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Prof. Dr. **Boby Johns G**

From The Chief Editor's Desk

I am happy to present before you the third issue of Pharmline, Vol.21, August 2022. First of all, I would like to acknowledge my forbearer Dr. CS Sathish Kumar for his dedication in carrying forward Pharmline to this point. It's my privilege to take the torch he led forward as the Chief editor of our Official publication.

It's a pleasure to acknowledge our dynamic President Dr. PK Sreekumar, Gen.Secretary, Mr. Abdul Nazeer PU, executive members and all other members of Kerala Pharmacy Graduates' Association for entrusting me with this task. I believe the official publication of any professional organization is the reflection of its presence and activities in the society. We hope to elevate the status of Pharmline to the next level with the support of all honorable members in the near future.

I am happy that KPGA is organizing various activities like seminars, webinars, various day celebrations, essay competitions and the like for the benefit of pharmacy students and pharma professionals. Many such activities are in the pipeline. We could conduct the general body meeting at our own prestigious premises at Thiruvananthapuram in the month of July,2022.

The general body meeting was a pleasant experience to all the members especially after the long pandemic season. The veterans in our profession were honoured which was an inspiration to all the budding members of KPGA.The meeting provided a platform for interaction between the younger and senior members, exchange of ideas, viewpoints etc. Various challenges especially related with our dream project pharma city were discussed in detail.

As we have celebrated the 76th Independence Day of our country, let us rededicate ourselves to work for the prosperity of our profession in our country and thereby keep the flag of KPGA flying high. Also, season's greetings to all...!!

Prof.Dr. **Boby Johns G**
Chief Editor, Pharmline

The President Speaks

Dr. PK Sreekumar

Dear Members,

Season's Greetings from KPGA !

I am so proud and glad of the contribution made by our esteemed members in joining our general body meeting conducted on 17/07/22. We all met after a disastrous covid affected time in our own beautiful hall at KPGA building, Trivandrum. We could meet our leaders who established our association and continue to guide us too. There was active interaction with our very senior professionals and younger generation. Many of our dedicated members travelled from outside Kerala, north and middle of Kerala exclusively for this purpose and all enjoyed the session with delicious food. It was a prestigious event during which some of our very seniors were honoured. This unity would strengthen and further nourish our association. Thank you one and all team KPGA, led by the dynamic general secretary for the sincere approach.

The brains behind our dream project "Pharmacity" presented the project and in the subsequent discussion it was evident that the profession has no future without Industry in Kerala. For the enormous number of students graduated from around 60 colleges in Kerala, outside Kerala and for the professionals related, including the management, we should take all efforts to create awareness to the management, pharma fraternity and public to get it materialized by the Government. The association is moving forward to this goal.

The relevant presentation on the "Kerala Pharmacy Conference" is another vital step for our association, and the assurance from the Principal and management, St James College of Pharmaceutical Sciences, Chalakudy is really appreciable and definitely will motivate others also to work hard towards it.

The keen interest advice and leadership from the coordinators on strengthening student's forum, funding the students on their projects, need to implement KPGA awards to professionals etc. are commendable and the contribution of Rs 50000/ by Sri. Jossy John from Australia Rs 25000/ By Sri Abdusamad, our Hon. Vice President and Rs 10000/ by Dr. Satheesh Kumar, our active leaders have contributed to the fund and there are no words to express our gratitude for their excellent service to the budding pharmacists and real professionals. The Editorial committee released the newly designed latest edition of "Pharmline" enriched with scientific articles. The work behind it by the Chief editor, editorial board, the new design work by Dr Boby is remarkable, I express my sincere thanks to all of them. The Editorial team was strengthened and best wishes to them.

For the first time, we have celebrated 75th anniversary of Independence day with new style and many of our members attended the virtual program and felt proud to be a part of an independent nation that has freedom of speech and freedom to live life in our own way. Also, we are celebrating World Pharmacists Day on 25th September, this time too through the slogan "Pharmacy united in action for a healthier world" which aims to showcase the Pharmacists positive vibe on the health of the society around the world and to further strengthen the solidarity among the professionals. Certain physical programs are also in the pipeline. Life is full of struggles and every day brings new challenges before us. To overcome these situations and achieve our desired success, we need support and appreciation from our professionals. I request all the members to unite under this platform to overcome the challenges and to propel our profession to higher altitudes.

Warm regards and best wishes,
Dr.**PK Sreekumar,**
President, KPGA

CYSTIC FIBROSIS: CURRENT TREATMENT APPROACHES AND FUTURE DIRECTIONS

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ABSTRACT

Cystic fibrosis (CF) is an autosomal recessive disease caused by mutations in the CF transmembrane conductance regulator (CFTR) gene. The subsequent CFTR protein defect causes abnormalities in both salt and fluid transport across epithelia, which in the lung, leads to dehydration of the airway surface and impaired mucociliary clearance. This review summarizes the current and upcoming pharmacological options for CF, such as those targeting the CFTR gene defect directly, including gene editing, CFTR correctors and potentiators; drugs targeting the epithelial sodium channels (ENaC inhibitors); repositioning of some existing drugs and evaluating their role in CF; and understanding the disease better by transcriptomic approaches and the role of gut microbiota in the disease process and severity.

KEYWORDS: Cystic fibrosis, CFTR, Chloride ion channels, Sodium epithelial channels

Introduction

Cystic fibrosis (CF) is a type of autosomal recessive disorder that causes severe damage to lungs, digestive system and other organs. The mutations in the CF transmembrane conductance regulator (CFTR) gene is known to be the reason for CF. Although CF is common in people of all races and ethnicity. CFTR which functions as a chloride ion trafficker in the plasma membrane of the epithelial cells of pancreas, liver, intestines, epididymis, sweat glands and lungs and this chloride transport across ion channels helps maintain the movement of water in tissues, necessary for production of thin, free flowing mucus[1]. CFTR is responsible for regulating sodium and chloride ion transport whereas it promotes the reabsorption of chloride in sweat glands. Gene defect of CFTR causes abnormal transport of glandular secretions and inadequately hydrated mucus which leads to ductal obstruction and finally tissue injury or infection[2,3,4.] There are about 30,000 people with cystic fibrosis in the United States and approximately 70,000 people worldwide. It is believed that 1 in 30 Americans is a carrier of CF and most common in Caucasians[5]. Diagnosis can be made by: new born screening, Genetic testing and sweat test, for carrying out abnormally high chloride levels measurement; and trans-epithelial nasal lining testing which may be used as a confirmatory test in which more negative trans epithelial potential difference across nasal epithelium is seen in diseased individuals[6]. Airway clearance therapy (ACT) has also proven useful in CF, is done by using a device called the "VEST. Any pancreatic insufficiency can be overcome by pancreatic enzyme replacement therapy (PERT) containing combinations of proteases, lipases and amylases[7].

Current Pharmacotherapy of cystic fibrosis

Main goal of CF therapy is on the correction of structural and functional abnormalities of the altered CFTR protein. For this CFTR modulators can be used some of them are Ivacaftor, lumacaftor, elexacaftor and tezacaftor, available as monotherapy or in combination with one another. Ivacaftor was the first targeted drug approved by Food and Drug Administration (FDA) in 2012. Mechanism of Ivacaftor is opening the Cl– channel and increase the duration, thus improving chloride transport. High cost of therapy is a limiting factor[8]. Lumacaftor is used along with ivacaftor as a combination therapy. The two drugs work together to restore and enhance the function of the CFTR channel protein at the cell membrane. Lumacaftor works by correcting the misfolded proteins and improving their transport the cell surface[9]. Elexacaftor and tezacaftor have been approved by USFDA in October 2019 as a combination therapy with ivacaftor. This drug is also available in combination with ivacaftor alone, under the brand name Symdeko[10,11,12].

Targeting gene defect

Gene replacement therapy is being actively researched as a one time treatment in CF patient. One major barrier is the lack of efficient vectors that can deliver functional CFTR gene without having immunological consequences[13].And the other one is Gene editing approaches are also being tried, by using nucleases to enzymatically correct the mutated genes in the naive cell.

- Targeting CFTR - Many other molecules having CFTR corrector potential are currently under trial.
- Drug repositioning in CF - The approach is Repositioning of existing drugs that are already in use for other diseases is an emerging concept in drug discovery programs.
- Targeting ENaC - Epithelial sodium channels (ENaC) are another important group of channels which are constantly working in opposition or in synchronization with the CFTR protein channels, depending upon the organ specific epithelial lining. ENaC is a heteromeric protein, composed of 3 homologous subunits (α, β, and γ). In the lungs CFTR defect contributing to thick and viscous airway secretions. ENaC is being considered as a novel therapeutic target, and its inhibition is theorized to increase hydration of mucus and enhance muco-ciliary transport in CF experimental models[14]. Some of these molecules show promise, several ENaC targeted therapeutics have failed in the clinical trials, despite showing promising pre-clinical results[15]
- Targeting transcriptome - Transcriptome is the study and identification of all the messenger RNA (mRNA) expressed by an organism. RNA-sequencing is sequence based and performs an unbiased quantification of all transcripts within a cell even without prior knowledge of a particular gene. It can also provide information on alternative splicing and sequence variation in the targeted genes[16].
- Targeting altered gut microbiome - In many experimental models, altered gut microbiome composition has been demonstrated. Decreased diversity of microflora, temporal instability and decreased abundance of taxa. In an effort to correct dysbiosis, bacteriotherapy like probiotics and prebiotics may be tried in CF. several studies have been carried out with probiotics, particularly Lactobacillus sp. to observe their effects on the intestinal health of CF patients. Results of these studies are awaited[16].

Conclusion

Cystic fibrosis is a life-threatening genetic disorder, affecting thousands of children and adults worldwide. Accordingly, its management is also multidimensional, keeping into account the disease course and its symptomatic management on a daily basis. Although with the advent of disease specific CFTR modulators the management of CF patients has improved, no single corrector drug is potent enough to fix the multi domain structure and function of CFTR protein on its own. A combination of drugs having varied mechanisms of action, can be used here. Due to the immense psychological and social burden of the disease, we need out-of-the-box approaches, by integrating genetic engineering and gene editing, with modern biological approaches like DNA nanotechnology, metabolomics, systems biology and intracellular protein kinetics.

Conflict of interest

The authors declared no conflict of interest with respect to the authorship, research or publication of the article.

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Cystic fibrosis: Current treatment approaches and future directions

GLIFLOZINS IN THE MANAGEMENT OF CARDIOVASCULAR DISEASE: A REVIEW

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ABSTRACT

Gliflozins, also called SGLT2 inhibitors, are a class of mediations that modulate sodium glucose transport proteins, act by inhibiting sodium glucose transport protein 2. The most important metabolic effect of this is to inhibit the reabsorption of glucose in the kidney and thus lowering the blood glucose levels. These medications are mainly used in the treatment of Type II DM. Type II DM is a known independent risk factor for cardiovascular disease and heart failure is one of the most important complication of diabetes. The gliflozin class of medication has shown significant improvement in cardiac functions in patients who have heart failure with or without type 2 diabetes and improve renal function, with fewer adverse effects. This review aimed to analyze the cardiovascular protective mechanisms of SGLT2 inhibitors.

Key words: SGLT2 inhibitors, Heart failure, Type II diabetes mellitus.

Introduction

Type 2 diabetes mellitus (T2DM) is a known independent risk factor for cardiovascular disease (CVD), including coronary, cerebral, and peripheral vasculopathy, a clinical condition that is globally represented as the primary cause of complications and death in patients with diabetes. Among the approved glucose lowering agents for clinical use sodium-glucose cotransporter-2 inhibitors, have shown beneficial effects on cardiovascular disease[1]. Their main effects are to reduce glycosylated hemoglobin (HbA1c), decrease pressure levels, and induce a weight loss of approximately 2 kg. Also, a reduction in cholesterol levels was seen in some animal studies[2]. In individuals having diabetes with impaired function of the left ventricle (LV), CHD, or congestive HF, the decrease in extracellular fluid and plasma volume with combined reduction of both afterload and preload contributed to cardiovascular benefits[3].

Mechanism of action

The mechanism of SGLT2 inhibitors on beneficial cardiac effects is not clear. In case of heart failure due to reduced mitochondrial glucose oxidation it was observed that there is a reduction in cardiomyocyte ATP production[4]. As the SGLT2 are inhibited, the circulating ketone levels are increased, which produces an effect that improves the mitochondrial function and increases the production of ATP, thus enhancing ventricular contractile performance[5]. The activity of sarcolemma sodium- hydrogen exchanger 1, and calcium calmodulin dependent protein kinase II, which impairs the cardiomyocyte contraction and relaxation are reduced by the SGLT2 inhibitors[6]. Frequent inflammations are seen in heart failure which is the leading cause of cardiac fibrosis[7]. SGLT2 inhibitors can activate of the nucleotide-binding domain, which stimulates inflammatory responses in experimental models of heart failure[8]. Blocking pro inflammatory–oxidative pathways, SGLT2 inhibitors can improve coronary endothelial function and increase flow-mediated dilatation [9].

Gliflozins and Heart Failure

SGLT2 inhibitors have been found to be a new class of compounds for the treatment of diabetic patients suffering from Heart failure, which is a common and serious comorbidity of Type II DM whose prevention is a necessary therapeutic goal[10]. SGLT2 inhibitors correct factors that provoke heart failure. The pharmacological effects of SGLT2 inhibitors including osmotic diuresis induced by glycosuria, decreased BP, concomitant increased Na+ excretion and, improved fluid overload in HF patients[11]. Also, gliflozins modulate afterload through reduction of arterial BP. Gliflozins shows many actions on the heart, such as the amelioration of LV mass and hemodynamics, reduction of myocardial inflammation, oxidative stress and fibrosis, and direct pleiotropic

effects on cardiomyocytes[12].

Gliflozin Benefit in HFpEF (Heart failure with preserved ejection fraction)

HFpEF described as a systemic syndrome mediated by risk factors and co-morbidities, resulting in a multi-organ pro-inflammatory state, It leads to myocardial dysfunction and profibrotic remodeling through a cascade of events involving cardiac micro circulation [13]. Nitrosative stress is a major mediator in the pathophysiology of HFpEF. An adequate level of intracellular NO is essential for the functioning of cardiomyocytes. On the basis of experimental findings, the improvement of myocardial microvascular function and amelioration of oxidative stress may be the mechanisms by which SGLT2 inhibitors act to prevent heart failure.

SGLT2 Inhibitors Combined with Other Drugs

Glucagon-like peptide 1 receptor agonists are also effective hypoglycemic agents having beneficial cardiovascular effects. The combination of an SGLT2 inhibitor and a glucagon like peptide receptor agonist appears to be safe and has an additive action in reducing glycated hemoglobin levels and possibly other end points as well.

Clinical implications

Adverse events of SGLT2 inhibitors

Most common adverse events are mycotic genital infections occurring frequently in women than men[14]. Less common adverse events include pyelonephritis, urinary tract infections, diabetic ketoacidosis (uncommon). Mainly euglycemic ketoacidosis is seen in patients taking SGLT2 inhibitors.

Conclusion

SGLT2 inhibitors, currently used for the management of Type II DM, have proven to have beneficial effects on patients with cardiovascular disease. SGLT2 inhibitors represents as a therapeutic option for non diabetic heart failure patients especially those with HFpEF. SGLT2 inhibitors in addition have glucosuric and natriuretic properties, also reduce the risk of end-stage kidney disease in patients with type 2 diabetes and chronic kidney disease. Further studies need to evaluate both safety and clinical efficacy to better understand the impact of gliflozins on elderly subjects characterized by numerous comorbidities[15].

Conflict of interest

The authors declared no conflict of interest with respect to the authorship, research or publication of the article.

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PERSPECTIVES ON THE USE OF STEM CELLS FOR AUTISM TREATMENT

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ABSTRACT

Autism spectrum disorders (ASDs) is a complex neurodevelopmental disorder. ASDs are clinically defined by deficits in communication, social skills, and repetitive and restrictive interests and behaviours. With the prevalence rates for ASDs rapidly increasing, the need for effective therapies for autism is a priority for biomedical research. Currently available medications do not target the core symptoms, can have markedly adverse side-effects, and are mainly palliative for negative behaviours. The development of molecular and regenerative interventions is progressing rapidly, and medicine holds great expectations for stem cell therapies. This review will focus on the potential use of the various types of stem cells: embryonic, induced pluripotential, fetal, and adult stem cells as targets for ASD therapeutics.

Key Words: Autism, ASD, ESC, Stem cells, WJC

Introduction

Autism Spectrum Disorders: Overview

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) published by the American Psychiatric Association, autism spectrum disorders (ASDs) are complex, severe, heterogeneous neurodevelopmental disorders[1]. The core characteristics of ASDs are dysfunctions in social interaction and communication skills, restricted interests, repetitive and stereotypic verbal and nonverbal behaviours[2,3]. Several biochemical and cellular events are associated with ASDs: oxidative stress, endoplasmic reticulum stress, decreased methylation capacity, limited production of glutathione, mitochondrial dysfunction, intestinal dysbiosis and inflammation, increased toxic metal burden, impaired detoxification, and dysregulations of the brain's intrinsic immune system (including autoimmunity and activation of neuroglial cells)[4,5]. Other available treatments for ASDs can be divided into behavioural, nutritional, and biomedical approaches, but a defined standard approach has not been generally accepted[6].

Novel findings of epigenetic, neuro immunologic, and environmental changes observed in ASDs suggest that stem cell therapies could be potential interventions for treating autistic syndromes, while enhancing early interventions for autism management in the future[7,8,9]

Stem cells in autism spectrum disorders

It is generally agreed that stem cell therapies represent the future of molecular and regenerative medicine for what would otherwise be untreatable human diseases. Stem cells are also suitable for developing cell based patient specific pharmacotherapies [10,11]. Thus, it is hoped that stem cells offer new treatment options for ASDS[12].The immune and neural dysregulations observed in ASDs provide specific targets for stem cell therapies. Stem cells possess several useful characteristics which suggests their potential therapeutic application for ASDs. This review will focalize on the major types of stem cells, embryonic, fetal, and the adult stem cells, that could offer specific advantages in cell transplantation for ASD treatment.

Embryonic stem cells

Apart from their ethical controversies, embryonic stem cells (ESCs) are pluripotent stem cells derived from early stages of embryonic development [13,14]. ESCs are obtained from the inner cell mass of the blastocyst-stage preimplantation embryo, single blastomeres of the morula stage. They derive their cell differentiation characteristics from the recipient environment. However, absent anti rejection medication would be expected to be rejected by the recipient immune system once HLA-II expression occurred [15]. The challenges of chimeric engrafting are far from understood in the paediatric population, and thus this potential outcome from ESCs is poorly characterized

in the scientific literature and a source of concern. While still at the embryonic stage of their development, they are, however, considered potent producers of paracrine activity [16].

In ASDs, it has been demonstrated that an altered immune cell ratio is sometimes associated with a decreased number of T lymphocytes [18]. The ability of ESCs to differentiate into hematopoietic cell lineages, giving rise to all blood cell types and subtypes of the immune system (i.e., T cells, NK cells, and dendritic cells), could be used in immune-altered pathologies, such as ASDs, which require induction of the immune response in an antigen-specific manner[17].

Fetal stem cells

Fetal stem cells (FSCs) are a subpopulation resident within fetal tissues. Fetal-derived tissues typically addition to the FSCs. These fetal tissues and their associated FSCs divide into 3 subtypes: ectodermal (including brain), mesodermal, and endodermal. They have great potential for clinical use; as they possess immune-regulatory functions as found in mesenchymal stem cells but exhibit a greater expansion capacity and enhanced plasticity [18,19]. Indeed, FSCs are more rapidly, easily, and efficiently reprogrammed to pluripotency than neonatal and adult cells. Early gestational fetal neuronal tissue is of particular interest to neurodegenerative disease therapies and may serve as a model for ASD interventions. In part, this is because early FSCs have minimal or no expression of MHC-I and no MHC-II [20]. Further, FSC-derived hematopoietic cells express HLA-G a factor in tolerance, thereby conferring increased viability post transplantation. These factors may contribute to the success of allogeneic FSC transplants in ASD therapies. Cells isolated from first trimester human fetuses have the capacity to survive after transplantation, acquire a mature neuronal phenotype, and mediate a functional effect [21].

Adult stem cell types

Mesenchymal Stem Cells

Mesenchymal stem cells (MSCs) transplantation or autologous reimplantation could be a useful therapeutic tool in the future of regenerative medicine [22]. They are self-renewing precursor cells of mesodermal origin found principally in the bone marrow and adipose of children and adults, which can differentiate into bone, fat, cartilage, and stromal cells of the bone marrow. Briefly, MSCs could stimulate the plastic response in the host damaged tissue, synthesize and secrete survival-promoting growth factors, restore synaptic transmitter release by providing local reinnervations, integrate into existing neural and synaptic network, and restoring plasticity [23].

Specific Mesenchymal Stem Cell Subtypes

Adipose-Derived Mesenchymal Stem Cells

Adipose-derived mesenchymal stem cells (AD-MSCs) are abundant in human adipose [24]. They are readily harvested with minimally invasive procedures (e.g., small volume lipo-aspirate). These cells gained much consideration for autologous cell therapy. AD-MSCs show anti-inflammatory characteristics and are able to differentiate into adipogenic, osteogenic, chondrogenic, and another mesenchymal lineage. Even though several clinical trials have been conducted using AD-MSCs, considerable uncertainty about their real clinical potential is still present. Their differentiation processes into cell lineages apart from adipocytes have not yet been definitively demonstrated in human's post reimplantation. Concerns on purity and molecular phenotype for AD MSCs have also been raised. It is likely that cell preparations contain heterogeneous populations of cells. This fact creates uncertainty over whether AD-MSCs themselves are responsible for observed effects[24].

Umbilical Cord-Derived MSCs

Other sources of stem cells include both umbilical cord and placenta [25]. These are abundant sources of stem cells, since the majority of post-delivery umbilical cords and placentas are discarded. Umbilical cord blood-derived mesenchymal stem cells are hematopoietic and have potential applications along those lines as previously discussed. The stroma of the cord is also a source of relatively primitive stem cells residing in the Wharton's jelly (WJCs). Their potential application resides in their low immunogenicity. WJCs express low levels of human leukocyte antigen (HLA)-ABC and no HLA-DR. WJCs are able to inhibit the proliferation of phytohemagglutinin - stimulated human peripheral blood lymphocytes and mouse splenocytes[25]. WJCs show also immunomodulation properties and act as trophic support to neighbouring cell populations. These cells have potential for future applications in CNS regenerative medicine, as well as in ASDs. Equally, their in vitro capacity to produce paracrine trophic factors should be explored.

Conclusion

Cellular therapies offer a needed and novel treatment modality in ASDs. Several stem cell types could be suitable for ASD therapy. Among them, MSCs and FSCs seem to show several biological advantages. However, long-term safety of cell-based therapies are not yet well established, and preclinical animal models are urgently needed to progress this area of research.

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ALCOHOL WITHDRAWAL SYNDROME: CURRENT PHARMACOTHERAPY AND NEWER AGENTS

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ABSTRACT

Alcohol withdrawal syndrome (AWS) can occur when an individual stops or even significantly reduces alcoholic consumption after a prolonged period of use. Depending upon the severity of withdrawal symptoms, patients may be treated in the inpatient or outpatient setting. Pharmacotherapy is often necessary for treating patients with AWS to manage the symptoms of withdrawal, prevent the progression to serious complications, and bridge these patients to treatment for maintaining long-term recovery. This review summarises the current pharmacotherapy being followed and the new propitious agents in therapy yet to be approved.

Key Words: Alcohol withdrawal syndrome, AWS, Pharmacotherapy, Benzodiazepines.

Introduction

Alcohol dependence use is among the leading causes of preventable death worldwide and also one of the most common psychiatric disorders, second only to major depression [1]. Globally alcohol consumption has increased in recent decades, with most of the increase in developing countries [2]. Alcohol use is associated with increased risk of accidents, workplace productivity losses, increased medical and mental health costs, and greater rates of crime and violence categorising alcohol as one of the most harmful drugs [3] .

The Alcohol withdrawal Syndrome (AWS) is a cluster of symptoms which occurs in alcohol-dependent people after cessation or reduction in heavy or prolonged alcohol use. Symptoms and signs of AWS includes mild to moderate tremors, irritability, anxiety, or agitation. The most severe manifestations of withdrawal include delirium, tremors, hallucinations, and seizures [4,5]. These happen due to alcohol-induced imbalances in the brain which result in excessive neuronal activity if the alcohol is withheld. Long-term exposure to alcohol causes adaptive changes in several neurotransmitters, including GABA, glutamate, and norepinephrine, among many others[5,6]. The diagnosis requires adequate history of the amount and frequency of alcohol intake, the temporal relation between cessation/reduction of alcohol intake and the onset of withdrawal symptoms. Patients suffering from mild to moderate AWS can be managed as outpatients treated in an inpatient setting [8,9].

Current Pharmacotherapy for Alcohol Withdrawal

BZDs is the gold standard and is associated with effective reductions in AWS symptoms, they are also associated with adverse effects, including excessive sedation, falls, respiratory depression, aspiration, delirium, and even mortality. Benzodiazepines work by enhancing the effect of the GABA neurotransmitter at the $GABA_A$ receptor [10].

Long acting agents like diazepam and chlordiazepoxide which have greater half-life (up to several days) has shown that it can provide a smooth course of treatment without the risk of rebound symptoms (seizures) that occur late during withdrawal as blood levels are reasonably uniform across the course of the day. But it's demethylation and hydroxylation metabolic pathways, the long half-lives, and the presence of active metabolites makes it likely that drug accumulation will occur in patients with liver disease [11].

Short-acting (for several hours) benzodiazepines like lorazepam should be used in patients with severe liver dysfunction and in patients who are at high risk of experiencing serious medical consequences following sedation, such as people with severe lung disease or elderly patients as it has no active metabolites and its metabolism is not much affected in liver, but are associated with a greater risk of rebound symptoms [12]. Anti-convulsant drugs may represent suitable alternatives [13]. Carbamazepine was found superior to benzodiazepines in prevention of rebound withdrawal symptoms and reducing post-treatment alcohol consumption [14]. Valproic acid significantly affects the course of alcohol withdrawal and reduces the need for treatment with a benzodiazepine but are limited by their side effects [15]. Adrenergic medications (centrally acting alpha-2 agonists like clonidine; and antagonist

like propranolol) are of value largely as adjuncts to BZD's in the management of AWS [16].

Adjunctive therapy of, thiamine administered intramuscularly is mandatory in all people with severe alcohol withdrawal, people with poor diet and signs of malnutrition [17].

FDA approved drugs for alcohol dependency

The acetaldehyde dehydrogenase inhibitor disulfiram was the first medication approved for the treatment of alcohol use disorder by the FDA, in 1951. Disulfiram leads to an irreversible inhibition of aldehyde dehydrogenase and accumulation of acetaldehyde, a highly toxic substance [18].

The next drug approved for treatment of alcohol use disorder was acamprosate; first approved as a treatment for alcohol dependence in Europe in 1989, there is evidence that acamprosate may be more effective in promoting abstinence and preventing relapse in already detoxified patients than in helping individuals reduce drinking[1]. A third drug, the opioid receptor antagonist naltrexone, was approved for the treatment of alcohol dependence by the FDA in 1994, has been found to be most effective in reducing heavy drinking[20].

Promising drugs for AWS

Numerous other medications have been used off label in the treatment of alcohol use disorder, and many of these have been shown to be modestly effective in meta-analyses and systematic reviews.

Topiramate lead to the possibility of starting treatment while people are still drinking alcohol, therefore serving as a potentially effective treatment to initiate abstinence rather than to prevent relapse in already detoxified patients. A concern with topiramate is the potential for significant side effects, especially those affecting cognition and memory, warranting a slow titration of its dose and monitoring for side effects. Ondansetron, a $5HT_3$ antagonist, have suggested to show a potential role in alcohol use disorder, but only in those individuals with certain variants of the genes encoding the serotonin transporter 5-HTT and the $5\text{-}HT_3$ receptor [21].

Gabapentin, which has structural similarity to GABA, Its low toxicity makes it a promising agent in AWS [7]. Baclofen is a $GABA_B$ receptor agonist, currently used to control spasticity and is also is able to prevent the sensitization of withdrawal anxiety caused by repeated withdrawals. Dexmedetomidine is a drug which acts on the noradrenergic system and is currently used in the US in the treatment of AWS in emergency set up. It may reduce the need for BZD and is a promising and effective adjuvant treatment for AWS [21].

Conclusion

Alcohol Withdrawal Syndrome results in people who are dependent on alcohol and either stop drinking, or reduce the alcohol consumption. This results from a shift in the neurotransmitter levels in the brain, from GABA inhibition to glutaminergic stimulation. Oral benzodiazepines are the best studied and most effective drugs for preventing a severe alcohol withdrawal syndrome, particularly the risk of seizures and delirium. While BZD's addictive properties limit their long-term use, the possibility of using other pharmacological agents is effective both for the treatment of AWS and the subsequent long-term program for alcohol relapse prevention i.e. carbamazepine, baclofen, gabapentin and topiramate. The newer medications yet to be approved have shown promising results in phase 2 or phase 3 medication trials. However, owing to the development of novel neuroscience techniques, a growing and exciting body of data is expanding the armamentarium of targets currently under investigation in animal models and/or in early-phase clinical studies.

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SCHIZOPHRENIA: OVERVIEW AND TREATMENT OPTIONS

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ABSTRACT

Schizophrenia is a complex, chronic mental health disorder characterized by hallucinations, delusions and disturbances in thought, perception and behavior. Peoples with schizophrenia may seem like they have lost touch with reality. The diagnosis and care of people with schizophrenia has improved in the last several decades. Effective treatments are available, antipsychotic medication is the mainstay of pharmacological treatment. This review provides an overview of schizophrenia, diagnosis and also discusses the available treatment options

Key Words: Schizophrenia, Diagnosis, Treatment

Introduction

Schizophrenia is a chronic remitting and disruptive disorders associated with significant abnormalities and the progressive deterioration of a wide variety of cognitive, psychosocial, vocational, and behavioral functioning. The fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) defines schizophrenia as a syndrome characterized by long duration, high relapse rate (70%), bizarre delusions and behaviors, negative symptoms, and sometimes a few mood problems. The onset of symptoms typically occurs in adolescence and young adulthood, with a worldwide[1].

Patients with symptoms of schizophrenia may experience additional limitations and negative conditions. Substance-abuse disorders occur most often among these patients; these disorders can involve a variety of substances, including alcohol, tobacco, and prescription medications[2]. Anxiety, depression, panic, and obsessive-compulsive disorder are also prominent in patients with schizophrenia and can exacerbate the symptoms of their disorder[3]. These patients also have a general lack of awareness of their illness. This mindset has been linked to high rates of nonadherence, relapse, poor psychosocial function, poor hygiene, and worse disease outcomes[4]. The prognosis for patients with schizophrenia is generally unpredictable. Only 20% of patients report favorable treatment outcomes. The remaining patients experience numerous psychotic episodes, chronic symptoms, and a poor response to antipsychotics. The diagnosis of this condition can be summarized as follow.

Diagnosis

The diagnosis of schizophrenia is reached through an assessment of patient-specific signs and symptoms, as described in the *Diagnostic and Statistical Manual of Mental Disorders,* Fifth Edition *(DSM-5).* The *DSM-5* states that "the diagnostic criteria [for schizophrenia] include the persistence of two or more of the following active-phase symptoms, each lasting for a significant portion of at least a one-month period: delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behaviour, and negative symptoms. "At least one of qualifying symptoms must be delusions, hallucinations, or disorganized speech. Moreover, the *DSM-5* states that, to warrant a diagnosis of schizophrenia, the patient must also exhibit a decreased level of functioning regarding work, interpersonal relationships, or self-care. There must also be continuous signs of schizophrenia for at least six months, including the one-month period of active-phase symptoms noted above. In addition, the clinician must confirm that the presenting symptoms are not a result of substance abuse or another medical condition[5].

Treatment

Nonpharmacological Therapy

The goals in treating schizophrenia include targeting symptoms, preventing relapse, and increasing adaptive functioning so that the patient can be integrated back into the community. Since patients rarely return to their baseline level of adaptive functioning, both nonpharmacological and pharmacological treatments must be used to optimize long-term outcomes. For that

reason, nonpharmacological treatments, such as psychotherapy, are also important[6].

Pharmacologic treatment

More than 70 antipsychotics have been introduced. They are mainly categorized into first- and second-generation agents and share a similar pharmacological mechanism in blocking the dopamine D-2 receptors[7]. Their blocking mechanisms or actions are linked to their efficacy against positive and disorganization symptoms of schizophrenia[8].The first-generation antipsychotics (FGAs), or typical antipsychotics (eg, chlorpromazine, fluphenazine, and haloperidol, included in the World Health Organization's list of Essential Medications in 2009) were first introduced for the treatment of schizophrenia in the 1950s. The second-generation (atypical) antipsychotics, SGA (eg, clozapine, olanzapine, and risperidone) introduced in the last three decades were believed to be more efficacious and tolerable than the FGAs, and a few have progressively replaced the older FGAs to become the first-line prescription or the standard of care. The first FGA invented chlorpromazine, has become the well-established and benchmark treatment for people with schizophrenia to facilitate their deinstitutionalization and has been used for more than 40 years[9]. Other commonly used FGAs such as trifluoperazine, thioridazine, sulpiride, pimozide, perphenazine, and fluphenazine were tested and confirmed to have similar and satisfactory efficacy in symptom reduction–mainly for positive symptoms (eg, delusions and hallucinations)[10]. However, there was limited evidence to support their efficacy at lower doses or in short-term treatment[11]. Major adverse events induced by FGAs generally include sedation, movement disorders, endocrine disturbance, and metabolic and electrocardiogram changes. however, there is little evidence to support their efficacy in reducing negative symptoms (eg, anhedonia, loss of volition, and social withdrawal) and cognitive functioning, which may contribute much to the functional disability of people with schizophrenia[12]. Second-generation (or atypical) antipsychotics (eg, clozapine and olanzapine) were believed to have good antipsychotic properties and minimal adverse effects compared with those noted with the use of FGAs. Some of them have been shown to be more efficacious and less problematic in terms of sedative and neurological effects than FGAs[13,14].

The Texas Medication Algorithm Project (TMAP) has provided a six-stage pharmacotherapeutic algorithm for the treatment of schizophrenia. Stage 1 is first-line monotherapy with an SGA. If the patient shows little or no response, he or she should proceed to stage 2, which consists of monotherapy with either another SGA or an FGA. If there is still no response, the patient should move to stage 3, which consists of clozapine monotherapy with monitoring of the white blood cell (WBC) count. If agranulocytosis occurs, clozapine should be discontinued. If stage-3 therapy fails to elicit a response, the patient should proceed to stage 4, which combines clozapine with an FGA, an SGA, or electroconvulsive therapy (ECT). If the patient still shows no response to treatment, stage 5 calls for monotherapy with an FGA or an SGA that has not been tried.

Finally, if stage 5 treatment is unsuccessful, stage 6 consists of combination therapy with an SGA, an FGA, ECT, and/or a mood stabilizer[15].

Combination therapy is recommended only in the later stages of the treatment algorithm. The routine prescription of two or more antipsychotics is not recommended because it may increase the risk of drug interactions, nonadherence, and medication errors[16].

ECT and other treatment

ECT is considered an alternative treatment for those with unfavourable responses to antipsychotics alone after receiving different courses of medical or psychological treatment, and/or those with very strong suicidality and catatonic features [17].It is an effective adjunct to clozapine in treating refractory schizophrenia[18].There is certainly no strong or conclusive evidence to suggest that ECT alone or as an adjunct to antipsychotics is superior to antipsychotics alone or to any combination of different treatment modalities for schizophrenia. In addition, ECT may cause short-term, or occasionally long-term, memory impairment and leaves many unanswered questions about its role and mechanisms in the treatment of schizophrenia. Similarly, transcranial magnetic stimulation (a procedure that uses magnetic fields to stimulate the depolarization or hyperpolarization of the neuron cells in the cortical regions of the brain) has shown preliminary positive evidence in treating refractory negative symptoms and auditory hallucinations[19,20].

Conclusion

Schizophrenia is a complex disorder that requires prompt treatment at the first signs of a psychotic episode. Antipsychotics (first- and/or second generation antipsychotics) are shown to be effective in reducing overall psychotic symptoms and relapse in patients with schizophrenia. Many patients with schizo phrenia often have unresolved life events and psycho-

logical distress, as well as illness related or drug-induced problems, which significantly affect their daily daily life. Research in the treatment of schizophrenia must proceed simultaneously along two fronts: the development of potentially superior treatments and the development of further knowledge and knowledge transfer to maximize the benefits from currently available treatments. The advances in the safe and effective use of currently available treatments can have a major impact on the lives of many people.

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EAT RIGHT... CHOOSE A HEALTHY LIFE

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India has a rich and highly varied cuisine, and its various diets are strongly related to social identity, religion and other cultural factors as well as local agricultural practices and availability of diverse foods. To lead a healthy and active life humans need a wide range of nutrients. An adequate, well balanced diet combined with regular physical activity is a cornerstone of good health.

But rapid urbanization or globalization has increased the consumption of processed foods and the changing lifestyles has led to a shift towards unhealthy dietary patterns. Also, people are consuming more foods high in energy, fats, free sugars or salt/sodium, and many do not eat enough fruits, vegetables and dietary fibers such as whole grains. So, these all factors are contributing to an imbalanced eating. It leads to an alarming increase in the rate of life style diseases notably Diabetes, Obesity, Hypertension, Rheumatoid arthritis, Cancer etc. India has the double burden of over and under nutrition.

Food safety in terms of chemical, biological and nutrient contents is hardly a matter of concern in the country's social fabric. The major food issues of concern are insufficient/ imbalanced intake of foods/nutrients. Foods can be categorized according to the function as,

- Energy rich foods (Carbohydrates and fats) whole grain cereals, millets, vegetable oils, ghee, nuts and oilseeds and sugars.
- Body building foods (Proteins)- Pulses, nuts and oilseeds, milk and milk products, meat, fish,
- Protective foods (Vitamins and minerals) - Green leafy vegetables, other vegetables, fruits, eggs, milk and milk products and flesh foods.

Using your 12-inch plate, imagine a line down the middle of the plate. Then on either side, draw one line each, perpendicular to first line. Now you will have will have 4 sections in your plate.

1.Fill one section with cooked vegetables such as spinach, carrot, green beans, or any locally available vegetables.

2.Fill another section with locally available fresh fruits like banana, guava, papaya etc.

3.In one of the remaining sections put cooked grains such as rice, wheat, ragi etc.

4.And then in the last section fill your protein such as pulses or meat or fish.

5.Add a serving of diary product (curd, yoghurt), if your meal plan allows.

Consolidated National Health Portal (NHP) and Indian Medical Association (IMA) guidelines on safe and healthy food diet here follows.

1.Reduce rice servings, use brown rice and whole wheat and avoid white rice and white bread. Maida products should be avoided. (Avoid carbohydrate rich food like rice and wheat). Rice yields approximately 70% and wheat yields approximately 60% of carbohydrate. Any excess carbohydrate is converted to fat by the liver and is stored within itself or as visceral fat primarily in the anterior abdominal wall. Do not re-heat food as far as possible.

2.Select locally available seasonal fruits and vegetables.

3.Avoid junk foods (HFSS- High Fat, high Salt, high Sugar), instead replace with traditional foods and snacks.

4.Use stainless steel/glass/high quality plastic water bottles.

5.Restrict Salt intake (All kind of bakery and processed food).

6.Restrict Sugar maximum transfer from unnatural sugars (jaggery, Palm candy etc.)

7.Fats and oils: Choose healthy fat like natural coconut oil, olive oil, butter etc. Do not re-use oil. Avoid trans-fats vanaspati, ghee etc.

8.Meat: Removing skin before preparing poultry reduces fat content. Any meat should be consumed only in moderation.

9.Fruits and vegetables: - Local and seasonal fruits and vegetables with minimum preservation should be preferred.

10.Consume safe Fish: Small fishes are much better than larger ones. Procure from places with no preservative contamination and consume fresh fish only.

11.Before purchasing packed milk, watch for labels regarding pasteurization and toning.

a. Pasteurized homogenized toned milk with milk fat 3.0% is ideal for tea/coffee.

b. Pasteurized standardized milk with milk fat 4.5% is ideal for the preparation of deserts and sweets. c.Pasteurized toned milk with milk fat 3.0% -mostly aimed for consumption by children in the form of milk.

d. Pasteurized double toned milk with milk fat 1.5% is ideal for elderly people and for weight reducing diet and diet for hypercholesterolemia.

12. Avoid re-use of plastic containers for food and water. Do not use plastic containers for re-heating purpose unless it is specifically meant for that.

13. Prefer food with minimum preservatives and chemical contaminants (local and seasonal food with minimum preservation should be preferred).

14. Food colours, stabilizers preservatives etc. lead to extra contamination.

15. Frozen dessert is not ice-cream. (Ice-creams are milk-based whereas frozen desserts which are fat based are unsafe and hence cannot be recommended for daily basis consumption).

16. The practice of consuming accepted food items in excess, as a cure for diseases is wrong and is discouraged. [for example, Irumbanpuli (Chemmeenpuli) in excess can cause renal failure. Avoid scam claims like “it cures cholesterol”. In a small amount it is consumable for curry but avoid large amount of “Irumbanpuli juice” as a medicine]

17. Restrict calories and prevent over-weight. [Limit carbohydrate (rice, wheat, packed cereals) and fat (oil, meat, fried items) intake, instead consume plenty of safe fruits and vegetables, ensure adequate protein intake (egg white, small fish, pulses, milk and meat in moderation.

18.Don’t go for uncontrolled fasting or starving methodical diets for sake of developmental of your complexion which will lead harmful effects on your physical and mental health. (Before taking any pattern of diet it is best to consult with experienced dieticians for better results).

19.During pregnancy and lactation phase, extra care should be required in diet intake of Calcium. Therefore, their diet should contain calcium rich foods such as milk, yogurt, cheese, green leafy vegetables, legumes and seafood.

a. Vitamin A is required during lactation to improve child survival. Apart from these, nutrients like Vitamin B12 and C are also needed to be taken by lactating mother.

b. Iron is needed for hemoglobin synthesis, and to provide immunity against diseases. Plant foods like green leafy vegetables, legumes and dry fruits contain iron. Iron can also obtain through sources like meat, fish and poultry products. Consume vitamin C rich fruits like gooseberries (amla), guava, oranges and citrus rich fruits for better absorption of iron from your diet.

c. Iodine deficiency during pregnancy results in still births, abortions and cretinism therefore use iodized salt in your food.

20. Elderly need more calcium, iron, zinc, vitamin A and antioxidants to prevent age-related degenerative diseases and for healthy ageing.

a. It is very essential to maintain your health as ageing process starts and it increases the life expectancy. It is very important for elderly people to exercise as it helps to regulate body weight and flexibility in the joints. Calcium rich foods like dairy products (low fat), milk (toned) and green leafy vegetables should be included in the daily diet to maintain bone health, so as to prevent osteoporosis and bone fractures. Consume pulses, toned milk, egg-white etc. in good quantities as they are rich in proteins.

b. Elderly people should cut down on their saturated fats, sweets, oily food, salt and sugar level. Use of ghee, oil, butter should be completely avoided. Also, avoid eating spicy food. The diet for elderly people needs to be well cooked, soft and should be less salty and spicy. Ensure to eat small quantities of food at more frequent intervals and drink water at frequent intervals to avoid dehydration and constipation.

c. Consult a doctor/dietician for an individualized diet depending upon the medical condition in the case of persons suffering from chronic diseases and bed ridden patients.

21. If you want follow any kind of research results, please take a while to consult with your dieticians. Pay attention to food safety norms and regulations which is approved by concerned authorities.

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Eat right, Choose a healthy life

What can the ayurvedic theory of tridosha teach us?

GUEST COLUMN

Dr. **T. Velpandian**
Professor & HOD, Ocular Pharmacology & Pharmacy, All India Institute of Medical Sciences, New Delhi.

Clinical medicine has entered an era of systemic approach. In this context, ayurveda has much to offer. Although disease management serves as a common point of interest for both conventional medicine and ayurveda, there are fundamental differences in their approaches. While conventional medicine simplifies complexity by reductionism, ayurveda manages human complexity by systems approach using broad based theories. The conceptual framework of V, P and K offers a different perspective of health and disease.

With a shift in focus from genes to cells, systems approach is not only revolutionizing cell biology, but is also providing impetus for clinical medicine to shift from a reductionistic to a holistic approach for efficient disease management. This inevitably brings into focus one of the longest unbroken healthcare systems in the world, namely Ayurveda, the medical system indigenous to Indian subcontinent. A distinctive feature of ayurveda is its systems approach to health and disease. Through the theoretical framework of vata, pitta and kapha, ayurveda offers a new paradigm for understanding the human system as a networked functional entity wherein system properties are integral components. An open-minded dialogue between the cell-centric systems biology and organism-centric ayurveda can open new exciting vistas for research beneficial to both sciences, which could leave a major imprint on clinical practice. It is now widely acknowledged that systems biology holds great promise for the future of healthcare and clinical medicine1. Data from the 'omics' technologies is redefining the understanding of cell as a system rather than as sum of its components. This has not only revolutionized the emerging field of systems biology but has also fueled growing interest in applying systems theory to clinical medicine. As these advances continue to broaden our understanding of human complexity and provide methodologies for patient-centric systems approach, it is pertinent to have a relook at the Indian medical system of ayurveda known to have an integrated approach to health and disease. The answer to how ayurveda deals with human complexity lies in its theoretical underpinnings. Ayurveda views the human system from a predominantly functional standpoint, for which it has identified three key functions namely, movement, metabolic transformation, and growth and support. These are referred to respectively as Vata (V), Pitta (P) and Kapha (K) in Sanskrit, the language of ayurveda13,14. The functions associated with V, P and K exist at all levels of biological organization. For example, movement exists at the level of cell (e.g. cell motility), organ (pumping of heart), entire system (walking), and also mind (movement of thoughts). Clinical relevance of the properties associated with V, P and K Although the association between temperature, pH and metabolism is well known, no precedent exists in modern biology or medicine for using properties like dryness and viscosity to describe physiological functions. Nevertheless, these parameters are well studied for their association with non-physiological functions in another subject. Functional modules of (a) Vata, (b) Pitta and (c) Kapha represented as networks areas. For example, dryness plays a dominant role in surface friction, an important characteristic affecting movement and discussed in great detail in subjects

such as fluid dynamics and engineering mechanics18. Friction is a universally influencing factor affecting motion of objects in contact, be it in mechanical or biological systems. In the latter, all movements in an organism from subtle (cellular movement) to gross (walking) are also influenced by friction, which in turn is affected by dryness. For example, friction between two joints will affect movement. This indicates the relevance of dryness in biology. Interestingly, many of these properties such as dryness, viscosity and adhesion used in ayurveda are increasingly being studied for their physiological roles and clinical relevance.

Theory to clinical applications

Ayurveda has incorporated the theory of VPK in an ingenious way into its diagnosis and therapeutic management. All biotic (plants, animals, food components), abiotic (activities, seasons) and clinical (symptoms) factors having a role in disease are classified and understood in terms of V, P and K44–46. For instance, wheat (food component) increases kapha and hence classified under K. Exercise (activity) increases V and pitta increases in all biological organisms during autumn making this season P related. Examples of classification of clinical symptoms are: cough – dry cough is V related and wet cough is of K origin; skin disorders – dryness involves V, burning sensation indicates involvement of P, and a K associated symptom is pruritus. VPK thus provides theoretical and practical frameworks within which all clinical symptoms can be classified and interpreted. No clinical symptoms lie outside the purview of this classification. V, P and K thus offer a common platform for all factors involved in a disease (Figure 4). From a clinical stance, VPK provides an interface facilitating easy conversion of all diagnostically and therapeutically relevant parameters to a common denominator, enabling VPK based diagnosis and treatment. Ayurvedic therapeutic strategy is therefore comprehensive, addressing all biotic and abiotic causative factors and incorporating all therapeutically relevant parameters such as medicines, diet, activities, etc. in the treatment protocol. A brief example of how the theory of VPK is translated to clinical practice is given below.

Therapeutics targeting properties

Taking the example of osteoarthritis (OA) – OA may be interpreted as a disorder where lubrication (K3) between joints is reduced and dryness (V1) has increased. The latter affects viscosity (K4) of the lubricating fluid between joints. Conventional medicine also opines the same, albeit using different terminologies. It says that alteration of visco elastic properties of synovial fluid is a possible causative factor for friction between joints resulting in their degeneration30. It is pertinent to note that visco elastic property comes under the ambit of kapha. According to ayurveda, there is a systemic increase in dryness (the causative factor) in OA but the clinical manifestation is through the patient's vulnerable part, i.e. the joint. The choice of treatment, therefore, would diagnosis plants lifestyle activities common platform of V,P, K animals clinical symptoms A \food ingredients environment (seasons; strategies involve such vata reducing medicines, diet and lifestyle regimens that would also be appropriate for the state of K and P in each individual. The treatment for OA therefore addresses dryness, both locally and systemically. While the latter prevents the subsequent involvement of other joints and organs, local treatment with medicated oils addresses dryness and tackles the already manifested clinical symptoms. Avoiding diet and activities known to increase V form an integral part of the treatment. Ayurvedic therapeutic strategies target system properties and are not organ specific but context-dependent. Although treatment for OA in ayurveda has been validated and documented over centuries of practice, recent clinical studies have also confirmed using scientific methodologies, the efficacy of ayurvedic treatments for arthritis.

Conclusion

Clinical medicine has entered an era of systemic approach. In this context, ayurveda has much to offer. Although disease management serves as a common point of interest for both conventional medicine and ayurveda, there are also fundamental differences in their approaches. While conventional medicine simplifies complexity by reductionism, ayurveda manages human complexity by systems approach using broad based theories. The conceptual framework of V, P and K offers a different perspective of health and disease. By networking system properties, ayurveda provides a new and comprehensive paradigm for managing health in an integrated manner.

From a contemporary scientific viewpoint, the concept of network of system properties applicable at multiple scales in the organism offers a novel approach to understand a biological system. It provides new biomarkers for diagnosis, treatment and prevention. A central feature of modern medicine is addressing disease at the molecular level. Ayurveda, on the other hand, understands and addresses disease at the level of organism using system properties. In this sense, ayurveda is systems biology at a higher level, in comparison to the current cellular-centric approach. All these raise interesting possibilities of dialogue between systems biology and ayurveda, adding new dimensions for understanding human complexity and variability. It can give rise to formerly unthought-of models and parameters for systems research in medicine benefiting both systems. The prospects are truly exciting.

[Dr.T Velpandian is a pioneer researcher in the field of ocular pharmacology and a visiting faculty at Haward MIT-Health Sciences & Technology, USA]

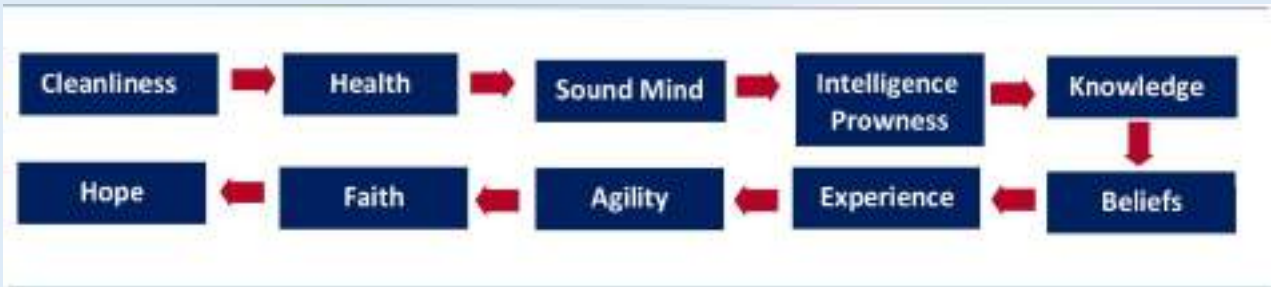
EXCELLENCE THROUGH CULTURE

Prof. **Subash Philip**

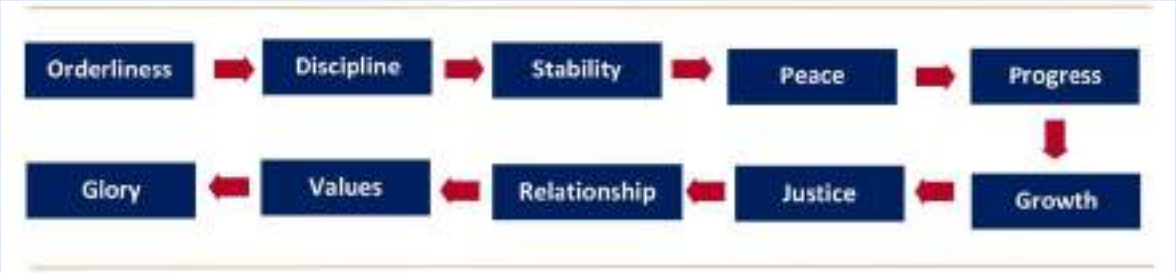
If we can hand over a culture which deeply engraves in the hearts of our new generation these qualities of cleanliness, orderliness and carefulness, then we are sure to have a future generation with universal cultural values that build good scientific temperament, strong relationships, and strong vision. Excellence can only be nurtured through a culture that is strongly rooted in profound values and a belief that constantly strives towards unearthing the ultimate truth.

The pharmaceutical world is one which constantly clamours for tighter controls over quality in every aspect of drug handling. From GMP to FDA approved plant to Six Sigma, man's quest for quality and perfection in design and excellence is moving through rapidly changing environs by adoption of newer technologies such as Artificial Intelligence (AI), machine learning and algorithms. Yes, we are always trying to change the environment which produces a quality product. As per WHO, quality cannot be inspected into a product but rather it should be built into a product. This environment that nurtures quality into a product can be called as the work culture of the company or institution. Every institution has its own culture. Culture can be broadly defined as the customs, beliefs and ideas of a particular society which has been handed down over many centuries and intrinsically ingrained in the depth of the individuals of a place. Culture can be defined as the 'way of life' including arts, beliefs and institutions of a population that are passed down from generation to generation. Thus, it is the learned and shared patterns of thought and behaviour characteristics of a given population including the material objects produced and used by that population. Culture has five basic characteristics: it is learned, shared, based on symbols, integrated and dynamic. Culture has three basic qualities that is embedded into its matrix, universally. They are cleanliness, orderliness and carefulness at the material level and gradually progresses over the years of a human life to three virtues: faith, hope and love demonstrated in the spiritual realm of the human being.

To explain it further, cleanliness practiced to perfection, instils in the mental sphere an environment of clean, pure and mighty thoughts which eventually gives a strong mind. When further practiced it evolves into intelligence, knowledge in the mental sphere and holiness in the spiritual realm and translates into unceasing humility and faith in the Creator. So, a clean body gives strong mind and deep faith. A thorough cleaning procedure ends in a wash water analysis showing no traces of previous batch. This is exactly how simple principles of GMP imparts a flawless product and deep faith (assurance) in the manufacturer in the process involved. Similarly, orderliness is also a deeply ingrained quality of every cultural model. Whether it be a dance form or art form like music the order of doing things and habituating oneself to the order in a meticulous fashion eventually culminates in making the artist's every performance a source of absolute bliss. We feel transformed, invigorated and elevated to a level through the rich and divine experience. When you order your life or time it is referred to as discipline. We know that without discipline we cannot achieve anything valuable. Similarly, without constant, disciplined practice we cannot excel in any profession or any walk of life. We feel highly elated when we go into a house or building which is neatly arranged, at the same time, we can get more things done correctly when we have an arranged desk. The benefit of orderliness is everywhere to be seen. An orderly traffic on the road creates fewer accidents.



Orderliness of the workflow is tantamount to prevent reverse flow of material in process and thus prevent cross contamination. To explain the statement further, equipment should place in the order of their processing. There should never be a backflow of materials and personnel movement. Orderliness at the material level, leads to discipline and stability in the mental realm and hope in the spiritual level. An orderly society imparts disciplined and visionary leaders who in turn instils peace, nurtures relationships and finally hope in the population for a bright future.



Finally let us look at carefulness as a virtue. To simply state, if we love an object, we will take care of it. The things we value we will be very careful to preserve it. Similarly, in the field of pharmaceuticals, careful study yields much results and serendipitous discoveries. Often laboratory work and research require careful handling of chemicals and equipment as well as careful quest (literature search) for hidden secrets. Carefulness as we all know reduces garbage load and strengthens the budget. Carefulness at the physical level unknowingly creates a culture of sustainability and experiential knowledge, which eventually builds a heritage, along with wisdom and finally love at the spiritual level. The love of our culture will further nurture and nourish the elements progressively to feed newer dimensions of technological and spiritual progress into it.

To sum it all, in this world where all things eventually die, three things remain – faith, hope and love. These values are amplified by imparting and observing three qualities in our homes and schools. As the human beings in the society matures, higher levels of values experienced at the mental levels should be inculcated and evaluated at the graduate and doctorate levels of education.

Just like Japanese children are taught to clean their surroundings in schools and Americans are taught the culture of long working hours, similarly we have to inculcate these values in our education system. Then there will be a sea change in the way the citizens of our country behave in public sphere and personal spaces.

To establish these values are in fact, the purpose of our lives on this earth. If we can hand over a culture which deeply engraves in the hearts of our new generation these qualities of cleanliness, orderliness and carefulness, then we are sure to have a future generation with universal cultural values that build good scientific temperament, strong relationships, and strong vision. Excellence can only be nurtured through a culture that is strongly rooted in profound values and a belief that constantly strives towards unearthing the ultimate truth.

[Prof. Dr. Subash Philip is the Vice -Principal of Dr. Marthoma Institute of Pharmaceutical Sciences & Research, Kattanam, Kerala, India]

Mr. **Abdul Nazeer PU**
Gen.Secretary, KPGA

BRIEF REPORT ON THE GENERAL BODY MEETING

The second General Body Meeting of the Association for the year 2021-2023 was held in the office premises of KPGA on 17th July 2022. The meeting began at 10.45 am and around 65 members of the Association were present. At the outset, the meeting started with a silent prayer. Dr. Kala D, Vice President, KPGA welcomed the gathering. Dr. P.K. Sreekumar presided over the meeting. After taking the chair, he introduced the discussion by appreciating the works done by each and every member of the Association for the past activities. He expressed his happiness for the wholehearted support of all KPGA members for making the GB a grand success. Dr. Satheesh Kumar C.S read the condolence message in the GB. We had a great loss in the last year, a great teacher and good professional Prof. Padmanabhan, former Professor and Head, College of Pharmaceutical Sciences, Medical College, Trivandrum. The meeting expressed all respect to the deceased soul with one minute silence. Mr. Abdul Nazeer P.U, Hon. General Secretary of KPGA presented a detailed activity Report and review of minutes of last GB for information to all members and it was passed in the meeting with applause of the members. Later, Mr. Sunil Kumar D, Treasurer of KPGA presented the finance details and the account statement was distributed among the members. After having a prolonged discussion on the report and the proposal for the maintenance & painting works of the building, the General Body unanimously approved and passed the account Statement as well as the proposal. Followed by the account statement, all the members introduced themselves in the meeting. After that, the meeting witnessed yet another golden moment of the Association i.e., the Release of 2nd issue of Vol. 21 (April, 2022) of Pharmline, the official publication of KPGA. Dr. Satheesh Kumar C.S congratulated Dr. Boby Johns G for his immense support in designing the Pharmline. The Chief Editor appreciated him for bringing out the journal with a new and professional look. The new edition was released in the GB by honorable Patron of the association Mr. S.S. Venkata Krishnan by handing over a copy to Prof. Chandrasekharan, immediate past Patron of the association. Later, Dr. Satheesh Kumar CS expressed his willingness for bringing Dr. Boby as the Chief Editor of the Journal. He has given reason for this proposal as he faces difficulty in finding time to spend more for the works of Journal due to his busy schedule. All the members unanimously supported this request and approved the decision to select Dr. Boby Johns G as the chief editor. Dr. Boby Johns G requested all members for their support and cooperation to get maximum numbers of articles for the upcoming issues of the Journal. He shared his dream to make PHARMLINE as one of the best Journals in Pharmaceutical Sciences with an ISSN number. As the Chief Editor of the Journal, he sought the help of two active Life Members of the Association, Dr. Subhash Philip and Ms. Jooly Kurien for supporting the Journal activities. Honoring the senior most life Members as well as Stalwarts of Pharmacy Profession in the State was another session in the GB. KPGA identified four seniors most members of the Association- (1) Prof.Chandrasekharan (Former Professor and Head, College of Pharmaceutical Sciences, Govt. Medical College, Trivandrum), (2) Mr. S.S. Venkata Krishnan (Former Drugs Controller and Licensing Authority, Kerala State), (3) Dr. Sudhakaran Nair (Former Professor & Head, College of Pharmaceutical Sciences, Govt. Medical College, Trivandrum) and (4) Prof. Pankajakshy (Professor, College of Pharmaceutical Sciences, Govt. Medical College, Trivandrum). Prof. Gireesh Chandran honoured Prof.

Chandrasekharan by adorning him with a Golden Shawl. Mr. S.S. Venkata Krishnan was honoured by Mr. Swarna Kumar, Dr. Sudhakaran Nair was honored by Mr. Jaleel K.A and Prof. Pankajakshy was honored by Smt. Valsala by adorning them with Golden Shawls. Dr. Nishith M.C, Joint Secretary presented the concept in the GB for the conduct of KPC in the State. The members in the GB unanimously supported this concept. St. James College of Pharmacy, Chalakkudy will be the venue for the Conference. Krishna Kumar KK, Principal of the College has offered full support for organizing the Conference in the College. He informed in the meeting that the accommodation of students will be done in other affiliated institutions of the Management such as Engineering Colleges and Devine Centre. Dr. Krishna Kumar will be the Coordinator of the Conference.

Pharma Park-The dream project of KPGA

Mr. Mathew Kokad and Mr. Suresh Kamath were presented the proof of concept of Pharma Park, yet to be started in the State. They handed over the project report to the President, Dr. Sreekumar P.K and released the report. They reported that it is a project with 2000 acres of land for brining all MNCs in Kerala. The proposed locations for starting the park will be Ernakulam/Kottayam/Idukki Districts. It will be a project with Private, Public and Government shareholders. For the infrastructure development, the investment may come around 1600 crores. The Pharma Park includes the facilities for API and formulations which requires around 1500 crores of investment. In total, it is a golden dream of Pharma Professionals with a total investment reaching around 22,000 crores in the State. This project will create 56,000 employment opportunities directly and 86,000 opportunities indirectly. This Park will have basic townships, theatres, hospitals, schools, solar panels etc. Mr. Sunil Kumar D opined that the support of Pharmacy Colleges Management is also inevitable as the student community gets seldom opportunities in Industry. Mr. Mathew Kokad suggested to call for a Press Conference for making aware the media and public for the need of this Project in the State. Mr. Subash Philip offered political support in this regard. Later, Dr. Subash Philip and Dr. Boby Johns G were invited to present a proposal for instituting KPGA Annual Awards. In the presentation, they said 10 prestigious awards will be given to KPGA members in the State. It includes-KPGA fellowship, Life Time Achievement Award, Academic Award, Researcher Award, Young professional award and award for Students. Dr. Nishith informed the Committee that an award for regulatory and Industry may be considered for this Award. Life member certificates to the members were distributed in the post lunch session. Mr. Venkata Krishnan SS, Adv. Unnikrishnan Panicker M.K, Dr. John Joseph, Mr. Anil Kumar, Prof. Bhanumathy L, Prof. Janeera Beegam, Mr. Sharafudheen and Mr. Abdul Raheem distributed certificates to the members. For the Bye-Law Amendment, President invited Dr. Nishith M.C to present the proposed amendment on inclusion of M. Pharm Students in Student Forum. After detailed deliberations on this subject, the GB opined that the proposed changes will be circulated to all members prior to present for approval. Accordingly, it is decided to frame draft on the proposed changes to be incorporated in bye law . The decisions on each proposed change will be taken thereafter. Dr. Sreekumar PK sought opinion among the members regarding the challenges faced by the Association. Mr. Mathew Kokad suggested that we should be very active and straight forward in all decisions and activities. Mr. Abdul Nazeer opined that KPGA Central zone need to be strengthened. Dr. John Joseph informed that activities of the Association should be increased. Dr. P.K Sreekumar said that we need to conduct physical programs, collaborating with Pharmacy Institutions. The prime importance for all members by giving a role in all of our programs. The meeting ended with vote of thanks proposed by Smt. Sangeetha R, Joint Secretary, KPGA.

News & Activities

The second General Body Meeting of the Association for the year 2021-2023 was held in the office premises of KPGA on 17th July 2022.The brief report is presented on page no.31.

The 76th Independence Day of our country was celebrated in a grand and different manner, virtually, in association with IPGA and IPA on 15th August 2022 at 11: 30 am. The Chief speaker was Mr. SS Venkatakrishnan, Patron of KPGA. Mr. Dileep G, executive member of KPGA welcomed the gathering. PK Sreekumar, President, KPGA presided the function. Dr. P Jayasekhar IPA Kerala branch president Dr. CS Satheesh Kumar, IPGA Kerala Branch president, and Dr. Mahalakshmi BK spoke on the occasion. Mr. Abdul Nazeer PU, Gen.Secretary, KPGA expressed the vote of thanks. Certificates were handed over to the new members joined on this auspicious day. All the speakers and participants reiterated their dedication to the prosperity of the Nation. The anchoring note of the program was done by Dr. Jeny Samuel in Hindi language.

Gallery

Through the General body meeting on 17th July, 2022 at Thiruvananthapuram

Gallery

Independence Day Celebration

|| Upcoming events ||

- World Pharmacists Day celebration will be celebrated on 25th September, 2022 on virtual platform. This year's theme will be "**Pharmacy united in action for a healthier world"**
- World Pharmacists Day will be celebrated by Kerala Pharmacy Graduates'' Association Jointly with Dr. Joseph Marthoma Institute of Pharmaceutical Sciences and Research, Kayamkulam in a grant manner on 24th Saturday, September,2022.
- The students' wing of KPGA will be conducting an online Poster competition in connection with World Pharmacists Day-2022.The topic of the competition is "Pharmacists: Help people to get the best from their medicines and stay healthy ".

Kerala Pharmacy Graduates' Association

PHARMLINE-The Official Publication Of Kerala Pharmacy Graduates' Association

PHARMLINE is the official publication of KPGA and is published since 1981. Pharmline is a triannual publication. The main aim of the publication is to keep pharmacists informed on current issues and best practices, as well as serving as a platform for the exchange of ideas, knowledge and opinion among pharmacists and related disciplines. The publishers welcome contributions of pharmaceutical relevance. Original articles are considered for publication on the condition that they have not been published, accepted or submitted for publication elsewhere. The editor reserves the right to edit manuscripts to fit articles with in space available and to ensure conciseness, clarity and stylistic consistency. All scientific articles submitted for publication are subject to a double blind review procedure.

Please send your articles to *kpgapharmline@gmail.com*

Contact us

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