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Review Article

Fibre Diet for Antipsychotic induced Hyperlipidemia: A review

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Abstract: The Dietary fibers are known for their cholesterol lowering effect. Dietary fibers are found in all plant based foods.. Soluble fibers pulls in water to form a gel in the digestive tract. This slows digestion, so that stomach and intestine don't absorb as much of some nutrients, like starch and sugar. Insoluble fiber can be found in the peels of fruits such as apples, blueberries and grapes. It acts as a natural laxative that speeds the passage of foods through the stomach and gives stool its bulk and helps it move quickly through the gastrointestinal tract. Dietary and pharmacological reduction in total and LDL cholesterol decreases the risk of coronary diseases and dietary intervention is the desirable approach. Antipsychotic medication shows some side effects generally weight gain, high cholesterol level and may increase in risk of diabetes, risk of heart disease, stroke and diabetes and common side effects are blurred vision, dry mouth, drowsiness muscle spasm or tremors. To control over these side effect of increased level of cholesterol lipid profile in the blood, soluble and insoluble fiber diets are administered which decreased the lipid level in the body. Fibers like guar gum has been found to be associated with a 10% reduction in apetite and increase in the feeling of satiety. Fiber reduces cholesterol by multiple mechanisms, namely, interruption of enterohepatic circulation of the bile acids with enhanced bile seceretion, and inhibition of cholesterol absorbtion leading to increased excretion of neutral sterols; additionally guar may entrap fat micelles thereby impending fat absorbtion. The present study highlights about the effect of soluble and insoluble fiber diet on atypical antipsychotic agents induced hyperlipidemia.
Keywords: Laxative, Total cholesterol, LDL cholesterol, Coronary disease, Drowsiness, Tremors, Postprandial glycemia, Insulinaemia, Enterrohepatic circulation, Cholestrol absorbtion, Neutral sterol

INTRODUCTION

Psychosis refers to an abnormal condition of the mind, and is ageneric psychiatric term for a mental state often described as involving a "loss of contact with reality". People suffering from psychosis are described as psychotic. Psychosis is the term given to the more severe forms of psychiatric disorder, during which hallucinations and/ or delusions, violence and impaired insight may occur.

The term "psychosis" is very broad and can mean anything from relatively normal aberrant experiences through to the complex and catatonic expressions of schizophrenia and bipolar type 1 disorder [1-2]. Moreover a wide variety of central nervous system diseases from both external substances and internal physiologic illness, can produce symptoms of psychosis. This led many professionals to say that psychosis is not specific enough as a diagnostic term. Psychosis (as a sign of a psychiatric disorder) is a diagnosis of exclusion. That is, a new-onset episode of psychosis is not considered a symptom of a psychiatric disorder until other relevant and known causes of psychosis are properly excluded [3]. "Psychosis" is generally given to noticeable deficits in normal behavior (negative signs) and more commonly to diverse types of hallucinations or delusional beliefs (e.g. grandiosity, delusions of persecution).

An excess in dopaminergic signaling is hypothesized to be linked to the positive symptoms of psychosis, especially those of schizophrenia; however, this hypothesis has not been definitively supportive. The dopaminergic mechanism is thought to involve the aberrant salience of environmental stimuli [4]. Many antipsychotic drugs accordingly target the dopamine system; however, meta-analyses of placebo-controlled trials of these drugs show either no significant difference in effects between drug and placebo, or a moderate effect size, suggesting that the pathophysiology of psychosis is much more complex than an overactive dopamine system [5-6].

People experiencing psychosis may exhibit some personality changes and thought disorder. Depending on its severity, this may be accompanied by

unusual or bizarre, as well as difficulty with social interaction and impairment in carrying out daily life activities.

SIGNS AND SYMPTOMS

People with psychosis may have one or more of the following: hallucinations, delusions, catatonia, or a thought disorder, as described below. Impairments in social cognition also occur [7-8].

- **Hallucination**: A hallucination is defined as sensory perception in the absence of external stimuli [9]. They are different from illusions or perceptual distortion, which are the misperception of external stimuli. Auditory hallucinations tend to be particularly distressing when they are derogatory, commanding or preoccupying. However, the experience of hearing voices need not always be a negative one. One research study has shown that the majority of people who hear voices are not in need of psychiatric help[10].

- **Delusions:** psychosis may involve delusional beliefs, some of which are paranoid in nature. Delusions are false beliefs which a person holds on to, without adequate evidence.
  It may be difficult to change the beliefs even with evidence to the contrary. Primary delusions are defined as arising suddenly and not being comprehensible in terms of normal mental processes, whereas secondary delusions are typically understood as being influenced by the person's background or current situation (e.g., ethnicity; also religious, superstitious, or political beliefs)[11]. Common themes of delusions are persecutory (person believes that others are out to harm him/her), grandiose (person believing that he/she has special powers or skills).

- **Catatonia**: Catatonia describes a profoundly agitated state in which the experience of reality is generally considered to be impaired. There are two primary manifestations of catatonic behavior. The classic presentation is a person who does not move or interact with the world in anyway while awake.

- **Thought Disorder**: It describes disturbance to conscious thought and is classified largely by its effects on speech and writing. Affected persons show loosening of association. In the severe form speech become incomprehensible and known as “word salad”.

PATHOPHYSIOLOGY

Psychosis has been traditionally linked to the neurotransmitterdopamine. In particular, the dopamine hypothesis of psychosis has been influential and states that psychosis results from an overactivity of dopamine function in the brain, particularly in the mesolimbic pathway. The two major sources of evidence given to support this theory are that dopamine receptor D2 blocking drugs (i.e., antipsychotics) tend to reduce the intensity of psychotic symptoms, and that drugs that boost dopamine activity (such as amphetamines and cocaine) can trigger psychosis in some people (amphetamine psychosis)[12]. However, increasing evidence in recent times has pointed to a possible dysfunction of the excitatory neurotransmitter glutamate, in particular, with the activity of the NMDA receptor.

This theory is reinforced by the fact that dissociativeNMDA receptor antagonists such as ketamine, PCP and dextromethorphan (at large overdoses) induce a psychotic state more readily than dopaminergic stimulants, even at "normal" recreational doses. The symptoms of dissociative intoxication are also considered to mirror the symptoms of schizophrenia, including negative psychotic symptoms, more closely than amphetamine psychosis. Dissociative induced psychosis happens on a more reliable and predictable basis than amphetamine psychosis, which usually only occurs in cases of overdose, prolonged use or with sleep deprivation, which can independently produce psychosis. New antipsychotic drugs that act on glutamate and its receptors are currently undergoing clinical trials.

The connection between dopamine and psychosis is generally believed complex. While dopamine receptor D2 suppresses adenylate cyclase activity, the D1 receptor increases it. If D2-blocking drugs are administered the blocked dopamine spills over to the D1 receptors. The increased adenylate cyclase activity affects genetic expression in the nerve cell, which takes time. Hence antipsychotic drugs take a week or two to reduce the symptoms of psychosis. Moreover, newer and equally effective antipsychotic drugs actually block slightly less dopamine in the brain than older drugs whilst also blocking 5-HT2A receptors, suggesting the 'dopamine hypothesis' may be oversimplified [13]. Soyka and colleagues found no evidence of dopaminergic dysfunction in people with alcohol-induced psychosis [14] and Zoldan et al. reported moderately successful use of ondansetron, a 5-HT_3 receptor antagonist, in the treatment of levodopa psychosis in Parkinson's disease patients[15].

TREATMENT OF PSYCHOSIS

The treatment of psychosis depends on specific diagnosis. The first line treatment for many psychotic disorders is antipsychotic medication and sometime hospitalization is needed. There are significant problems associated with this class of drugs. There is evidence that they can cause brain damage including pre frontal cortex atrophy, long lasting parkinsonism symptoms and personality change.

The treatment of psychosis depends on the specific diagnosis (such as schizophrenia, bipolar disorder or substance intoxication). The first line treatment for many psychotic disorders is antipsychotic medication (oral or intramuscular injection), and sometimes hospitalization is needed. However, there are significant problems associated with this class of drugs. There is evidence that they can cause brain damage including prefrontal cortex atrophy, long-lasting parkinsonian symptoms (tardive dyskinesia), and personality change [16]. Nancy Andreasen has argued for an association between antipsychotic drugs and smaller grey matter volumes independent of illness severity[17]. Furthermore, antipsychotic drugs can themselves induce psychotic symptoms if they are administered for a long time and then discontinued [18].

There is growing evidence that cognitive behavior therapy [19] acceptance and commitment therapy [20-21] and family therapy [22] can be effective in managing psychotic symptoms. When other treatments for psychosis are ineffective, electroconvulsive therapy or ECT (also known as shock treatment) is sometimes applied to relieve the underlying symptoms of psychosis due to depression. There is also increasing research suggesting that animal-assisted therapy can contribute to the improvement in general well-being of people with schizophrenia [23].

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Antipsychotic drugs have been used for treatment of psychosis. They are of two type:

- Atypical antipsychotics
- Typical antipsychotics

Drugs used in treatment of psychosis are-

- Olanzapine (Zyprexa)
- Apriprazole (Abilify)
- Risperidone (Risperdal)
- Ziprasidone (Geodon)
- Clozapine (Clorazil)
- Chlorpromazine (Thoazine)
- Haloperidol (Haldol)
- Perphenazine (generic only)
- Fluphenazine (generic only)
- Quetiapine (Seroquel)

MECHANISM OF ACTION

All antipsychotic drugs tend to block D_2 receptors in the dopamine pathways of the brain. This means that dopamine released in these pathways has less effect. Excess release of dopamine in the mesolimbic pathway has been linked to psychotic experiences. It has also been proven[less dopamine released in the prefrontal cortex in the brain, and excess dopamine released from all other pathways, has also been linked to psychotic experiences, caused by abnormal dopaminergic function as a result of patients suffering from schizophrenia or bipolar disorder. Various neuroleptpics such as haloperidol and chlorpromazine suppress dopamine chemicals throughout its pathways, in order for dopamine receptors to function normally.

In addition of the antagonistic effects of dopamine, antipsychotics (in particular atypical neuroleptics) also antagonize 5-HT_{2A} receptors. Different alleles of the 5-HT_{2A} receptor have been associated with schizophrenia and other psychoses, including depression [24-25]. Higher concentrations of 5-HT_{2A} receptors in cortical and subcortical areas, in particular in the right caudate nucleus have been historically recorded. This is the same receptor that psychedelic drugs agonize to various degrees, which explains the correlation between psychedelic drugs and schizophrenia.

Typical antipsychotics are not particularly selective and also block dopamine receptors in the mesocortical pathway, tuberoinfundibular pathway, and the nigrostriatal pathway. Blocking D_2 receptors in these other pathways is thought to produce some unwanted side effects that the typical antipsychotics can produce. They were commonly classified on a spectrum of low potency to high potency, where potency referred to the ability of the drug to bind to dopamine receptors, and not to the effectiveness of the drug. High-potency antipsychotics such as haloperidol, in general, have doses of a few milligrams and cause less sleepiness and calming effects than low-potency antipsychotics such as chlorpromazine and thioridazine, which have dosages of several hundred milligrams. The later have a greater degree of anticholinergic and antihistaminergic activity, which can counteract dopamine-related side-effects.

Atypical antipsychotic drugs have a similar blocking effect on D_2 receptors, however, most also act on serotonin receptors, especially 5-HT_{2A} and 5-HT_{2C} receptors. Both clozapine and quetiapine appear to bind just long enough to elicit antipsychotic effects but not long enough to induce extrapyramidal side effects and prolactin hypersecretion. 5-HT_{2A} antagonism increases dopaminergic activity in the nigrostriatal pathway, leading to a lowered extrapyramidal side effect liability among the atypical antipsychotics.

SIDE EFFECTS OF ANTIPSYCHOTICS

- Sedation
- Hypotension
- Anticholinergic effects
- Extrapyramidal symptoms
- Psedoparkinsonism
- Akathisia
- Dystonic reactions
- Tradive Dyskinesia
- High cholesterol level
- Increase risk of diabetes
- Blurred vision
- Dry mouth
- Drowsiness
- Muscle spasms or temors
- Hyperprolactinemia
- Cardiac arrhythmias

ANTIPSYCHOTICS INDUCED HYPERLIPIDEMIA:

The atypical antipsychotic vary in their propensity to cause hyperlipidemia, with clozapine and olanzapine showing the greatest effects, risperidone and quetiapine having intermediate effects and aripiprazole and ziprasidone having normal effects. However, the conseus statement acknowledges the caveat that aripiprazole and ziprasidone have fewer longer term data due to limited amount of time they have been on the market. Both risperidone and ziprasidone are non-benzodiazepene AAP, and appear to have minimal effects on serum lipids.

Clozapine and olanzapine, but not risperidone, were associated with increase in cholesterol and triglycerides level at the end of an 8 week treatmentin patients with first episode schizophrenia, similar changes due to olanzapine or clozapine, but not amisulpride or ziprasidone, were reported as early in the fourth week of treatment. In the clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), olanzapine was associated with greater and significant adverse effects on lipids, while ziprasidone was the only antipsychotic associated with improvement in these metabolic variables.

HIGH FIBRE DIET AGAINST HYPERLIPIDEMIA:

Dietary fiber or ruffage is the indigestible portion of food derived from plants and waste of animals that eat dietary fiber. There are two components :

- **Soluble fiber** dissolves in water. It is readily fermented in the colon into gases and physiologically active byproducts and can be prebiotic and/or viscous. Soluble fibers tend to slow the movement of food through the system.
- **Insoluble fiber**, which does not dissolve in water. It can be metabolically inert and provide bulking, or it can be prebiotic and metabolically ferment in the large intestine. Bulking fibers absorb water as they move through the digestive system, easing defecation [26]. Fermentable insoluble fibers mildly promote stool regularity, although not to the extent that bulking fibers do, but they can be readily fermented in the colon into gases and physiologically active byproducts. Insoluble fibers tend to accelerate the movement of food through the system.

Dietary fibers can act by changing the nature of the contents of the gastrointestinal tract and by changing how other nutrients and chemicals are absorbed [27]. Some types of soluble fiber absorb water to become a gelatinous, viscous substance which is fermented by bacteria in the digestive tract. Some types of insoluble fiber have bulking action and are not fermented [28]. Lignin, a major dietary insoluble fiber source, may alter the rate and metabolism of soluble fibers. Other types of insoluble fiber, notably resistant starch, are fully fermented[29].

Chemically, dietary fiber consists of non-starchpolysaccharides such as arabinoxylans, cellulose, and many other plant components such as resistant starch, resistant dextrins, inulin, lignin, waxes, chitins, pectins, beta-glucans, and oligosaccharides. The term "fiber" is something of a misnomer, since many types of so-called dietary fiber are not actually fibrous.

Food sources of dietary fiber are often divided according to whether they provide (predominantly) soluble or insoluble fiber. Plant foods contain both types of fiber in varying degrees, according to the plant's characteristics.

Advantages of consuming fiber are the production of healthful compounds during the fermentation of soluble fiber, and insoluble fiber's ability (via its passive hygroscopic properties) to increase bulk, soften stool, and shorten transit time through the intestinal tract.

Disadvantages of a diet high in fiber is the potential for significant intestinal gas production and bloating. Constipation can occur if insufficient fluid is consumed with a high-fiber diet

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DEFINITION OF FIBRE

- Originally, fiber was defined to be the components of plants that resist human digestive enzymes, a definition that includes lignin and polysaccharides. The definition was later changed to also include resistant starches, along with inulin and other oligosaccharides.

Organization (reference)	Definition
Institute of Medicine [30]	Dietary fiber consists of nondigestible carbohydrates and lignin that are intrinsic and intact in plants. Functional fiber consists of isolated, nondigestible carbohydrates that have beneficial physiologic effects in humans.
American Association of Cereal Chemists [31]	Dietary fiber is the edible parts of plants or analogous carbohydrates that are resistant to digestion and absorption in the human small intestine, with complete or partial fermentation in the large intestine. Dietary fiber includes polysaccharides, oligosaccharides, lignin, and associated plant substances. Dietary fibers promote beneficial physiologic effects including laxation, and/or blood cholesterol attenuation, and/or blood glucose attenuation.
CodexAlimentarius Commission [32]	Dietary fiber means carbohydrate polymers1 with ≥10 monomeric units2, which are not hydrolyzed by the endogenous enzymes in the small intestine of humans

TYPES AND SOURCES OF DIETARY FIBRE

- Water insoluble dietary fibre:

Sources of soluble fibre

Nutrient	Food additive	appearance / preparation
β-glucans (a few of which are water soluble)		
Cellulose	E 460	cereals, fruit, vegetables (in all plants in general)
Chitin	—	in fungi, exoskeleton of insects and crustaceans
Hemicellulose		cereals, bran, timber, legume
Hexosane	—	wheat, barley
Pentosane	—	rye, oat
Lignin	—	stones of fruits, vegetables (filaments of the garden bean), cereals
Xanthan	E 415	production with Xanthomonas-bacteria from sugar substrates

Sources of insoluble fibre

Nutrient	Food additive	appearance / preparation
Fructans		replace or complement in some plant taxa the starch as storage carbohydrate
Inulin	—	in diverse plants, e.g. topinambour, chicory, etc.
Polyuronide		
Pectin	E 440	in the fruit skin (mainly apples, quinces), vegetables
Alginic acids (Alginates)	E 400–E 407	in Algae
Natriumalginat	E 401	
Kaliumalginat	E 402	
Ammoniumalginat	E 403	
Calciumalginat	E 404	
Propylenglycolalginat (PGA)	E 405	
agar	E 406	
carrageen	E 407	red algae
Raffinose	—	legumes
Xylose	—	monosacharide, pentose
Polydextrose	E 1200	synthetic polymer, ca. 1kcal/g
Lactulose	—	Synthetic disacchride

FIBER CONTENT IN FOOD:

Dietary fibre is most found invegetables and fruit. The exact amount of fibre contained in the food can be seen in the following table of expected fibre in USDA food groups/subgroups [33].

FOOD GROUP	SERVING MEAN	FIBER g/SERVING
Fruit	0.5 cup	1.1
Dark green vegetables	0.5 cup	6.4
Orange vegetables	0.5 cup	2.1
Cooked dry beans (legumes)	0.5 cup	8.0
Starchy vegetables	0.5 cup	1.7
Other vegetables	0.5 cup	1.1
Whole grains	28g (1 oz)	2.4
Meat	28g (1 oz)	0.1

FIBRE SUPPLEMENTS

These are a few example forms of fiber that have been sold as supplements or food additives. These may be marketed to consumers for nutritional purposes, treatment of various gastrointestinal disorders, and for such possible health benefits as lowering cholesterol levels, reducing risk of colon cancer, and losing weight.

Soluble fiber supplements may be beneficial for alleviating symptoms of irritable bowel syndrome, such as diarrhea or constipation and abdominal discomfort [34]. Prebiotic soluble fiber products, like those containing inulin or oligosaccharides, may contribute to relief from inflammatory bowel disease, [35] as in Crohn's disease, [36] ulcerative colitis, [37, 38] and *Clostridium difficile* [39] due in part to the short-chain fatty acids produced with subsequent anti-inflammatory actions upon the bowel [40-41]. Fiber supplements may be effective in an overall dietary plan for managing irritable bowel syndrome by modification of food choices [42].

One insoluble fiber, resistant starch from high amylose corn, has been used as a supplement and may contribute to improving insulin sensitivity and glycemic management [43-45] as well as promoting regularity [46] and possibly relief of diarrhea [47-49]. One preliminary finding indicates that resistant corn starch may reduce symptoms of ulcerative colitis [50].

PHYSIOCHEMICAL PROPERTIES

Dietary fibers has distinct physiochemical properties. Most semisolid foods, fiber and fat are a combination of gel matrices which are hydrated or collapsed with microstructural elements, globules,solutions or encapsulating walls. Fresh fruit and vegeatables are cellular materials [51-53].

- The cells of cooked potatoes and legumes are gels filled with gelatinized starch granuls. The cellular structures of fruits and vegetables are foams with aclosed cell geometery filled with a gel, surrounded by cells walls which are composites with an amorphous matrix strengthened by comlex carbohydrate fibres.
- Particlesize and interfacial interactios with adjacent matrices affect the mechanical properties of food composites.
- Food polymers may be soluble in and/or plasticized by water. Water is the most important plasticizer ,particularly in biological systems thereby changing mechanical properties.
- The variables include chemical structure,polymerconcentration, molecular weight, degree 6of chain branching , the extent of ionization (for electolytes), solution pH, ionic strength and temperature.
- Cross linking of different polymers, protein and polysachhrides , either through chemical covalent bonds or cross links through molecular entanglement or hydrogen or ionic bond crosslinking.
- Cooking and chewing food alters these physiochemical properties and hence absorbtion and movement through the stomach and along the intestine.

MECHANISM OF FIBRE

Dietary fibres have three primary mechanism:

- Bulking
- Viscosity
- Fermentation

Dietary fibres can change the nature of the contents of the gastrointestinal tract, and to change how other nutriets and chemicals are absorbed through bulking and viscosity.Some types of soluble fibres bind to bile acids in the small intestine making them less likely to renter the body; this in turn lowers cholesterol levels in the blood from the actions of cytochrome P-450 mediated oxidation of cholesterol. Viscous soluble fibres may also attenuate the absorbtion of sugar, reduce sugar responseaftereating, normalize blood lipid levels and , once fermented in the colon, produce short chain fatty acids as byproducts with wide ranging physiological activities. Insoluble fibre is associated with reduced diabetes risk, but the mechanism by which this occurs is unknown.

DIETARY FIBRE AND THE UPPER GASTROINTESTINAL TRACT

A slowly eaten meal will enter the absorptive phase of the gastrointestinal tract more slowly than a ralidly eaten meal fo similar composition. Many of the differences between between low and high glycemic foods would disappear if meal was eaten slowly [54].

The chemical and physiochemical nature of the meal will also influence the gastric emptying of food multiphase system. Fatty foods and hypertonic solutions empty slowly. The movement of food, i.e., chime, along the gastrointestinal tract, polymer flow and diffusion becomes important

Following a meal, the stomach and upper gastrointestinal contents consist of

- Food compounds
- Complex lipid/micellar/aqueous/hydrocolloid and hydrophobic phases
- Hydrophilic phases
- Solid, liquid, colloidal an gas bubble phases[55].

Two mechanisms bring nutrients into contact with epithelium:

1. Intestinal contractions create turbulence and
2. Convection currents direct contents from the lumen to the epithelial surface.

CONCLUSION

Regular intake of antipsychotic drugs for the treatment of psychosis disorders like schizophrenia, Hallucinations,etc. result into the higher lipid level in the body and increase lipid profile in the blood. The higher lipid will result into hyperlipidemia which affect the body weight and body size. There will be increase in body weight and causes many other problem in the body including cardiac problem,etc. To control over this side effect,hyperlipidemia, of antipsychotic medications, the fibre diet has been administered regularly along with antipsychotic medication so that there will be a normal levels of lipid in blood. Fibre diets are of two types: Soluble fibre and Insoluble fibre which act by different mechanism like Bulking, Viscosity and Fermentation.Advantages of consuming fibre are the production of healthful compounds during the fermentation of soluble fibre and insoluble fibre's ability to increase bulk,soften stool and shorten transit time through intestinal tract. Disadvantages of a diet fibre is the potential for significant intestinal gas production and bloating.constipation can occur if sufficient fluid is consumed with ahigh fibre diet.

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