Review Article

Mental Illness: Treatments and Associated Adverse Drug Reactions

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ABSTRACT

Mental illness encompasses a broad spectrum of conditions that impact an individual's mood, thinking, and personality. Since, ancient era often Mental illness is connected with the evil possession in the person as the evolution of the medicinal field the view of Mental health have been changed and medication as well as non-medical treatment intervention have been developed and the myth regarding it have been changed progressively. In this article, we study regarding various common mental health conditions like Psychosis, Depressant, Anxiety and Bipolar disorder with its treatment. Additionally, the adverse drug reactions and management of the adverse drug reaction have been studied.

Keywords: Mental illness, Adverse Drug Reaction, Management of ADR, Psychosis.

1. INTRODUCTION

Drugs the substances other than food that produce the changes in physiological and psychological condition of patients. That is intended to reduce the abnormality or disease condition of a patient by properly diagnosing then preventing and treating it. Adverse drug reactions are unintended or untoward which is caused due to intervention of the medicinal product. Adverse drug reactions (ADRs) continue to be a problem in modern medicine, especially in the context of growing multi-morbidity, aging populations, and more sophisticated therapies.[1] (Coleman JJ, 2016 Oct;16(5))

Pharmacovigilance and drug safety are nevertheless significant fields in medicine and science. According to the World Health Organization (WHO), pharmacovigilance is described as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem".[2] (WHO, 15)

James Lind's first clinical experiment, which was recorded in 1747, proved that lemon juice was effective in reducing scurvy.[3] (Bhatt., 2010) When Hannah Greener, a 15-year-old girl, came for the surgical removal of a toenail on January 28, 1848, she was given chloroform which caused the death of the girl. It was later proven that it was due to the side effect of anesthesia that produced cardiac arrest.[4] (Paul R Knight 3rd, 2002 May;96(5)) Pregnant women with nausea were frequently treated with thalidomide. The 1960s witnessed the discovery that hundreds of children receiving thalidomide had serious birth abnormalities.[5] (James H Kim, 2011 Jul;122(1)) Numerous studies have proven the side effects related to the drugs.

1.1 Mental Illness Theories

Fortunately, the development of mental disease has been cyclical rather than linear or progressive. The context of behavior determines whether it is deemed normal or deviant, and this context varies depending on the time and society in question. Three broad hypotheses about the cause of mental disease have been proposed historically. They are supernatural, somatogenic, and psychogenic.

According to supernatural theories, mental illness can be caused by demons or bad spirits possessing a person, gods being angry, eclipses, planetary gravitational pull, curses, and sin. Somatogenic theories identify disturbances in physical functioning resulting from either illness, genetic inheritance, or brain damage or imbalance. Psychogenic theories concentrate on skewed perceptions, regressive learning associations and cognition, and catastrophic or traumatic events. The care and treatment that mentally ill people get is determined by etiological theories of mental illness.

2. Mental illness

Mental health diseases, commonly referred to as mental illness, cover a wide variety of psychiatric disorders that affect a person's behavior, emotions, and thought processes. In India, one of the primary contributors to the burden of nonfatal diseases is mental illness. In 2017, mental illnesses of different kinds affected one in seven Indians.[6] (India State-Level Disease Burden Initiative Mental Disorders Collaborators. The burden of mental disorders across the states of India: The global burden of disease study 1990-2017., 2020) Pharmacovigilance can be very helpful in psychiatric units in detecting adverse drug reactions (ADRs) and informing medical professionals about the possibility and circumstances of these events that prevent patients from being harmed unnecessarily by

avoidable injury. Consequently, ADR monitoring minimizes the cost of therapy by assisting in the formulation of acceptable interventional programs to manage, prevent, and restrict the risk of developing ADRs.[7] (Jaspreet Kaur Sidhu, 2023)

ADRs for psychiatric medications are frequent. When receiving extended treatment, noncompliance is common. This may result in physical morbidity, stigma, therapy cessation, and a decline in standard of life. The majority of adverse drug reactions (ADRs) are influenced by patient factors and dosage. Anti-psychotics differ in the prevalence and severity of adverse drug reactions.[8] (Dhanya Thirookaran Harichandran, Aug 2016)

The Mental Care Act of India was enacted on April 7, 2017, and it became effective on May 29, 2018. This was an updated version of the 1987 Mental Health Act. The legislation was described in the first paragraph as "an act to provide for mental healthcare and services for persons with mental illness and to protect, promote and fulfill the rights of such persons during delivery of mental health care and services and for matters connected therewith or incidental thereto"

2.1 Psychosis

Psychosis is a collection of mental health conditions that lead to a person losing their sense of reality. This feature is shared by a number of medical, neuropsychiatric, psychiatric illnesses, neurologic and neurodevelopmental. Medical professionals increasingly address psychosis as their primary therapeutic objective because it can bring patients and their loved ones a tremendous lot of distress.[9] (Jordan Calabrese, 2023) It is treated by anti-psychotic drugs.

Anti-psychotic medications frequently alleviate the severity of hallucinations and delusions and enable the person with schizophrenia to operate in an atmosphere of acceptance, but they are not curative and do not cure chronic thinking disorders. [10] (Whalen, 2019)

2.1.1 Pathophysiology

Excess dopamine in the mesolimbic tract is thought to be the source of the alluring symptoms associated with psychotic illnesses. Another excitatory neurotransmitter involved is glutamate. Numerous investigations have revealed that the NMDA glutamate receptor is functioning less well.[11] (Geddes AE, 2011) Gamma-aminobutyric acid (GABA), a significant inhibitory neurotransmitter, has also been mentioned in studies.[12] (Kinon BJ, 2011) Certain examinations involving schizophrenic patients have shown signs of dysfunction. Finally, the consequences suggest an acetylcholine imbalance.[13] (Freedman R, 2008)

2.1.2 Symptoms

Hallucinations, disorganized thought, delusions, catatonia, disorganized behavior, and negative symptoms like the decline in emotions, words, movements, or motivation (anhedonia).[14] (Ditzell, 2023)

2.1.3 Treatment

Anti-psychotic Drugs, Talking Therapies, Cognitive behavioral therapy, Family intervention, self-help groups, and rehabilitation from psychosis.[15] (Ninan A, 2014)The combination of multiple antipsychotic drugs had a greater effect on renal function than monotherapy.[16] (Sun, 2022)

Anti-psychotic drugs:

TYPICAL ANTI-PSYCHOTIC DRUGS: Chlorpromazine, Triflupromazine, Thioridazine, Trifluoperazine, Haloperidol, Trifluperidol, Fluephethixol, Pimozide, Loxapone.

ATYPICAL ANTI-PSYCHOTIC DRUGS: Clozapine, Risperidone, Olanzapine, Quetiapine.

ADVERSE DRUG REACTIONS: CNS effect - Drowsiness, Lethargy, Mental confusion. Weight gain and increased appetite. CVS effect - QT Prolongation, Postural hypotension, inhibition of ejaculation common in thioridazine. Hyperprolactinemia is common with typical neuroleptics and risperidone. Elevated levels of blood glucose. The extrapyramidal effect is the most frequent side effect with neuroleptic drugs.

2.2 Depression

Sadness and/or a loss of interest in once-enjoyable activities are symptoms of depression.

2.2.1 Introduction

Depression is classified into different categories based on their influence on symptoms, such as disruptive mood disorder, disruptive behavior, and persistent depressive disorder.

2.2.2 Etiology

First-degree relatives of depressed people are almost threefold more likely to have depression than the general population, even though depression can strike anyone without a family history of depression. The diseases of Alzheimer's and Parkinson's and other neurological conditions like stroke, multiple sclerosis, seizures, cancer, macular degeneration, and chronic pain are associated with greater rates of depression.

2.2.3 Pathophysiology

Serotonin (5-HT) activity in the central nervous system has a significant impact on physiological research, both preclinical and clinical. Norepinephrine (NE), dopamine (DA), glutamate, and brain-derived neurotrophic factor (BDNF) are more related neurotransmitters.[17] (Pham TH, 2019)

2.2.4 Symptoms

An evaluation of neurodegenerative symptoms, such as irregular sleep patterns, appetite, and energy levels, is part of an introduction to depressed symptoms. The signs of depression can vary in severity and include things like difficulty sleeping, Reduced interest or enjoyment,

sentiments of worthlessness or shame, Changes in energy/fatigue, decreased focus/attention, and changes in appetite/weight.[18] (Suma P Chand, 2023)

2.2.5 Evaluation

Physical examination results and medical history are used to diagnose depression. The following laboratory tests may be performed the measurement of the fluid level of calcium, magnesium, blood urea nitrogen (BUN), creatinine, thyroid-stimulating hormone (TSH), vitamin B-12, rapid plasma regain (RPR), HIV test, and complete blood count (CBC). Brain computed tomography (CT) or magnetic resonance imaging (MRI) is the differential diagnosis involving organic brain syndrome or hypopituitarism.[19] (Mangla K, 2019)

2.2.6 Treatment

Combination therapy was linked to far higher rates of compliance, an improvement in quality of life, and a reduction in depressive symptoms. Empirical evidence also supports CBT's capacity to deter recurrence. The related treatments include CBT, antidepressants, and Electroconvulsive therapy (ECT)**.** [20] (Rootes-Murdy K, 2019)

TRICYCLIC ANTIDEPRESSANTS (TCAs): Imipramine, Amitriptyline, Clomipramine, Doxepin, Dothiepin, Reboxetine

ADVERSE DRUG REACTIONS: Anticholinergic effects, increased appetite and weight gain, sedation, mental confusion and weakness, sweating, postural hypotension, cardiac arrhythmia, sexual distress.

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs): Fluoxetine, Sertraline, Escitalopram, Sertraline, Dapoxetine

ADVERSE DRUG REACTONS: Nausea, Anxiety, Drowsiness, Insomnia, Sexual dysfunction

REVERSIBLE INHIBITORS OF MOA-A (RIMA): Moclobemide, Clorglyine.

ADVERSE DRUG REACTIONS: Nausea, dizziness, head ache, insomnia.

SEROTONIN AND NORADRENALINE REUPTAKE INHIBITORS (SSRIs): Venflaxine, Desvenflaxine, Duloxetine

ADVERSE DRUG REACTIONS: Nausea, sweating, anxiety, dizziness, impotence and withdrawal reactions.

2.3 Anxiety

Fear is an automatic neurophysiological state of alertness characterized by a fight-or-flight response to the cognitive assessment of an existing or imminent threat (real or perceived). Anxiety is related to fear and manifests as an anticipatory mood state consisting a comprehensive system of cognitive, emotional, physical and behavioral reactions related to preparation for perceived threatening events or conditions.[21] (Lahousen T, 2018)

2.3.1 Etiology

A variety of bio-psycho-social factors seem to contribute to the development of anxiety disorders. Clinically significant syndromes are the result of the interaction between genetic vulnerability and stressful or traumatic conditions.

The following circumstances may result in anxiety: medications, natural remedies, substance misuse, trauma, early life events, and panic attacks. [22] (Domhardt M, 2019)

2.3.2 Pathophysiology

The amygdala is a key component in reducing anxiety and terror. Patients suffering from anxiety disorders have been shown to have an elevated amygdala response to anxiety disorders. Prefrontal cortical regions are linked to limbic system and amygdala structures, and pharmacological or psychological therapies can rectify anomalies in prefrontal-limbic activity.[23] (Chand SP, 2023)

2.3.3 Symptoms

Cognitive symptoms: Fear of losing control; fear of being physically hurt or killed; fear of "going crazy"; fear of others' unfavorable opinions; frightening ideas, visions, or memories; feeling of detachment or unreality; inability to focus, getting lost, or becoming distracted; memory loss; and trouble speaking.

Physiological symptoms: elevated heart rate, palpitations, rapid breathing, shortness of breath, pressure in the chest, a sense of suffocation, vertigo, sweating, heat, or cold, nausea, upset stomach, diarrhea, trembling, tingling in the hands and feet, weakness, unsteadiness, fainting, tense muscles, stiffness, and dry mouth. [24] (Cosci F, 2015)

2.3.4Treatment of anxiety [25] (Chapdelaine A, 2018)

1. Anti-anxiety medications

Acute anxiety may require treatment with a benzodiazepine. Treatment for chronic anxiety consists of psychotherapy, drug therapy, or a combination of these. Medical treatment includes various medications.

BENZODIAZEPINES: Diazepam, Lorazepam, Chlordiazepoxide, Alprazolam, Flurazepam

ADVERSE DRUG REACTONS: Respiratory depression, Drowsiness, Confusions, Headache, Nausea or vomiting, Diarrhoea, Tremor.

AZAPIRONES: Buspirone, Gepirone, Isapapirone

SEDATIVE ANTIHISTAMINIC: Hydroxyzine

β- ADRENERGIC BLOCKER: Propranolol

2.3.2. Psychotherapy

Cognitive-behavioral therapy is one of the most successful methods of psychotherapy. This type of therapy is structured, focused on goals, and didactic. Its major objective is to assist clients in understanding and modifying common maladaptive thought patterns and beliefs that lead to and perpetuate symptoms. The primary

objective of this type of treatment is to help patients become more adept at managing their behavior in order to react and behave more correctly in situations that cause anxiety.

2.4 Bipolar Disorder

Bipolar disorder (MA) is characterized by chronic episodes of mania or hypomania alternating with depression, often misdiagnosed at first.

2.4.1Etiology

It is believed that abnormalities in intracellular signaling systems that control mood as well as monoaminergic neurotransmitters, specifically dopamine and serotonin, are the cause of borderline personality disorder (BD). There hasn't been any evidence of a neurotransmitter system malfunction though.

2.4.2Pathophysiology

Bipolar disorder's pathogenesis is unclear; however, it is believed to entail interactions between a number of genetic, neurochemical, and environmental variables.[26] (S., 2022)

2.4.3 Symptoms

Irritability and aggression, Sleep disturbances, proactivity[27] (McGuffin P, 2003)

2.4.4 Treatment of bipolar disorder

There are many clinical practice guidelines available for treating and managing bipolar disorder, yet there is enough uniformity. Make a model known as "metaconsensus". "The lack of common language and recommendations in current guidelines may be an additional complicating factor in the implementation of evidence-based treatments for BD," the authors of the systematic review found. [28] (Miklowitz DJ)

2.4.4.1 Medications

Medications that can aid in mood stabilization and guard against manic episodes and sadness. They also support mood maintenance without getting in the way of job, school, or social obligations. Any manic or depressed episode lasting many days or weeks is treated with these medications.[29] (Skjelstad DV, 2010) Antipsychotic agents that may have superior efficacy or more rapid action than the mood stabilizer. Continuing to enhance advancements antimanic drugs with improved effectiveness through medical trials with better short or long-term tolerance. [30] (Yildiz A, 2011)

LITHIUM CARBONATE

ADVERSE DRUG ACTIONS: Side effects are common, but are mostly tolerable. Toxicity occurs at slightly elevated levels compared to therapeutics only.

ANTICONULSANTS: Sodium Valporate, Carbamazepine, Lamotrigine

ATYPICAL ANTIPSYCHOTICS: Olanzapine, Risperidone, Quetiapine, Aripiprazole.

2.4.4.2 Maintenance treatment

Extended maintenance therapy is usually necessary for bipolar disorder patients in order to prevent relapses in symptoms and to return to normal functioning. [31] (Betcher HK, 2019)

3.ADVERSE DRUG REACTIONS ASSOCIATED WITH MENTAL ILLNESS

In a retrospective analysis conducted in 2021, Sneha Ambwani et al. found that antipsychotics accounted for the bulk of adverse drug reactions (ADRs), followed by antidepressants and antiepileptics. Sedation was the most frequent adverse drug reaction, followed by weight gain, akathisia, and excessive salivation.[32] (Ambwani S, 2021)

Adverse drug reaction in Children:

Children are being prescribed more psychotropic drugs than ever before, and each child is being prescribed a greater variety of medications. Younger persons are more likely than adults to experience additional pyramidal unpleasant events, and children may be more sensitive to negative events than adults.[33] (Chand SP A. H., 2024) Regardless of when they received treatment, pediatric patients had a higher risk of developing dyslipidemia, drowsiness, involuntary movements/EPS, and seizures.[34] (Jerrel., 2010) Additionally, pediatric patients with anxiety disorders and depressants are more likely to experience headaches and headache syndromes.[35] (Crawley SA, 2014)

Adverse Drug Reaction in Pregnant Women:

Mental health issues are frequently present throughout pregnancy and lactation. Treatments for these illnesses are crucial since they might affect a mother's and child's health.[36] (Marano G, 2011) Most antipsychotic medications used during pregnancy and their harmful effects on the unborn child. It is also advised that women continue their treatment with less dangerous medications.[37] (Reutfors J, 2020) Prochlorperazine is mostly used to treat nausea in the early stages of pregnancy, according to a study on the incidence and usage trends of antipsychotic medications during pregnancy in ten countries on four continents. Antipsychotic medication use peaked before and at the start of pregnancy.[38] (Ellfolk M, 2020) Prenatal exposure to antipsychotic medicines of the second generation has been linked to a higher risk of pregnancy problems, specifically altered glucose metabolism. Newborn issues are frequent and manifest similarly in SGA and FGA users.[39] (Vancampfort D, 16)

Adverse Drug Reactions associated with Anti-psychotic Drugs:

Considering the exception of aripiprazole and amisulpride, all antipsychotics have been linked to a high incidence of diabetes, and the rate of diabetes is higher in those using first- or second-generation antipsychotics than in the general population.[40](I.G.Holt., 2019) Antipsychotics work

therapeutically by antagonistically binding to D2 dopamine receptors; they also effect on adrenergic, histamine, and serotonin receptors. These receptors control intermediate metabolism and body weight.[41] (Babu GN, 2015 Jul) Psychotropic medications may have adverse effects on the cardiovascular system that are probably more prone to cardiac toxicity. Psychotropic medications cause cardiovascular problems, and their effects on antidepressant treatment with a prior medical history are noted.[42] (Liu HC, 2018) Individuals with schizophrenic illness who also take immune-suppressive drugs are more vulnerable to TB. When combined with other antipsychotic medications, clozapine reduces tuberculosis risk more effectively than when used alone.[43] (DL., 2003) Contrary to first-generation antipsychotics, which are linked to neurological ADR, second-generation antipsychotics are linked to metabolic ADR. [44] (Szabo., 2011) Furthermore, it was discovered that clozapine had greater rates of ADR-induced liver enzymes, whereas risperidone and haloperidol caused extrapyramidal symptoms.[45] (Bender S, 2004)

An increased probability of glucose intolerance appears to be connected with treatment with clozapine, olanzapine, or risperidone. Anticholinergic medications could load to urinary retention and should be steered clear of in causes of obstructive genitourinary issues Also, the phenothiazine group of antipsychotic medications increases the risk of hypotension in patients with chronic kidney disease and second-generation antipsychotic medications are considered to be safe in renal diseases as most of them metabolized in the liver.[46] (Dalal PK, 2022)

The impact of several antipsychotic medication combinations on renal function was higher than that of monotherapy. The adverse events seen with clozapine were gastrointestinal disturbance, hypersalivation, dizziness and fatigue.[47] (Association, Association, Endocrinologists, & Obesity., 2004)

Adverse Drug Reaction associated with Anti manic Drugs:

The most prevalent adverse reactions of mood stabilizers for bipolar illnesses include sleepiness, weight gain, and cognitive impairment. These effects can be lessened by utilizing more recent medications, such as Topiramate, which is also linked to weight loss.[48] (Gupta S, 2000) The most common medication for mood disorders is lithium. Its therapeutic index is quite narrow, and adverse effects are observed in numerous organ systems. Nephrogenic diabetic insipidus is the result of lithium intoxication.[49] (Şenocak Taşçi E, 2019)

Adverse Drug Reaction associated with Anti-depressant Drugs:

According to research, 22% of kids and teens of both sexes experience psychological side effects after SSRI medication, and 21% of kids receiving treatment for serious depressive disorders have been found to experience behavioral side effects from sertraline.[50] (Donnelly CL, 2006) Link between long-term Imipramine use and Q-switched and picosecond laser therapy for photo disrupted hyperpigmentation. Even after stopping their medications, some individuals may experience pigmentation that does not go away for years.[51] (Hamid RN, 2021) Tricyclic antidepressants should be avoided by patients on immunosuppressants. Furthermore, medications such as fluoxetine inhibit CYP3A4 enzymes in the liver and raise the plasma level of calcineurin inhibitors, therefore SSRIs and SSNRIs should be used cautiously. Youngsters treated with antidepressants frequently report having headaches. According to Rawlims MD et al. (1988), three individuals who were taking fluoxetine, clomipramine, and lithium together experienced serotonin syndrome. (ii) Mianserin with sertraline. (iii) Mianserin and Citalopram, which manifested symptoms such as (i) agitation, tremor, and confusion. (ii) Perplexity and hyperreactivity (iii) fever, myoclonus, and confusion.[52] (MD., 1988)

4. MANAGEMENT of ADVERSE DRUG REACTIONS:

Aburamadan et al. conducted research on the need for ongoing patient monitoring of ADR and, if feasible, cautious selection of treatment alternatives.[53] (Aburamadan HAR, 2021) To control side effects, such as encouraging healthy lifestyles, using low-risk antipsychotics or switching to them, or adding weight-loss drugs. It also entails encouraging patients to make the required adjustments, such as giving up smoking, starting a nutritious diet, and engaging in regular exercise.[54] (Maayan L, 2010)

Atypical antipsychotic adverse drug reactions (ADRs) have significantly decreased, with olanzapine and risperidone being linked to the highest number of ADRs, respectively.[55] (Pinaki Chakravarty, 2016) Upon reviewing antipsychotic patients' case histories, it was discovered that there was a developing risk of hypertension. Even though this ADR is uncommon, BP must be closely monitored in order to prevent it from happening.[56] (Alves BB, 2019) Given that fluoxetine may block clozapine metabolism, administering fluoxetine with clozapine at the same time raises clozapine plasma concentrations and improves the pharmacological effects of clozapine.[57] (Ferslew KE, 1998) Dosage reduction is the therapeutic strategy for symptomatic hyperprolactinemia caused by antipsychotics. Aripiprazole is an option that can be used if the clinical risk of dose reduction is deemed too high. This medication has been demonstrated to lower prolactin levels in patients receiving risperidone. [58] (Maher S, 2016) Fludrocortisone is frequently used to treat orthostatic hypertension and has also been successfully utilized to alleviate orthostatic hypotension brought on by clozapine.[59] (Jr., 1994) Since dystonia is extremely upsetting and unpleasant, the best course of treatment is prevention. Anticholinergic drugs are the cornerstone of dystonia prevention. Prophylactic benztropine administration is beneficial for strong antipsychotics.[60] (Stern TA, 1979) nonetheless, it might not work with low potency drugs.[61] (Swett C Jr, 1977)

Bipolar patients were administered more drugs overall when they had cardiometabolic disease. Therefore, cutting back on the amount of prescription drugs will aid in lowering the frequency of ADRs.[62] (Weinstock LM, 2014) Antipsychotic extrapyramidal side effects can be treated by combining antidotes with medications that have a proven adverse drug reaction (ADR), such as anticholinergic medicines.[63] (Erden A, 2013)

DICUSSION

The co-occurrence of mental illness and chronic illnesses results in polypharmacy, or the use of many medications, which raises the risk of drug interactions. Health care professionals must be vigilant sufficiently knowledgeable about how medications work. The psychiatric dosage ought to be determined by the patient's etiology and mental state. Appropriate counseling should be used to guarantee patient adherence. Because patients often refuse to acknowledge their condition and refuse to take their medications while acting well, it is important to regularly monitor them to ensure compliance. They can utilize tools like pill boxes and frequent reminders to make sure the medication is followed. In order to prevent ADRs associated with improper drug storage, they should also get education on this topic. For mental health issues, complementary and alternative therapy include electrical stimulation, yoga, and dietary supplements like kava and omega-3s. These methods could improve overall wellbeing, lessen anxiety, lessen depressive symptoms, and promote relaxation.

CONCLUSION

The nature of mental disorders has existed hotly debated throughout history. The belief that "mental illness is brain illness," which was made nearly two centuries ago, had a significant impact on the development of the more recent medical knowledge of mental illness. Significant advances in brain imaging and genetics over the past 20 years have reinforced biological psychiatry and helped to validate mental illnesses as brain diseases. Mental health practitioners and efforts to improve public understanding of the mentally ill have been impacted by the prominence of the almost exclusively bio genetic conceptual framework for understanding mental illness. Consequently, the proverb "mental illness is like any other illness" is now almost universally accepted and, as such, it stands for an uncontested fact.

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