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VISION :

To emerge as one of the premier pharmacy colleges in the country and produce pharmacy professional of global standards.

MISSON :

•To deliver quality academic programs in Pharmacy and empower the students to meet industrial standards.

•To build student community with high ethical standards to undertake R&D in thrust areas of national and international standards.

•To extend viable outreach program for the health care need of the society.

•To develop industry institute interaction and foster entrepreneurial spirit among the graduates

ANAESTHESIA INDUCED DEMENTIA

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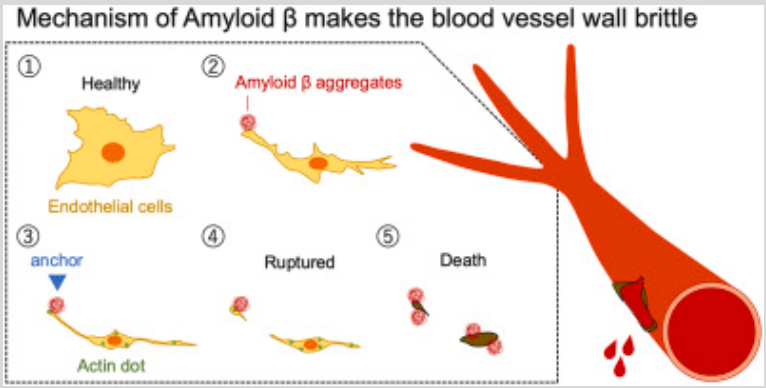
INTRODUCTION :

ANAESTHESIA- It means loss of sensation.Drugs that cause anaesthesia are known as anaesthetics these are used during surgical operations to prevents pain,discomfort and induce sleep

DEMENTIA -The loss of cognitive functioning such as thinking,remembering,and reasoning which interfere with a day to day activities

MOA OF DEMENTIA :

Anaesthetics activate memory loss receptors in the brain which causes loss of sensation. Anaesthetic drugs has clinical benefits and neurodegenerative complications. Invitro and magnetic resonance studies shown that inhaled anaesthetics promote amyloid β peptide(Aβ) oligomerisation which results in Aβ induced neurotoxicity.The risk of dementia increases in patients who received IV or IM anaesthesia & general anaesthesia.

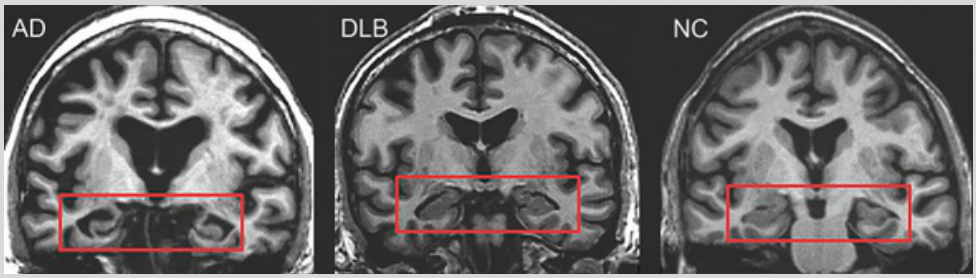


EPIDEMIOLOGY:

Dementia is more prevalent among old peoples . in 2001 nearly 24 million peoples are suffered from dementia in the world. the estimated prevalance in the year 2020 & 2040 is 42 millions & 81 millions.every year there are nearly 10 million new cases.

DISCUSSION:

Inhalation anaesthetics such as Sevoflurane can induce temporary memory impairment. Propofol,Midazolan,Thiopental or Ketamine etc. are the anaesthetic drugs which are used before surgery.Fronto Parietal Cortex is the major target site for anaesthetics .Symptoms includes decline in memory,confusion,poor judgement & reasoning skills, changes in language & behaviour, sudden mood swings etc.. Physicians can diagnose dementia by using MRI or CT scans or even detect signs of dementia before symptoms appear.The first line treatment for dementia is acetyl cholinesterase inhibitors such as Donepezil, Rivastigmine & Galantamine etc.. thes drugs increase acetyl choline levels which are responsible for memory & cognitive functioning .



Ginkgo Biloba enhances memory by increasing circulation to brain . Regular excercise, balanced diet, having regular contact with others, quit alcohol & smoking etc.. are the life style modifications for dementia. We can protect our brain from anaesthesia induced dementia by developing brain-healthy habits before & after surgery. They are :

- Eat plenty of fruits, vegetables, lean proteins & healthy fats.
- Avoid inflammatory foods such as refined carbohydrates, sugar, fried foods & excessive alcohol.

There is no specific method or treatment that is proven to prevent dementia. CONCLUSION: The invitro & animal studies shown that anaesthesia & surgery can increase production of Aβ & tau proteins & cause alzheimer disease. It was suggested that anaesthesia & surgery may increase risk of dementia but it is not clear that anaesthesia & surgery can cause cognitive impairment such as dementia & alzheimer disease. Further studies are required to confirm the relationship between anaesthesia, surgery & neuro degenerative complications.

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A REVIEW ON FLOUROQUINOLONES INDUCED TORSADES DE POINTES [QT INTERVAL ELONGATION]

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ABSTRACT:

Fluoroquinolones (FQs) are very potent bactericidal antibiotics that can produce adverse cardiac events such as QT interval elongation, which can lead to the dangerous arrhythmia disease known as TORSADES DE POINTES.

Torsades de pointes is a life-threatening variant of polymorphic ventricular tachycardia.It can be diagnosed by a twisting pattern on an ECG and an irregular cardiac rhythm.It might be acquired [via drug usage] or congenital.

The QT interval is the time it takes for the ventricles to depolarise and repolarise a heartbeat.It is the interval between the start of the QRS complex [ventricular depolarization] and the end of the t-wave. These flouroquinolone medications may interact with cardiac ion channels, causing QT elongation by inhibiting HERG potassium channels, resulting in delayed cardiac repolarization. These pharmaceuticals may also interact with other medications, causing QT elongation.

Women are more susceptible to this condition than males. Moxifloxacin and levofloxacin may have a greater risk of torsades de pointes than other fluoroquinolones. Some of the risk factors include advanced age, female gender, pre-existing cardiac conditions, electrolyte imbalances, concomitant use of other QT-prolonging medications, and genetic predispositions. In a study reveals that FQ administration in critically ill patients resulted in a high rate of QTc prolongation (119/139, 85.6%).

KEY WORDS : Flouroquinolones, Torsades de pointes, polymorphic ventricular tachycardia, HERG Potassium channels, Venticular depolarisation

INTRODUCTION:

Fluoroquinolones, a class of antibiotics known for their broad-spectrum antimicrobial activity and high oral bioavailability, have been linked to serious cardiovascular adverse effects, particularly QT interval prolongation.[1][2]. Health authorities like the FDA and MHRA recommend restricting fluoroquinolone use for uncomplicated infections, emphasizing the importance of weighing benefits against risks.[2]. Understanding and managing the risks associated with fluoroquinolones causing QT prolongation is crucial.[3].

This article explores the link between fluoroquinolones and QT prolongation, focusing on safer therapeutic alternatives. It discusses QT prolongation mechanisms, comparative risks, high-risk population identification strategies, and recent research's impact on clinical guidelines for safer fluoroquinolone use.

TORSADES DE POINTES:

Torsades de pointes (TdP) is a life-threatening polymorphic ventricular tachycardia requiring immediate intervention due to an acquired or congenitally prolonged QT interval, often caused by drugs causing prolonged ventricular repolarization.[22]

The QT interval on ECG is the time taken by ventricles to repolarize after depolarization. Predisposing factors for prolonging the QT interval include old age, females, cardiac diseases, electrolyte imbalances,

diabetes, and drug elimination abnormalities. Drug-induced QT prolongation often results from blockage of the Ikr, a rapid component of delayed rectifier current, which brings action potential to resting membrane potential. Drugs that block Ikr include thioridazine, cisapride, terfenadine, astemizole, and sertindole. The alpha sub unit of the IKr is encoded by the human ether-a-go-go related-gene (hERG), and alteration in hERG channel trafficking can also cause QT prolongation.[22]

Sodium channel blockers, such as quinidine, procainamide, and other class1A antiarrhythmic drugs, can increase the width of the QRS complex and cause QT prolongation. Some Na+ channel blockers also interfere with Ikr currents, causing wide QRS complex and QT prolongation. Cocaine, for example, blocks both Na+ and K+ channels, making abusers more prone to QT prolongation and TdP.Inhalational anesthetic drugs like halothane, isoflurane, enflurane, and sevoflurane can prolong QT interval by blocking IKs, while 16 β2 adrenoceptor agonistis like epinephrine, salbutamol, terbutaline, and salmeterol can also prolong QT interval.[22].

THE ROLE OF FLOUROQUINOLONES

Fluoroquinolones are highly effective antibacterial agents, known for their broad-spectrum properties and their significant role in treating various infections due to their mechanism of action and pharmacokinetics.

Mechanism of Action:Fluoroquinolones are antibacterial agents that inhibit type II DNA topoisomerases, specifically DNA gyrase and topoisomerase IV, which are essential for bacterial DNA replication and transcription, thereby preventing cell division and DNA replication leading to bactericidal activity [4][5].

Spectrum of Activity: This medication is effective against various aerobic gram-positive and gram-negative organisms, including Staphylococci, Streptococcus pneumoniae, Enterococcus faecalis, Neisseria, Haemophilus, Enterobacteriaceae, Pseudomonas, and Vibrio. [4] They also exhibits activity against notable pathogens such as Haemophilus influenzae, Moraxella catarrhalis, Mycoplasma species, Chlamydia species, Legionella species, and Mycobacterium tuberculosis, among others [5]. Delafloxacin, a fluoroquinolone, is a broad-spectrum antibiotic effective against gram-negative and gram-positive bacteria, MRSA, atypical respiratory tract pathogens, and anaerobes.[5].

PHARMACOKINETICS:

Fluoroquinolones are well-absorbed orally, with most being metabolized in the liver and excreted in urine. Moxifloxacin is primarily eliminated in bile [5] . They are
distributed extensively, reaching most extracellular and intracellular fluids, with prostate, lung, and bile concentrations[5]. However, oral absorption can be reduced by coadministration of polyvalent cations like aluminum, magnesium, calcium, zinc, and iron, impacting their effectivenes[5].Fluoroquinolones, despite their potency and broad antibacterial activity, have led to an increase in antimicrobial resistance. They also carry risks of serious side effects and drug-drug interactions, necessitating careful prescription [2].

Treatment with fluoroquinolones is associated with increased risks of sudden deaths, ventricular arrhythmias, and cardiovascular deaths per million treatment courses.[6].

Understanding QT Elongation :

Understanding QT Elongation involves the exploration of its causes, manifestations, and potential risks.

This section delves into the intricacies of QT interval prolongation (QTIP) and its implications, particularly in the context of fluoroquinolone use.

Causes and Mechanisms:

QT elongation may be classified into two types: congenital, which is commonly caused by genetic abnormalities affecting ion channels (potassium, calcium, or sodium), with over 15 known mutations, and acquired, which can occur from electrolyte imbalances or pharmacologi lated with the lowest risk of QT prolongation and TdP rate. [1].

Diagnosis:

The QT interval is measured on an electrocardiogram (ECG), including U waves if large and prominent. Recent advancements suggest that automated QT algorithms could enhance the detection of subtle T-wave changes, potentially replacing manual measurements [11].

Risk Factors:

High-risk indicators include a corrected QT interval (QTC) of >500ms or an increase in QTC of >60ms. Factors elevating the risk of medication-induced QT prolongation encompass a family history of TdP, gender, age, certain medications, and conditions causing electrolyte imbalances [10] QT elongation can escalate the risk of abnormal heart rhythms, notably torsades de pointes (TdP), which may lead to sudden cardiac death [9]

LINK BETWEEN FLUOROQUINOLONES AND QT ELONGATION

Variability in QT Prolongation Risk Among Fluoroquinolones:

Moxifloxacin is a significant risk factor for Torsades de Pointes (TdP) in cardiac patients due to its higher potential for QT interval prolongation [12].. Levofloxacin, Ofloxacin, and Ciprofloxacin have a lower risk of causing QT interval prolongation, thereby reducing the risk of TdP. [12].Gemifloxacin, like moxifloxacin, is prescribed cautiously to cardiac patients due to its potential for QT prolongation [8]

Mechanism of Action on Cardiac Ion Channels:

Fluoroquinolones prolong the QT interval by inhibiting the delayed rectifier potassium current (IKr), mediated by hERG [1]. Moxifloxacin has a more potent effect on QTcF prolongation and affects the J-Tpeakc, affecting cardiac repolarization [14]. Levofloxacin's effect on J-Tpeakc is minimal, suggesting a difference in QT prolongation mechanism compared to moxifloxacin. Moxifloxacin inhibits both IKs and IKr potassium channels, while levofloxacin primarily affects IKr channels [14].Fluoroquinolone use can lead to QT elongation, a condition where the heart's electrical activity is prolonged. High-risk populations include those over 60 years old and females,[17][13]those with low left ventricular ejection fraction, left ventricular hypertrophy, and ischemia [15]. Genetic factors, such as silent gene mutations or congenital Long QT Syndrome, can also increase the risk of QT prolongation [15]. Additionally, concurrent drug use, such as antiarrhythmics, antipsychotics, antibiotics, or any combination of drugs known to prolong the QTc interval, can amplify the risk [15] [13]. Dose adjustments are crucial for patients with renal impairment to avoid exacerbating QT prolongation risks [5].

Healthcare practitioners, including cardiologists, internists, family practitioners, psychiatrists, nurses, physician assistants, and clinical pharmacists, play a pivotal role in identifying high-risk populations and ensuring proper QT interval measurement and monitoring [15]. This multi-disciplinary approach is crucial for minimizing the risks of QT elongation and the subsequent development of life-threatening arrhythmias in patients requiring fluoroquinolone therapy.

IMPACT ON PATIENT HEALTH :

The impact of fluoroquinolones on patient health extends beyond their antibacterial efficacy, encompassing a range of adverse effects that can significantly affect quality of life. These effects are broadly categorized into physical and mental health impacts, as well as specific conditions associated with fluoroquinolone use:

Musculoskeletal Effects:

Tendinitis and tendon rupture, with the FDA placing its strongest warning on drug packaging due to the higher chance of these conditions [16].Muscular pain, joint pain, and swelling, which may lead to reduced mobility and quality of life [16].

Cardiovascular Effects:

Increased risk of sudden cardiac death among patients receiving hemodialysis when treated with respiratory fluoroquinolones compared to amoxicillin-based antibiotics [20].A higher incidence of ruptures or tears in the aorta, posing a significant risk to cardiovascular health [16].

Neurological and Sensory Effects:

Numbness or tingling in arms and legs, muscle weakness, which can impair daily functioning [16].Vision problems and ringing or buzzing in ears, affecting sensory perception and quality of life [16].

Gastrointestinal and Skin Reactions:

Common adverse effects like nausea, diarrhea, and headache [16].Serious anaphylactic and skin reactions, ranging from minor rash to Stevens-Johnson syndrome or toxic epidermal necrolysis [7].

GUIDELINES FOR SAFE USE

Recommendations for Prescribing Fluoroquinolones:

Fluoroquinolones are not recommended for uncomplicated infections like acute rhinosinusitis, uncomplicated cystitis, and acute bronchitis due to potential risks.For severe infections, a thorough assessment is necessary. [2] Avoid prescribing fluoroquinolones for non-severe or self-limiting infections or non-bacterial conditions.Ciprofloxacin or levofloxacin should not be used for uncomplicated cystitis unless other antibiotics are available [18].

Special Considerations:

In children, fluoroquinolones should only be used for treating infections caused by multidrug-resistant organisms where no safe and effective alternatives exist [21].The coadministration of corticosteroids with fluoroquinolones is advised against due to increased risks of tendinitis and tendon rupture [18] [19].

Healthcare professionals should discontinue treatment at the first signs of a serious adverse reaction and inform patients about potential side effects [18].

Precautions When Prescribing Fluoroquinolones:

Patient Screening: Before prescribing fluoroquinolones, a thorough patient history should be conducted to identify any past adverse reactions or predispositions to conditions that may be exacerbated by these medications [17].

Informed Consent: Patients should be informed about fluoroquinolones' potential side effects, long-term health effects, and signs/symptoms requiring immediate medical attention, ensuring they are fully aware of potential health risks [17].

Monitoring: Patients should be closely monitored for adverse effects during treatment, including regular follow-ups and potentially more frequent testing for pre-existing conditions that may be negatively affected by fluoroquinolones. [17].

Alternatives to Fluoroquinolones:

When possible, alternative antibiotics with a lower risk profile should be considered, especially for conditions where fluoroquinolones are not the only effective treatment option. The choice of antibiotic should be guided by the infection type, patient health status, and local antibiotic resistance patterns [17].

For UTIs: Consider trimethoprim/sulfamethoxazole, nitrofurantoin, or fosfomycin as first-line treatments in regions where resistance patterns support their use [17].

- For Respiratory Infections: Macrolides or doxycycline can be effective alternatives, depending on the specific pathogen and resistance patterns [17].
- For Skin Infections: Clindamycin, doxycycline, or TMP/SMX may be suitable alternatives, particularly in cases of MRSA, where fluoroquinolones would not be the first choice anyway [17].

CONCLUSION;

This article looks at how fluoroquinolones are used to treat bacterial infections and the possible cardiovascular hazards they provide. It describes the mechanics of QT prolongation, underlines the hazards associated with various fluoroquinolones, and emphasises the need of identifying high-risk groups in order to implement safer therapy options. The report also emphasises the significance of using fluoroquinolones wisely and keeping healthcare practitioners informed in order to successfully limit hazards. The article's ramifications go beyond individual patient treatment, impacting future research and policy decisions to improve the safety and efficacy of antibacterial medications. It advocates for educated decision-making and the exploration of safer options to protect patient health while preserving the treatment arsenal against recalcitrant bacterial infections. The essay encourages healthcare practitioners and researchers to contribute to a future in which antibiotic therapy is both effective and safe.

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TRUQAP (CAPIVASERTIB)- A NEWLY APPROVED DRUG FOR THE TREATMENT OF BREAST CANCER

SWATHI M, KABEER AHAMED Z,
Pharm D IVth year

BRAND NAME: - Truqap
GENERIC NAME: - Capivasertib
MOLECULAR FORMULA: - C21 H25ClN602
DRUG CLASS: - AKT inhibitor
MANUFACTURER COMPANY:
Astra Zeneca Pharma India Limited. And Aptus therapeutics
DATE OF APPROVAL: - 16/11/2023
DOSAGE FORM AND STRENGTH: Tablets 160mg and 200mg
ROUTE OF ADMINISTRATION: Oral (swallow tablets whole, do not chew)

INDICATION:

TRUQAP, in combination with fulvestrant, is indicated for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with one or more PIK3CA/AKT1/PTEN-alteration as detected by an FDA-approved test following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.

MECHANISM OF ACTION:

Mechanism of Action: Capivasertib is an inhibitor of all 3 isoforms of serine/threonine kinase AKT (AKT1, AKT2, and AKT3) and inhibits phosphorylation of downstream AKT substrates. AKT activation in tumors is a result of activation of upstream signaling pathways, mutations in AKT1, loss of phosphatase and tensin homolog (PTEN) function, and mutations in the catalytic subunit alpha of phosphatidylinositol 3-kinase (PIK3CA)

PHARMACOKINETICS:

- Absorption Tmax: 1 to 2 hours
- Bioavailability: 29%
- Effects of food: Not clinically meaningful Distribution of Protein binding, plasma proteins: 22% Vd, oral: 1847 L
- Metabolism: capivasertib is primarily metabolized by CYP3A4 and UGT2B7
- Excretion Renal clearance: 21% of total clearance Renal excretion, oral: 45% Fecal excretion, oral: 50% Total body clearance, oral: 50 L/hr.
- Half-life: The half-life of capivasertib is 8.3 hours.

ADVERSE DRUG REACTION:

- Nausea
- Vomiting
- Hyperglycemia
- Fatigue
- Decrease appetite
- Erythema multiforme
- Rash
- Stomatitis
- Diarrhea

Contra indications:

TRUQAP is contraindicated in patients with severe hypersensitivity.

DRUG INTERACTIONS:

Concurrent use of CAPIVASERTIB and STRONG CYP3A4 INDUCERS may result in reduced capivasertib exposure and reduced efficacy of capivasertib. o Fetal risk may occur when used during pregnancy.

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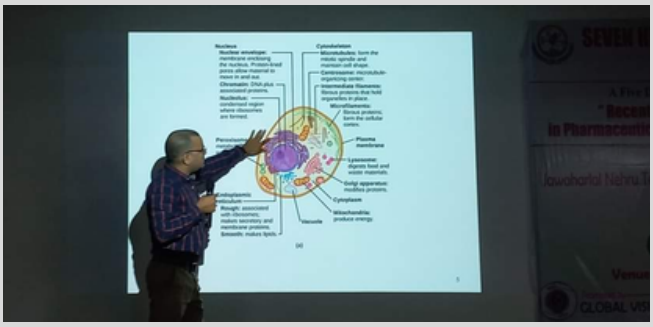
Departmental Activities in November - 2023

PERFECT CLICK

“Phytopharmaceuticals in Drug Discovery: Advances & opportunities”

“Cancer Physiology and Molecular Pharmacology of Cancer & its drugs”.



"Current Scenario of Diabetes Care" on the ocassion of World Diabetes day.

National Pharmacy Week Celebrations 2023, the Department of Pharmacology & NSS unit had organized "Blood Donation Camp"