily as a fruiting shade tree. The *Zizyphus jujuba* tree originated in China where it has been cultivated for several thousand years. Its precise natural distribution is uncertain due to extensive cultivation, but is thought to be in southern Asia, Pakistan northern India, Bangladesh, the Korean peninsula, and southern and central China. *Zizyphus jujuba* date has long been used in Chinese traditional medicine for the treatment of anxiety and insomnia. The fruits are used in Chinese and Korean traditional medicine, where they are believed to alleviate stress,[36] and traditionally for sedative,[37] antioxidant, immunostimulant, and Wound healing properties[38]. *Zizyphus jujuba* is widely used in Chinese traditional medicine for the treatment of insomnia and anxiety. *Zizyphus jujuba* is promoted as having a calming effects. A number of compounds are present in *Zizyphus jujuba*, including saponins, jujubosides and triterpenoic acids. *Zizyphus jujuba* is used in the Orient for its calming effects. This herb does appear to have some relaxation potential although others herbs such as passion flower, kava, and supplements such as 5-HTP, tryptophan, serotonin, and theanine are good options. Compounds in *Zizyphus jujuba*, called jujubosides, have inhibitory effects on glutamate-mediated excitatory signal pathway in the hippocampus and probably act through their anti-calmodulin action. Glutamate is the major excitatory neurotransmitter in human brain. After binding to NMDA receptors it open calcium ion channel and increases entry of calcium ions. These calcium ions interacts with calmodulin and regulate the release of glutamate by increasing the formation of NO (nitric oxide) through nitric oxide synthetase. So by showing anti-calmodulin action, Zizyphus jujube can be used to reduce glutamate mediated excitotoxicity in schizophrenia.

Crocus sativus

Crocus sativus L. (Iridaceae), commonly known as saffron, is a perennial stemless herb that is widely cultivated in Iran and other countries such as India and Greece. Saffron is used for depression in Persian traditional medicine[39-41]. Characteristic components of saffron are crocin - (responsible for the color), picrocrocin- (responsible for the bitter taste), and safranal- (responsible for odor and aroma)[42]. Saffron contains more than 150 volatile and aroma-yielding compounds. It also has many non-volatile active components, many of which are carotenoids including zeaxanthin, lycopene, and various α- and β-carotenes.[43] The volatiles with a very strong odor are consistent of more than 34 components that are mainly terpenes, terpene alcohols, and their esters. Non-volatiles include crocins 14 that are responsible for the red or reddish brown color of stigmas together with carotenes, crocetin, picrocrocin (a glycosidic precursor of safranal), the bitter substance and safranal the major organoleptic principle of stigmas Pistils of saffron are generally used in traditional Indian medicine as analgesics and cardio-protective agents, as well as in the treatment of various kinds of mental illnesses. A crude extract of pistils of saffron improves recovery in ischemia/reperfusion injury and learning and memory in rats. The efficacy of petal of *C. sativus* was assessed in the treatment of mild-to-moderate depression. Saffron was compared to the drug fluoxetine; it was found that the saffron performed as well as the drug in the treatment of depression. The saffron extract and two of its main ingredients, crocin and crocetin, improved memory and learning skills in ethanol-induced learning behavior impairments in mice and rats. Oral administration of saffron may be useful in the treatment of neurodegenerative disorders and related memory impairment[44]. Modern pharmacological studies have demonstrated that saffron extract or its constituents have antidepressant,[45] anti-inflammatory, anti-tumor effects, radical-scavenging, learning and memory improving properties[46-48].

Ginseng

Ginseng is the dried root of various species of panax, like *P.ginseng, P.japonica, P. notoginseng*, and *P. quinquefolium*. It grows widely in korea, China, Russia. Ginseng contain a mixture of several saponin glycoside, belonging to triterpenoid group. They are grouped as Ginsenosides, panaxosides, chikusetsusaponin. Constituents found in most ginseng species include ginsenosides, polysaccharides, peptides, polyacetylenic alcohols, and fatty acids. Most pharmacological actions are attributed to the ginsenosides that belong to a group of compounds known as steroidal saponins, steroid molecules with attached sugar residues. More than 20 ginsenosides have been isolated. Ginseng is an immunomodulatery drug. It increases the natural resistance and enhances the power to overcome the illness. It has both stimulant and sedative properties. Data from animal studies suggest that ginseng may have beneficial effects in the central nervous system. Ginsenosides prevented scopolamine-induced memory deficits in laboratory animals by increasing central cholinergic activity. They may also protect neurons from ischemic damage and facilitate learning and memory by enhancing nerve growth. The effect of ginseng on pain pathways needs further investigation. Ginsenosides appear to modulate neurotransmission through -aminobutyric acid (GABA), and by inhibiting neurotransmitter reuptake.

Ashwagandha

It consists of dried root and stem bases of *Withania somnifera*, belonging to family Solanaceae. This plant grows wildly in all dry parts and subtropical India. It occur in Madhya Pradesh, Uttar Pradesh, Punjab plains and North Western parts of India like Gujarat and Rajasthan. The main constituents of ashwagandha are alkaloids and steroidal lactones. Withianine is main constituents of it. Ashwagandha has sedative and hypnotic effects. It is an immune-modulatory agent and have been shown to possess anti-stress activity. Scholars at Banaras Hindu University, located in Varanasi, India, have conducted research that has shown that many of the elements of ashwagandha are antioxidants. The researchers looked at the effects these elements have on the brains of test animals and found that ashwagandha led to larger amounts of three different natural antioxidants: superoxide dismutase, catalase and glutathione peroxidase. The scholars conclude, “These findings are consistent with the therapeutic use of W. somnifera as an Ayurvedic rasayana (health promoter). The antioxidant effect of active principles of W. somnifera may explain, at least in part, the reported anti-stress, cognition-facilitating, anti-inflammatory and anti-aging effects produced by them in experimental animals, and in clinical situations." For years, Indians have prescribed ashwagandha as a treatment for cerebral disorders in the elderly, including memory loss. Scholars from the University of Leipzig looked at the effects of ashwagandha on the brain. They dosed rats with ashwagandha and then looked at their brains to see if ashwagandha affected neurotransmitters. The research showed that ashwagandha led to more acetylcholine receptor activity. The scholars concluded that the increase of activity in that particular neurotransmitter could account for the increase in cognitive ability and memory that is attributed to ashwagandha. Researchers at the University of Texas Health Science Center also looked at the effects of ashwagandha. They found that extracts of the shrub had activity that was similar to GABA, which could explain why the plant is effective in reducing anxiety. Another study, conducted in 2002, found that ashwagandha leads to increased growth of axons and dendrites. Another study in 2001 found that the plant can enhance memory. A 2000 project indicated that ashwagandha reduced anxiety and depression in animals.

5. DIETARY SUPPLEMENTS

Along with Herbal supplements, symptoms of schizophrenia can be improved by dietary supplements.

5.1 list of dietary supplements

Glycine

Glycine (an amino acid sold as a dietary supplement) has been a subject of research for over 15 years as a potential treatment for the negative symptoms of schizophrenia. Only a handful of human clinical trials with fewer than 50 people in each trial, have been completed (though one trial with 150 people has recently completed and has not yet been published). The trials published to date are reporting that the results have been quite positive, showing a significant reduction (averaging around 24%) in negative and cognitive symptoms based on the PANSS (Positive and Negative Schizophrenia Symptoms) scale. The clinical trials have shown that Glycine did not help people who are taking Clozapine, but it did help (in reducing negative symptoms) in people who were taking risperidone (Risperdal), and olanzapine (Zyprexa). The biggest downside to taking glycine seems to be upset stomach and nausea which, researchers tell us, is quite common in people who take 60 grams of glycine a day for a month or two.

One hypothesis of schizophrenia pathology suggests that NMDA-receptor dysfunction (a special kind of glutamate receptor in the brain) may contribute to disordered synapses and brain atrophy, which ultimately result in the visible symptoms. The NMDA receptor has a number of modulatory sites that affect its activity. Within the channel, there is a binding site for the dissociative anesthetics such as phencyclidine (PCP, “angel dust”) and ketamine, which serve as noncompetitive antagonists and produces symptoms of schizophrenia[49]. There is also a strychnine-insensitive binding site for the co-agonist glycine, which must be occupied in order for glutamate to open the ion channel. Glycine is known to act as an agonist for NMDA. It is believed that supplementing with glycine may not only have antispastic activity but it may also have antipsychotic activity along with anti-oxidant

and anti-inflammatory properties. Glycine may turn out to be a very beneficial supplemental treatment (when added to standard antipsychotic medications) for some people with schizophrenia. We hope to see longer and larger trials for glycine supplemental treatments. A number of small, randomized control trials have been done looking at the effect of adding glycine to atypical antipsychotics and the impact that would have on symptoms.

Antioxidant vitamins

Some studies reported that there is increase in free radical generation in schizophrenia and antioxidant defense is impaired[50]. The free radical plays an important role in the genesis of neuronal membrane that could be responsible for the beginning and aggravation of the basic disease[51-52]. It was also reported that neurotransmitter like dopamine induces oxidative stress in neuron with glutathione deficits[53]. Researchers have found a positive correlation between superoxide generation and the negative symptoms of schizophrenia, indicating a possible role for oxidative stress in the development of the disease (and the potential for antioxidants to help in decreasing the risk or severity of the disease). "There are several lines of evidence to support the contribution of oxygen free radicals in schizophrenia, including increased lipid peroxidation, fatty acids, and alterations in blood levels of antioxidant enzymes. A fall of the activities of the secondary antioxidant enzymes (glutathione-S-transferase, glucose-6-phosphate dehydrogenase, caeruloplasmin, Ferroxidase) and as well as an in increase in the peroxidation of the lipid was noted among schizophrenic patients[54].

Higher than normal intake of foods known to have a high content of antioxidants, as well as supplements of high antioxidant vitamins (Alpha Lipoic Acid, Vitamin E, Vitamin C) may have some beneficial impact on the incidence and progression of the disease - anecdotal evidence suggests as much as 5% to 10% improvement for some individuals. Oral supplementation of vitamin C with atypical antipsychotic reverses ascorbic acid levels, reduces oxidative stress, and improves BPRS (brief psychiatric rating scale score), hence both the drugs in combination can be used in the treatment of schizophrenia. Foods high in antioxidants include blue berries (frozen or fresh), dried plums, spinach and strawberries.

Vitamin E and other antioxidants (for tardive dyskinesia)

Tardive dyskinesia is a neurological syndrome caused by the long-term use of neuroleptic drugs - especially the older "typical" medications. Tardive dyskinesia is characterized by repetitive, involuntary, purposeless movements. Features of the disorder may include grimacing, tongue protrusion, lip smacking, puckering and pursing, and rapid eye blinking. Rapid movements of the arms, legs, and body may also occur. Impaired movements of the fingers may appear as though the patient is playing an invisible guitar or piano. There is no standard treatment for tardive dyskinesia. The first step is generally to stop or minimize the use of the neuroleptic drug. Replacing the neuroleptic drug with substitute drugs may help some patients. Other drugs such as benzodiazepines, adrenergic antagonists, and dopamine agonists may also be beneficial.

In the last 10 years, preclinical studies of the administration of antipsychotics to animals, as well as clinical studies of oxidative processes in patients given antipsychotic medications, with and without tardive dyskinesia, have continued to support the possibility that neurotoxic free radical production may be an important consequence of antipsychotic treatment, and that such production may relate to the development of dyskinetic phenomena. In line with this hypothesis, evidence has accumulated for the efficacy of antioxidants, primarily vitamin E (mixed-tocopherols), in the treatment and prevention of tardive dyskinesia. Because there is increased oxidative damage from antipsychotic medications, but not the effectiveness of vitamin E, especially in cases of long-standing tardive dyskinesia, alternative antioxidant approaches to the condition may be warranted. These approaches may include the use of antioxidants as a preventive measure for tardive dyskinesia or the use of other antioxidants, such as melatonin, for established tardive dyskinesia.

EPA omega-3 fish oils

While the research is somewhat conflicting (some positive studies, some negative studies) there is some early scientific research that suggests that people that have schizophrenia may benefit by a reduction in symptoms when they take fish oil capsules that are high in the EPA (a type of Omega-3 fatty acid) form of oil.

N-methylglycine (also called sarcosine)

One hypothesis of schizophrenia pathology suggests that NMDA-receptor dysfunction (a special kind of glutamate receptor in the brain) may contribute to disordered synapses and brain atrophy, which ultimately result in the visible symptoms. Glycine (or glycine-like supplements such as Sarcosine) may turn out to be a very beneficial supplemental treatment (when added to standard antipsychotic medications) for some people with schizophrenia. In a recent (2004) Harvard Medical School study with consumers who suffer from schizophrenia it was revealed that patients who received N-methylglycine (sarcosine) treatment had significant (on the order of 10 to 15%) improvements in their positive, negative, cognitive, and general psychiatric symptoms. This looks very promising, but the research needs to be duplicated with some larger sample groups of people. N-methyl glycine (Sarcosine) is apparently an amino acid tested. This derivative acts by increasing the synaptic availability of glycine by inhibiting its reuptake through a compound called the glycine transporter – 1 or GlyT-1. Sacrasine is a natural amino acid that appears to have those properties. In one study[55] this hypothesis was successfully proved.

Although evidence of the efficacy of certain herbal preparations and dietary supplements in the treatment of psychiatric conditions is growing, translating the results of efficacy studies into effective treatments for patients is hampered by the chemical complexity of the products and the lack of standardization of commonly available preparations. In particular, well-controlled studies comparing herbal remedies with conventional medications are few. As a result, it is difficult for psychiatrists to recommend herbal remedies and dietary supplements over established conventional treatments. Research has been carried out to compare effectiveness of herbal supplements and conventional treatments. Herbal supplements and conventional treatments alone were not found very effective but in combinations better results were obtained[56]. So to improve therapeutics of schizophrenia, further research is required in the field of herbal treatment. SO that patients can get treatment plans that use herbs, conventional medications and lifestyle changes to promote health.

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