A Quarterly News Letter of Krupanidhi College of Pharmacy, Bangalore | FOR PRIVATE CIRCULATION ONLY

SYNERGIA

Updates | Zeitgeist | Fun

EDITORIAL

Dear all,

In an effort to make your reading experience more immersive *Synergia* will be sporting a new look and increased content. From this issue *Synergia* will be 12 paged, with themed content.

We at *Synergia* passionately believe that exchange of ideas is the best way to professional development. We have envisioned *Synergia*, to be forum, where budding and seasoned clinical pharmacists and clinicians can learn and can continue their learning. This is not possible without the involvement of the most important stakeholder – you the reader.

In a happy moment to KCP, the graduation ceremony, which happened during May, saw the graduation of more than 100 students form the Diploma to Doctoral programs of our college, many of them with high academic acclaims. We also with equal fervor welcome the freshers to our institution.

Synergia requests you to be forthcoming and consider contributing or sending your feedback to us. *TeamSynergia* looks forward to it.

Rajeswari R
Editor

FDA APPROVALS

Brand Name (Active Ingredient)	Indication	Sponsor	Approval
Cardiology/Vascular Diseases			
Byvalson (Nebivolol And Valsartan)	Hypertension	Allergan	June 2016
Dermatology			
Taltz (Ixekizumab)	Plaque Psoriasis	Eli Lilly	March 2016
Ameluz (Aminolevulinic Acid Hydrochloride	Actinic Keratoses	Biofrontera Pharma	May 2016
Hematology			
Idelvion (Coagulation Factor IX (Recombinant), Albumin Fusion Protein	Hemophillia B	CSL Behring	March 2016
Kovaltry [Antihemophilic Factor (Recombinant)]	Hemophillia A	Bayer	March 2016
Venclexta (Venetoclax)	Chronic Lymphocytic Leukemia With 17p Deletion	Abbvie	April 2016
Afstyla (Antihemophilic Factor (Recombinant), Single Chain)	Hemophillia A	CSL Behring	May 2016
Hepatology			
Defitelio (Defibrotide Sodium)	Veno-Occlusive Disease With Renal Or Pulmonary Dysfunction	Jazz Pharmaceuticals	March 2016
Ocaliva (Obeticholic Acid)	Primary Biliary Cholangitis	Intercept Pharmaceuticals	May 2016
Immunology			
Odefsey (Emtricitabine, Rilpivirine, And Tenofovir Alafenamide)	HIV-1 As Initial Therapy	Gilead Sciences	March 2016
Descovy (Emtricitabine And Tenofovir Alafenamide)	HIV-1 Infection	Gilead Sciences	April 2016
Afstyla (Antihemophilic Factor (Recombinant), Single Chain)	Hemophillia A	CSL Behring	May 2016
Vaxchora (Cholera Vaccine, Live, Oral)	Active Immunization Against Cholera	Paxvax	June 2016
Oncology			
Cabometyx (Cabozantinib)	Advanced Renal Cell Carcinoma	Exelixis	April 2016
Venclexta (Venetoclax)	Chronic Lymphocytic Leukemia	Abbvie	April 2016
Lenvima (Lenvatinib)	Advanced Renal Cell Carcinoma	Eisai	May 2016
Opdivo (Nivolumab)	Hodgkin Lymphoma	Bristol-Myers Squibb	May 2016
Tecentriq (Atezolizumab)	Urothelial Carcinoma	Genentech	May 2016
Psychiatry/Psychology			
Nuplazid (Pimavanserin)	Hallucinations And Delusions Associated With Parkinson's Disease Psychosis	Acadia Pharmaceuticals	May 2016

Source: Centerwatch, USFDA, Current as on 30 June 2016

Geriatrics - certitude for drug use essential

Nataraj G.R
Assistant Professor
Department of Pharmacology & Pharmacy Practice,
SJM College of Pharmacy
Chitradurga – 577502, KA
itsnattu007@gmail.com

Prescribing a drug for geriatric use is a really a challenging job. They are the most vulnerable population to have drug related issues. A small negligence during the course of treatment can cause greater impact on their daily livelihood or even for their life too.

The Hippocratic Oath tells us, *"First, do no harm"*. In the older population, the susceptibility to the Adverse Drug Reactions (ADRs) is higher than younger adults. The principle of Geropharmacology is based on the appropriate use of drugs to give most benefit to older person while avoiding or decreasing ADR and drug interactions.

In our society, the percentage of elderly people in the population has increased dramatically during recent decades and is likely to increase further in the coming decades. However, a large proportion of older people are confronted with one or more disabilities or disease condition. The older population consumes more number of drugs when compare to younger adults.

Physiological changes in Elderly

Geriatric populations have a reduced body organ system performance due to which an altered pharmacokinetic and pharmacodynamic action for drugs is seen. The age relate changes in the geriatric populations like reduced water content, increased body fat, reduced heart muscle strength, reduced intrinsic heart rate, decreased elasticity of vessel walls, decreased blood flow may alter the postural adoption response by geriatrics, wane of receptor and pathway slows the motor coordination among elderly. Decreased GI secretion and motility which will affect the ADME of drugs. Decreased immune response in geriatrics may cause increased susceptibility for infection and increased use of antibiotics. Decreased or depletion of calcium level, loss of which increases the use of NSAIDs drugs among older population. Reduction of renal mass, blood flow may prolong the effect of drugs which may contribute to ADRs. Visual and hearing impairment as aging may contribute for noncompliance/ nonadherence towards the prescribed drugs. The other reasons for drug related problems among elderly population are drug-disease interaction, drug- drug interactions, inappropriate drug selection, inadequate monitoring, lack of medication adherence, overdosage, poor communication, under prescribing, adverse drug reaction etc. Like this there are many facts to be known about geriatrics which help the health care team to provide better treatment and at most care for our elderly population.

Dosing of drugs in elderly

Drug dose should be reduced in elderly patients because of a general decline in body function with age. A general equation that allows calculation of maintenance dose for a

$$\frac{\text{(Weight in KG) } 0.7 \times (140 - \text{age in years})}{1660} \times \text{Adult dose}$$

Successful pharmacotherapy means using the correct drug with the correct dose for the correct indication and for correct duration in an individual patient. Dose adjustment for renal & hepatic impairment must be strictly followed.

The clinical pharmacists' consultations can improve geriatric patients' drug regimens and compliance. One important aspect of quality care for older adults is managing their medications to assure the maximum beneficial results from medication therapy while avoiding adverse complications. The main guidelines to prescribing medication for the older patient are "to start with a low dose of medication and step up the dose as one goes along to achieve an optimum therapeutic end point". The prescriber must keep the principles in Geropharmacology in mind if their prescriptions are to have intended effect and not to create iatrogenic problems.

EXPERT REVIEWS

Principles of Prescribing in the geriatric population

- Review patient's medical record
- Avoid prescribing prior to diagnosis.
- Follow Beers Criteria Start with a low dose and titrate slowly.
- Avoid starting 2 agents at the same time.
- Reach therapeutic dose before switching or adding agents.
- Consider non-pharmacologic management
- 'Old drugs for old people' – It is safer to use drugs that have been time tested
- Keep in mind possible drug interactions including Over The Counter preparations
- Use less frequent dosing intervals (OD or BID dosing is preferable)
- Use formulations that are easy to administer
- Drugs should be dispensed in easy-to-open containers
- Clear instruction about how to administer the drug should be given
- Treat adequately; do not discontinue a drug without achieving adequate therapeutic concentration unless ADR intervene.
- Always continuously evaluate the need for each of the drugs that the patient is taking
- Be sensitive to the patient's concerns and reports of ADRs
- Foster a good Physician-Pharmacist-patient relationship

Pharmacovigilance Programme of India (PvPI) launches updates on social media

/ Ncc-Pvpi Ipc

+917042343309

Disability Adjusted Life Expectancy, DALE

Dr. S C Basak
Professor,
Department of Pharmacy,
Annamalai University,
608002, TN
scbconnect@gmail.com

Life expectancy at birth measures the average number of years that a newborn baby can expect to live. Life expectancy statistics are used for many purposes of annual assessment of world health. However, life expectancy (LE) estimates are based on the overall length of life based on mortality data only.

What Is DALE?

DALE is disability-adjusted life expectancy, developed by WHO in 1999, which measures the equivalent number of years of life expected to be lived in full health, also called healthy life expectancy. To calculate DALE, the years of ill-health are weighted according to severity and subtracted from expected overall life expectancy to give the equivalent years of healthy life. Following is the formula used to estimate DALE:

DALE = LE – DLE.

Where LE is total life expectancy based on average numbers of years males and females could expect to live in each country.

DLE is expected years lost due to disability – an estimate of the total equivalent lost of years of good health.

Why healthy life expectancy?

Life expectancy at birth increased dramatically during 20th century and will continue to rise as soon as cancer and other life-threatening diseases are conquered. However higher life expectancy is desirable only if it is linked to acceptable level of quality of life. With a longer life span the subject of ***healthy years of life*** to be lived has become an important issue.Sociologists and other scientists of every country are interested higher level not only life expectancy, but also years of healthy life. Hence disability-adjusted life expectancy, DALE has become more salient. Health outcomes, in terms of DALE, is directly linked to access to medicines (The World Medicines Situation 2004). In recognition of present day need, the DALE indicator developed by WHO is an important sociological tool and it will further promote analysis of health performance of poorly performing health systems of the world.

Scleroderma

Scleroderma is a chronic disease of unknown etiology that affects the microvasculature and loose connective tissue. It is characterized clinically by fibrous deposition and obliteration of vessels in the skin, lungs, gastrointestinal tract, kidneys, and heart. Scleroderma literally means “hard skin” and was first reported by William and Robert Watson in 1754. The diffuse thickening and induration of the skin in the systemic sclerosis (SSc) is accompanied by fibrosis and vascular obliteration of internal organs. Its course is often progressive and fatal.

Here is a case report that describes a patient with scleroderma, interstitial lung disease and pulmonary arterial hypertension with low vitamin D with osteoporosis.

A 55 year old female patient from West Bengal reported to the clinical immunology and rheumatology department with chief complaints of severe burning pain over the right toe, along with pain over the finger tips. She has persistence of breathlessness. Present effort tolerance is 10-15 steps and 100m on level ground. No H/o increased breathlessness on lying down. She also complained of persistent cough, which increase during swallowing.

Patient has been symptomatic since 1996 (19 years). Her symptoms started as bluish discoloration of the fingers on exposure to cold. Following a nail infection, which was excised in 1996, she developed acute onset gangrene of the left index finger tip, which was later operated.

Early in 1997, she noticed skin tightening over her face and extremities. Gradually she developed breathlessness on exertion. She noticed difficulty in climbing stairs beyond the first floor. She was evaluated locally in Kolkata and diagnosed to have scleroderma and started on therapy (details not available). She was asymptomatic on treatment.

In 2007 while on treatment she developed a reddish, painful lesion over her right lateral malleolus, which ulcerated with white discharge and later on became a moderate size non-healing ulcer. It took almost 5-6 months for this ulcer to heal. Subsequently she developed other ulcers around the same region and on left leg medial malleolus, which healed with multiple dressing 3-4 months later. Ulcers used to be extremely painful. Her breathlessness on exertion progressed gradually during this time period. She also developed painful ulcers over the finger tips, which used to heal leaving pitting scars. She also complained of cough

No H/o pain or swelling over joints or photosensitivity or melar rash. No H/o proximal muscle weakness. She complained of dryness of mouth. No H/o dry eyes. No H/o chest pain or palpitations. No H/o dry cough or hemoptysis.

In 2010 she was diagnosed to have scleroderma with interstitial lung disease and pulmonary arterial hypertension and started on steroid with second line immune suppression. She fared well on these medications and continued to have regular follow up visits.

In April 2014, she developed pain over the left shoulder and diagnosed to have periarthritis and was administered intra articular steroid, which relieved her symptoms. Towards later May 2015 she noticed reappearance of the reddish lesions over her malleoli. She also developed black discoloration of the right leg toe, which was extremely painful. Progressed to reddish in color, followed by ulceration at the tip of the finger under the nail. H/o severe burning pain over the ulcer.

She has a H/o jaundice in 1980. Appendicectomy in 1982. H/o ASD repair in 1985. H/o mumps in 1992 following which she has menopause at an early age- 32 years with no issues. She has been on steroid, MMF and tadalafil. She has a family history of mother died at her childhood due to some problem in liver.

On physical examination, patient was conscious and well oriented. Salt and pepper pigmentation over bridge of nose. Hypopigmented patch over the forehead. Generalized skin tightening present. mRSS- 2/51. Pitting scars over tips of left index and right middle finger. Pinched nose appearance. Mouth opening- 2 fingers.

Reddish discoloration over lateral malleoli. Calcinosis cutis over lateral malleoli. Non healing ulcer over right big toe tip. Reddish discoloration of right big toe distal part.

On systemic examination, no JVP elevation. In CVS, S1 normal and S2 wide split (+). ESM in pulmonary area. In respiratory system, bilateral scattered crackles present. No other abnormality detected.

Laboratory investigations revealed low haemoglobin (10.2 g/dl), low platelet count (1.16 lakh cells/cu.mm), high ESR (59 mm/1 hr) and high CRP (13.1 mg/L). Echo showed no evidence of interstitial lung disease while spirometry revealed minimal improvement in FVC.

In general, disease heterogeneity (stage, severity, and pace

CASE REPORT

image courtesy: http://www.hopkinsmedicine.org/

With the manifestation of Reynaud's phenomenon calcium channel blockers, angiotensin Type II receptor blocker, surgical sympathectomy will be the choice of treatment. Cases with digital ulcer, skin fibrosis, arthritis, myositis, drugs like immunosuppressive, non-steroidal anti-inflammatory drugs, low dose of steroids are given. In severe cases, where there is renal crisis and pulmonary hypertension, angiotensin-converting enzyme inhibitors are given as treatment modalities.

The drugs prescribed throughout the hospital stay were Tab. Amoxiclav and Tab. Metronidazole for infection, Tab. Pantop, Tab. Tadalafil and Tab. Nicardia which is a calcium channel blocker for hypertension, Tab. Aceclo, Tab. Pregab and Tab. Calpol for pain management, Tab. Ostocalcia as a calcium supplement, Tab. Mycophenolate which is an immuno suppressant, Tab. Ecospirin-AV and Tab. Omnacortil which is a corticosteroid hormone.

During hospital stay, she discontinued steroids and developed pain and swelling over her peripheral joints. Steroid was restarted on lower doses and planned to continue with a gradual tapering schedule.

Discharge medications were prescribed for 3 months. The drugs included Tab. Deflazacort, Tab. MMF, Tab. Bosentan, Tab. Nicardia R, Tab. Ecospirin, Tab. Atorvastatin, Tab. Pregabalin, Tab. Amitryn, Tab. Aceclo, Tab. Pantop. Tab. Deflazacort was given in tapered dose as 12 mg once daily after breakfast for 2 weeks. Followed by 9 mg once daily for 2wks, then 6 mg once daily for 1 month and then reduce the dose to 3 mg once daily for the last one month. She was asked to review after 3 months.

Scleroderma is an autoimmune disorder involving multiple systems with oral and cutaneous manifestation. Pulmonary manifestations of systemic sclerosis include interstitial lung disease, pulmonary hypertension, pleuritis and pleural effusion, and aspiration pneumonia. Dyspnea and non productive cough in a patient with systemic sclerosis will raise the possibility of lung disease, and a work up for interstitial lung disease should be performed. Physicians and patients should be more attentive to the potential risk factors for organ damage.

Reference:

1. Shah AA, Wigley FM. My approach to the treatment of scleroderma. Mayo Clin Proc 2013;88:377-93.
2. Mark H, Robert B. 1999. The Merck Manual of Diagnosis and Therapy. 17 ed. Merck and Co. USA.
3. Naylor WP. Oral management of the scleroderma patient. J Am Dent Assoc 1982;105:814-7.

Joice Samuel, Pharm D Intern
Krupanidhi College of Pharmacy, Bangalore

OncoQuiz

How well do you know your Oncology? A Round-up of the current practice notes, therapeutic options and ADRs

QUESTION 1

On day 14 after allergenic stem cell transplant, the patient complains of right-upper-quadrant pain. He has gained 10 kg over the past 3 days. The preparative regimen for his AML was cyclophosphamide and busulfan. What is the most likely cause of the pain?

A. Cytomegalovirus hepatitis

B. Graft-versus-host disease

C. Veno-occlusive liver disease

D. Acute cholecystitis

QUESTION 2

A 50-year-old male presents to the emergency department with a temperature of 39.4°C, severe hypotension, and chills. The patient has a history of hypertension, diabetes, and coronary artery disease. He received paclitaxel and carboplatin 9 days ago for non-small-cell lung cancer. His absolute neutrophil count is 56cells/mm^3. Which of the following interventions would be most appropriate for this patient?

A. Cefepime

B. Imipenem and filgrastim

C. Ceftriaxone and filgrastim

D. Ciprofloxacin and aztreonam

QUESTION 3

Which of the following chemotherapy agents has been associated with severe extravasations injury?

A. Bleomycin

B. Cyclophosphamide

C. Methotrexate

D. Vincristine

QUESTION 4

A 68-year-old female has been recently diagnosed with stage IV breast cancer. Her tumor is found to be estrogen- and progesterone-receptor positive. Which of the following is recommended for initial hormonal management?

A. Anastrozole 1 mg PO q.d.

B. Aminoglutethimide 250 mg PO q.i.d.

C. Tamoxifen 40 mg PO b.i.d.

D. Exemestane 25 mg PO q.d

QUESTION 5

Which of the following combination chemotherapy regimens is considered first-line treatment for adults with acute non lymphocytic leukemia?

A. Mitoxantrone and Cytarabine

B. Cytarabine and doxorubicin

C. Mitoxantrone and daunorubicin

D. Cytarabine and daunorubicin

QUESTION 6

Which of the following chemotherapy agents has been associated with severe extravasations injury?

A. Bleomycin

B. Cyclophosphamide

C. Methotrexate

D. Vincristine

QUESTION 7

When an investigational drug is being studied in a phase II clinical trial which of the following choices best characterizes the appropriate endpoints of the study?

A. Efficacy and dose limiting toxicity (DLT)

B. Pharmacokinetic and Pharmacodynamics parameters

C. Response rate and safety

INTERN NOTES

QUESTION 8

A new physician joins the Oncology Division at your hospital. He has several research protocols that involve the use of gene transfer products and he has submitted these to the IRB for approval. You sit on the IRB and have concerns about the safety and proper handling of these agents. Which of the following publications would provide the best information about the dangers involved in handling these gene transfer agents and precautions that should be taken to ensure the safety of those preparing them?

A. CDC/NIH publication - Biosafety in Microbiological and Biomedical Laboratories

B. ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs

C. OSHA Technical Manual - Controlling Occupational Exposure to Hazardous Drugs

D. JCAHO publication - Comprehensive Accreditation Manual for Hospitals

QUESTION 9

It is recommended that patients who have had basal cell carcinoma of the skin or those who are at high risk for skin cancer use a minimum sun block of SPF:

A. 5.

B. 15.

C. 30.

D. 45.

QUESTION 10

You are participating in an annual patient education program sponsored by your employer. You have been asked to help staff the booth focusing on current cancer screening guidelines. A woman asks you about the latest recommendations for the screening of gynecologic cancers. Which of the following statements accurately represents the American Cancer Society (ACS) cervical cancer screening guidelines?

A. At age 30 or after, women who have a single normal or negative cytology result can receive subsequent screening human papillomavirus (HPV) DNA testing in conjunction with cytology smears.

C. Women should begin cervical cancer screening no later than age 21 or within 3 years of becoming sexually active, whichever occurs first.

D. All women who are 70 years of age or older with an intact uterus no longer require cervical cancer screening.

QUESTION 11

With regard to treatment trials, the primary purpose of the informed consent process is to provide:

A. information regarding the treatment and the financial costs associated with trial participation.

B.liability coverage for the institution and the participating investigators.

C. a contract between the investigator and a person participating in the trial.

D. sufficient information for a potential subject to make a

Solutions:- Q1:C; Q2: B;Q3: D; Q4:A;Q5:D; Q6:A;Q7:C; Q8:A; Q9:B; Q10:C; Q11:D

Renoy Philip, Pharm D Intern
Krupanidhi College of Pharmacy, Bangalore

Caution and rational use is advised on the long term use of Proton Pump Inhibitors (PPI):

- Iron deficiency anemia -caused due to malabsorption of iron.
- Hypochlorhydria -increased susceptibility to bacterial or parasitic infections.
- Hypergastrinemia - elevated gastrin levels and possibly a predisposition to cancer.
- Osteoporosis -due to its effects on vitamin B 12
- Kidney disease- unclear mechanism
- Heart disease-negative effect on vascular function.
- Dementia -increase the risk of Vitamin B12 deficiency.
- PPIs also interact with various drugs like acetaminophen,

Nancy Ashok, Pharm D Intern
Krupanidhi College of Pharmacy, Bangalore

Computer Aided Drug Design: *An Inevitable and Economical Tool for Drug Modeling and Designing - PART 1*

The most fundamental goal in drug design is to predict whether a given molecule will bind to a target and if so how strongly. Molecular mechanics or molecular dynamics are most often used to predict the conformation of the small molecule and to model conformational changes in the biological target that may occur when the small molecule binds to it.

Drug design, often referred to as rational drug design or simply rational design, is the inventive process of finding new medications based on the knowledge of a biological target. Drug design that relies on the knowledge of the three-dimensional structure of the bio-molecular target is known as structure-based drug design.

The phrase "drug design" is to some extent a misnomer. A more accurate term is ligand design (i.e., design of a molecule that will bind tightly to its target)

Traditional Drug Discovery (known as forward pharmacology), which rely on trial-and-error testing of chemical substances on cultured cells or animals, and matching the apparent effects to treatments, rational drug design (also called reverse pharmacology) begins with a hypothesis that modulation of a specific biological target may have therapeutic value.

Drug design with the help of computers may be used at any of the following stages of drug discovery:

1. Use of computing power to streamline drug discovery and development process
2. Leverage of chemical and biological information about ligand and/or targets to identify and optimize new drugs
3. Design of *in silico* filters to eliminate compounds with undesirable properties (poor activity and/or poor Absorption, Distribution, Metabolism, Excretion and Toxicity, ADMET) and select the most promising candidates.

A Brief History of CADD

1900: The receptor and lock-and-key concepts P. Ehlrich (1909) and E. Fisher (1894);

1970s: Quantitative structure-activity relationships (QS- AR), Limitations: 2-Dimensional, retrospective analysis;

1980s: Beginning of CADD Molecular Biology, X-ray crystallography, multi-dimensional NMR Molecular modeling, computer graphics;

chemistry, High-throughput screening.

A major aspect of the utilization of the information will be the provision of small molecules which will recognize selected sequences, perhaps with the goal of switching off particular genes as in cancer chemotherapy. For some time, antibiotics such as netropsin have been known to bind preferentially to sequences rich in A-T pairs. A variant based on this research has been to try to design a bioreductive ligand based upon netropsin. The idea of bioreductive anti-cancer agents, starts with the fact that tumours receive less blood and hence less oxygen than normal tissue.

Underpinning all the work is the availability of high quality computer graphics, largely supported on workstations leading to Computer Aided Drug Design (CADD). It is expected that the power of CADD will grow as the technology continues to evolve.

How Does CADD Work?

Target Identification---> Structure Determination-->Biological assays-->Synthetic Chemistry-->ClinicalTrials-->FDA Approval

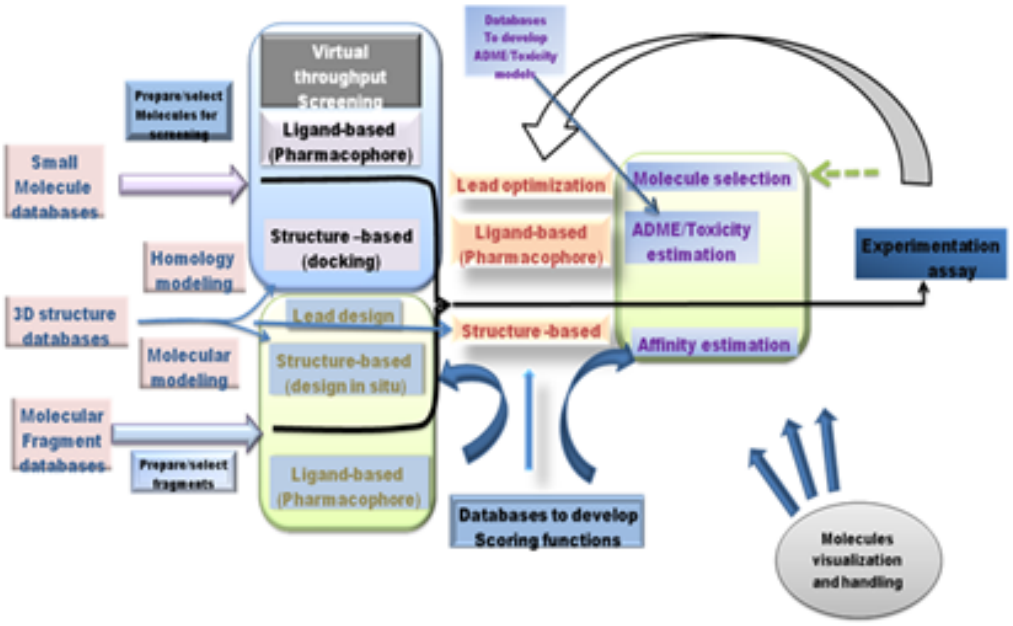
CADD Strategies in the Drug Discovery Process

Strategies for CADD vary depending on the extent of structural and other information available regarding the target (enzyme/receptor) and the ligands. “Direct and indirect” designs are the two major modeling strategies currently used in the drug design process. In the indirect design comparative analysis of the structural features of known active and inactive compounds. In the direct design the three-dimensional features of the target (enzyme/receptor) are directly considered.

CADD in Search of Lead molecule - Ligand-based Drug Design

Ligand-based drug design (or indirect drug design) relies on knowledge of other molecules that bind to the biological target of interest. These other molecules may be used to derive a pharmacophore model that defines the minimum necessary structural characteristics a molecule must possess in order to bind to the target. In other words, a

knowledge of what binds to it, and this model in turn may be used to design new molecular entities that interact with the target. Alternatively, a quantitative structure-activity relationship (QSAR), in which a correlation between calculated properties of molecules and their experimentally determined biological activity, may be derived.



Structure-Based Drug Design

Structure-based drug design (or direct drug design) Within many of the rational drug design projects in the group, computer-aided methods, such as virtual screening and de novo design techniques, play an important role. NMR and Mass spectroscopy in conjunction with molecular modeling and other spectroscopic methods allows investigations to be made into molecular mechanisms of ligand-target recognition at the atomic level. This information is a necessary component in the design of novel therapeutics and in prediction of interactions of drugs with the targets. Also over the years, the group has studied details of binding of ligands to the minor groove of DNA, such as Hoechst 33,258, or to tRNA.

3D Structure Prediction of Unknown Drug

In the early stage of a drug discovery process, researchers may be faced with little or no structure activity relationship (SAR) information. At this point, assay development and screening should be undertaken immediately by the high-throughput screening (HTS) group. The compounds screened could be commercially available, natural products, collections of in-house synthesized compounds or emerge from combinatorial libraries.

CADD and Bioinformatics

A few years ago, the National Institutes of Health (NIH) created the Biomedical Information Science and Technology Initiative (BISTI) to examine the current state of bioinformatics in the United States. BISTI's working definition of bioinformatics included its use in biomedical research, in particular for drug discovery and development programs. Computer-Aided Drug Design (CADD) is a

by the high-throughput screening (HTS) group. The compounds screened could be commercially available, natural products, collections of in-house synthesized compounds or emerge from combinatorial libraries.

CADD and Bioinformatics

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Ranganath MK, Professor & HoD, Department of Pharmaceutical Analysis
Krupanidhi College of Pharmacy, Bangalore
ranga9rpc@gmail.com

Please send your contributions, feedback and suggestions to : synergia.kcp@gmail.com

Cefazolin: Cost-Effective Alternative for Treating MSSA Infections

Methicillin-susceptible Staphylococcus aureus (MSSA) is a major pathogen in community-acquired infections, although methicillin resistance is increasing (1). These strains can be treated with either Nafcillin or Cefazolin which are generally considered as first line therapies for effective management of the infection.

Cefazolin is a first generation cephalosporin which has been used for the treatment of MSSA infections since the 1970s. It falls into the category of β-Lactam (beta-lactam)antibiotics and works by inhibiting cell wall synthesis of the bacteria by binding to penicillin-binding proteins. Nafcillin is second-generation penicillin which is used to treat moderate-to-severe bacterial infections caused by penicillinase-producing bacteria. It is highly resistant to inactivation by penicillinases. Nafcillin was also approved for use in the 1970s and is still widely used to treat severe staphylococcal infections.

While some case reports suggest that Cefazolin is associated with treatment failure due to efficient hydrolysis by S. aureus-produced β-lactamase (2, 3), Nafcillin use has been linked with rare yet clinically apparent cases of idiosyncratic liver injury (4). Previously conducted tolerability and effectiveness studies of the drugs have indicated that Nafcillin treatment was associated with higher rates of both premature antimicrobial discontinuation (PAD) as well as drug-emergent events (DEEs) compared with cefazolin treatment (5, 6).

According to Dr.Maggie Monogue, Pharm D, a clinical pharmacy fellow at Hartford Hospital Center for Anti-infective Research and Development, switching to cefazolin instead of nafcillin to treat MSSA infections not only saves a considerable amount of money but also allows the patients to leave the hospital earlier (7).

Cefazolin is a lot less expensive than nafcillin; it ranges from10 to 13 times less expensive. Some infections call for at least four to six weeks of treatment; when we factor in the price variation and multiply that with the number of treatment days, it attributes to significant cost savings.

A retrospective, non-inferiority cohort study comparing treatment failure rates between nafcillin and cefazolin in patients with MSSA bacteriawas conducted by Dr.Monoguein Parkland Health and Hospital System, Dallas. The researchers observed142 patients affected by MSSA bacteria, with an equal number of patients in the nafcillin and the cefazolin arms. Nafcillin-treated patients showed a treatment failure rate of 14% (10/71), which was greater than the 8.4% failure rate observed among those treated with cefazolin (6/71; 95% CI, –0.032 to 0.145). The cost difference at Parkland to treat 71 patients with nafcillin over cefazolin was around $100,000. This will definitely peak the interests of Hospital administrators because we attain a mutual benefit when we combine drug efficacy with cost savings.

These findings definitely reveal financial benefits, but more importantly, cefazolin is the more tolerable option. The drug is prescribed in less frequent doses; and patients can leave the hospital on an oral dose sooner than those taking nafcillin, making it a favourable option for both patients and hospitals.

References

1. Miro J. M., et al. 2005. Staphylococcus aureus native valve infective endocarditis: report of 566 episodes from the International Collaboration on Endocarditis Merged Database. Clin. Infect. Dis. 41:507–514.
2. Bryant R. E., Alford R. H.. 1977. Unsuccessful treatment of staphylococcal endocarditis with cefazolin. JAMA 237:569–570.
3. Quinn E. L., et al. 1973. Clinical experiences with cefazolin and other cephalosporins in bacterial endocarditis. J. Infect. Dis. 128:S386–S389.
4. Drug Report- Naficillin Available at: http://livertox.nih.gov/Nafcillin.htm - overview
5.Youngster I, Shenoy ES, Hooper DC, Nelson SB. 2014. Comparative evaluation of the tolerability of cefazolin and nafcillin for treatment of methicillin-susceptible Staphylococcus aureus infections in the outpatient setting.Clin Infect Dis. 1; 59(3):369-75.

Judith Baskar, Pharm D Intern
Krupanidhi College of Pharmacy, Bangalore

The Botswana Experience

I had the opportunity of doing my Internship in the country of Botswana, located in southern African continent. My experience had been a fruitful one as I was able to grasp the knowledge of HIV and the antiretroviral therapy to a higher extent. As I had only prior theoretical knowledge of HIV, the practical experience I gained there was remarkable.

It was all thanks to the support of the staff members who helped and guided me throughout. They were always ready to lend their valuable guidance and also insights to various medication related issues also.

Apart from HIV, the experience regarding therapy of other ailments also was a learning point. The difference in therapy, effects and also other aspects of medication therapy in the other race was a good learning point. Medical team also was engaging in deciding course of therapy and would consider the pharmacist's opinion on any drug related aspect for the patients. I was lucky enough to participate too and give my views which were also accepted by them. They would often enquire the practices followed back here in India, and I would tell them about which they found insightful. Mostly they were open to the opinions provided by the pharmacy team and took it in stride to apply it in practice.

As the country had laid down their guidelines for medication use, pharmacists were engaged in making sure that only the aforementioned drugs would be given to the patient, thereby promoting rational use of medications and improving the quality of life of patients.

I was able to attend the routine HIV follow–up clinics where I was able to participate with my pharmacy team to enquire patients about their drug history, side-effects, and other related effects and would electronically document the same. Patients were able to tell about their experience with the drugs and were quite knowledgeable about their condition and medication effects. Pharmacists are involved in providing counseling to patients always while dispensing their medications. Patient counseling was a vital part of dispensing and was practiced by all pharmacists, I too was able to engage in the same and dispense. We used to have daily meetings as the entire pharmacy team would discuss about pharmacy related issues and their methods to resolve them. There were even presentations by members on drugs, diseases, changes in guidelines etc, as part of the CME's. Towards the end I could see that pharmacists there played an integral role and were actively participating in patient care and was proud to be one of them even for a short while that I was there.

Ahmadi Naaz, Pharm D Intern
Krupanidhi College of Pharmacy, Bangalore