SPECIAL TOPIC:

RHEUMATOID ARTHRITIS

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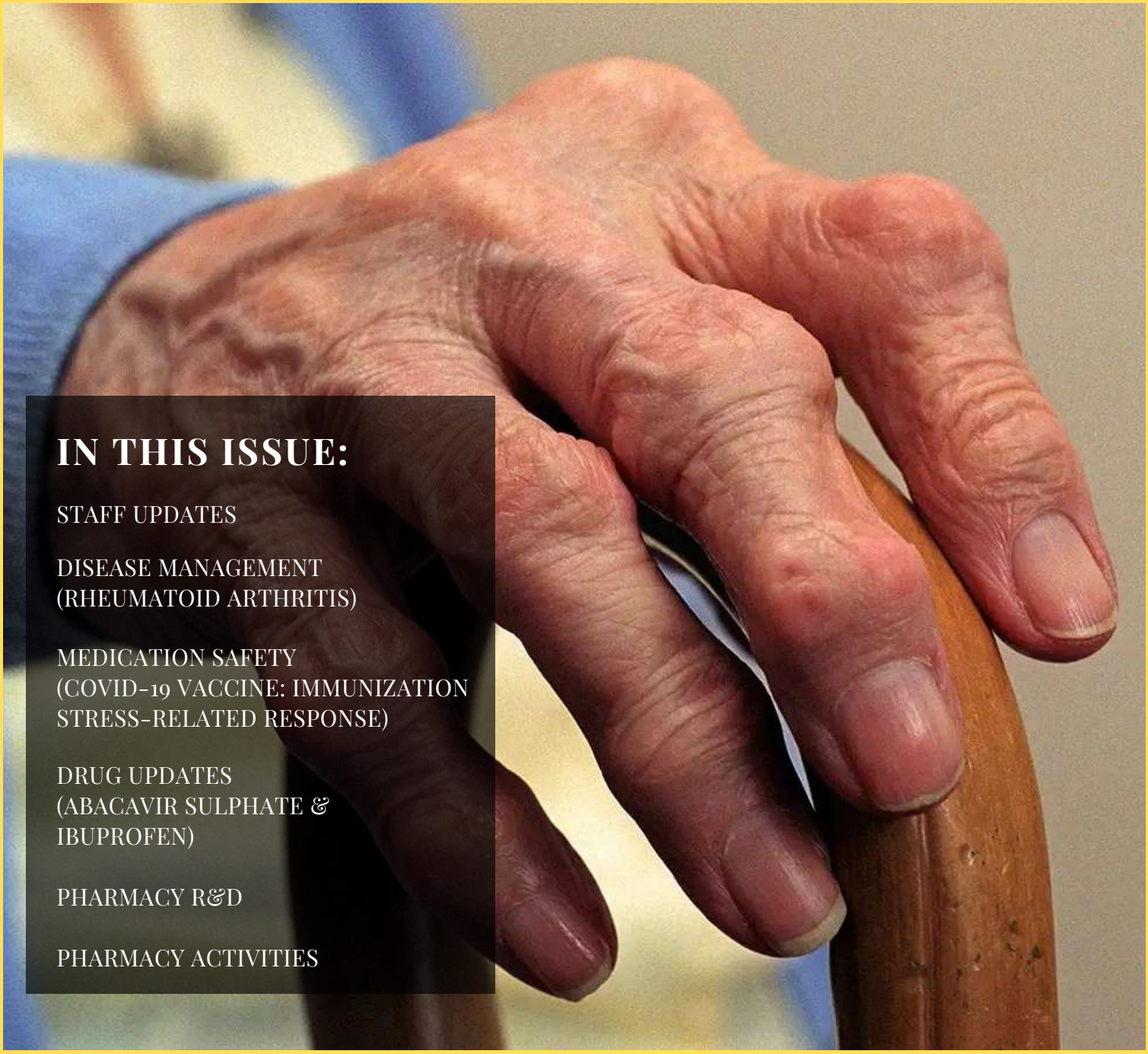

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RHEUMATOID ARTHRITIS

By Noor Shuhaidah binti Shukhaimy & Nurlisya Rafiha binti Anuar

BACKGROUND [6]

Rheumatoid arthritis (RA) is a chronic and progressive autoimmune disease which primarily affects the joints. When a person has an autoimmune disease, such as RA, the immune system misidentifies the body's cells as foreign invaders and releases inflammatory chemicals to fight them. RA is characterized by dysregulated inflammatory processes in the synovium of the joint that eventually leads to the destruction of both cartilaginous and bony elements of the joint, which results in pain and disability. Systemic inflammation of RA is associated with a variety of extra-articular comorbidities including cardiovascular disease, resulting in increased mortality in patients with RA.

RA affects 1-3% of the population worldwide with a peak prevalence between the age of 30-50 years old. For unknown reason, it is more common in women than men. Having a family member with RA increases the odds of developing RA.

AETIOLOGY [7]

RA is theorized to develop when a genetically susceptible individual experiences an external trigger (eg, cigarette smoking, infection, or trauma) that triggers an autoimmune reaction. Socioeconomic, psychological, and lifestyle factors may influence disease development and outcome.

PATHOGENESIS [4,5]

CD4 T-cells, mononuclear phagocytes, fibroblasts, osteoclasts, and neutrophils play major cellular roles in the pathophysiology of RA. B cells produce autoantibodies. Abnormal production of numerous cytokines, chemokines, and other inflammatory mediators has been demonstrated in patients with RA, including the following:

Cytokines	Pathogenic role
TNF-α	• Activates leukocytes, synovial fibroblasts, endothelial cells and osteoclasts • Induces production of inflammatory cytokines • Enhances metalloproteinase expression • Suppresses Treg cells
IFN-γ	• Increases antigen presentation • Activates macrophages • Increases chemokine secretion
IL-1	• Activates leukocytes, synovial fibroblasts, endothelial cells and osteoclasts • Induces production of matrix proteinases
IL-6	• Activates leukocytes and osteoclasts • Stimulates antibody production
IL-17	• Induces production of inflammatory cytokines • Activates innate immune cells • Increases osteoclastogenesis • Stimulates neutrophil recruitment
IL-21	• Activates Th17 and B cells

Intracellular signalling pathways are also involved in the pathogenesis of RA. Examples of intracellular signalling pathways include the the Janus kinases (JAK) pathway, the signal transducers and activators of transcription (STAT) pathway, and the nuclear factor κ-light-chain enhancer of activated B cells (NF-κB) pathway. Intracellular signalling pathways are essential for a normal immune response, and aberrations in these pathways may contribute to autoimmune disease.

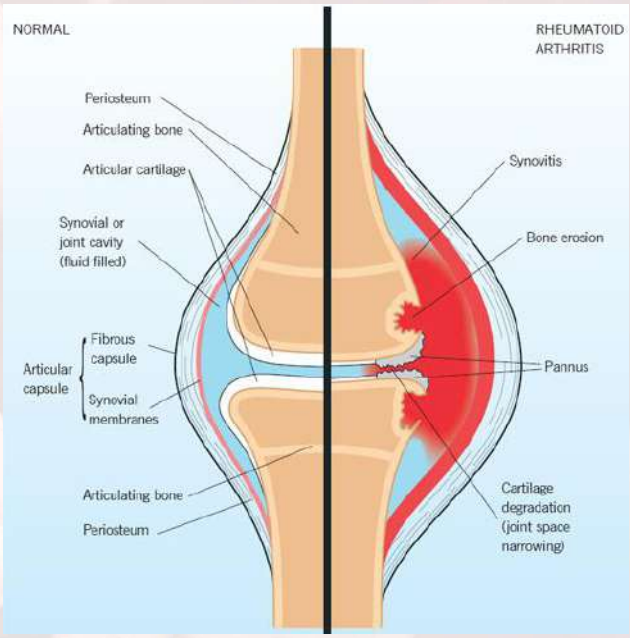

Figure 1: A healthy joint (Figure 1A, left side) is composed of two adjacent bony ends covered with a layer of cartilage. The space between ends is called articular cavity, which is bounded by the synovial membrane on both sides and contains synovial fluid. This autoimmune reaction exacerbates in the synovium, where leukocytes infiltrate and cause synovial membrane inflammation (rheumatoid synovitis).

SYMPTOMS [2]

- Joint pain, tenderness, swelling or stiffness that lasts for six weeks or longer.
- Morning stiffness that lasts for 30 minutes or longer.
- Myalgia, fatigue, weight loss, low-grade fever, depression
- More than one joint is affected.
- Small joints (wrists, certain joints in the hands and feet) are typically affected first.

MANAGEMENT AND TREATMENT [1]

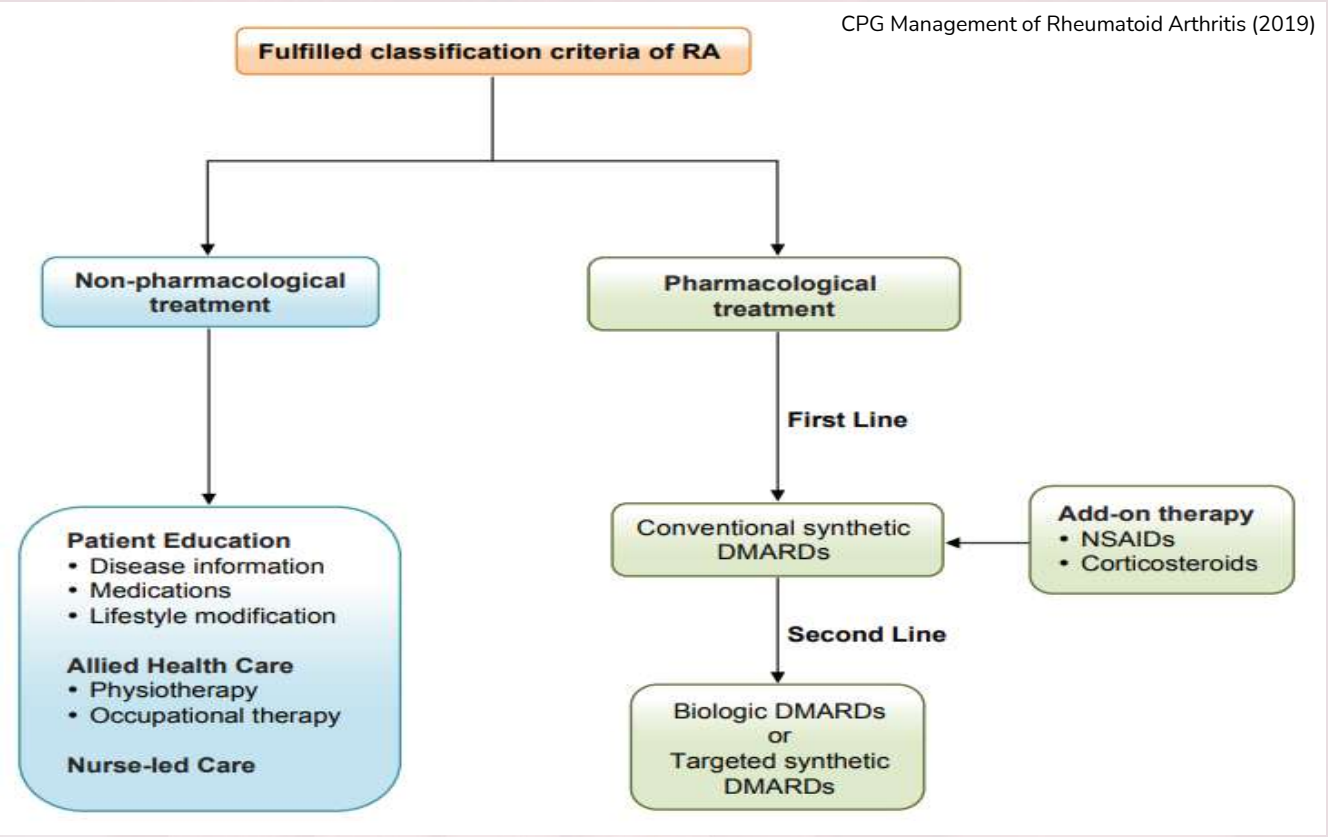

Figure 2: Optimal care of patients with RA consists of an integrated approach that includes both non-pharmacological and pharmacological treatments.

PHARMACOLOGICAL TREATMENT : DMARDS IN RHEUMATOID ARTHRITIS [1,2,3]

a) Conventional Synthetic DMARDS

Drug	Mechanism of Action	Dose	Possible Side Effects
Methotrexate	Inhibits dihydrofolate reductase and prevents formation of tetrahydrofolate, which is involved in thymidylate and purine formation, thus preventing DNA synthesis, repair and cellular replication.	Initial dose: 7.5-15 mg once weekly. Increase dose by 2.5 to 5 mg/week every 4 to 12 weeks if needed based on response. Max dose: 25 mg/week.	Bone marrow suppression, loss of appetite, headache, oliguria, alopecia, acne, gynaecomastia.
Leflunomide	Inhibits pyrimidine synthesis by inhibiting dihydroorotate dehydrogenase enzyme activity resulting in antiproliferative and anti-inflammatory effects.	LD: 100 mg once daily for 3 days; MD: 20 mg once daily, may reduce dose to 10 mg once daily if higher dose is not tolerated. Max dose: 20 mg once daily.	Diarrhoea, headache, alopecia, dry skin, weight loss, peripheral neuropathy.
Sulfasalazine	Forms into active 5-aminosalicylic acid (mesalazine) and sulphapyridine. Involved in modulation of chemical mediators in the inflammatory response and inhibit the tumour necrosis factor.	Initial dose: 500 mg once daily or 1 g/day in 2 divided doses, increase weekly. MD: 2 g/day in 2 divided doses. Max dose: 3 g/day.	Abdominal pain, diarrhoea, dyspepsia, fever, anorexia, dizziness, headache, insomnia.
Hydroxychloroquine	The mechanism of action in the treatment of RA has not been fully elucidated.	200 to 400 mg daily as a single daily dose or in 2 divided doses.	Retinopathy, bronchospasm, alopecia, hypersensitivity reactions.

PHARMACOLOGICAL TREATMENT : DMARDS IN RHEUMATOID ARTHRITIS [1,2,3]

b) Targeted Synthetic DMARDs (tsDMARDs)

Drug	Mechanism of Action	Dose	Possible Side Effects
Baricitinib	Inhibits JAK1 and JAK2, which leads to reduced phosphorylation and activation of STATs and decreased in serum IgG, IgM, IgA, and CRP.	2 mg once daily	Neutropenia, lymphopenia, anaemia, nausea, URTI.
Tofacitinib	Inhibitor of Janus kinase (JAK) enzymes (JAK1, JAK2, JAK3) that results in suppression of immune response, reduced activation of T lymphocytes and release of a range of pro-inflammatory cytokines.	IR tablet: 5 mg twice daily ER tablet: 11 mg once daily	Fatigue, joint swelling, headache, insomnia, dyspnoea, cough, rash, erythema.

c) Biological DMARDs (bDMARDs)

Drug	Mechanism of Action	Dose & Regimen	Possible Side Effects
Infliximab	Binds with high affinity to the TNF-α thereby inhibiting binding of TNF-α to its receptors.	3 mg/kg at 0, 2, and 6 weeks, followed by MD of 3 mg/kg every 8 weeks.	Chills, fever, dyspnoea, chest pain, urticaria, pruritus, hypersensitivity.
Etanercept	Binds to TNF and blocks its interaction with cell surface TNF receptors, thus preventing cellular responses by rendering TNF inactive.	Once-weekly dosing: 50 mg once weekly. Max dose: 50 mg/week. Twice-weekly dosing: 25 mg twice weekly	Nausea, vomiting, dyspepsia, headache, dizziness, asthenia, allergic reactions, fever.
Adalimumab	Binds to human TNF-α, thus interfering with cytokine-driven inflammatory processes.	Initial: 40 mg every other week Selective patients with an inadequate response: may up to 40 mg every week or 80 mg every other week.	Sinusitis, headache, alopecia, liver failure, pancytopenia, aplastic anaemia.
Golimumab	Binds to TNF-α and inhibits the induction of IL-6 and IL-8, granulocyte-colony stimulating factor, and granulocyte-macrophage colony stimulating factor, which are proinflammatory cytokines responsible for several chronic inflammatory diseases.	IV: 2 mg/kg at weeks 0, 4, and then every 8 weeks thereafter . SC: 50 mg once a month.	Pancytopenia, leukopenia, thrombocytopenia, dizziness, weakness.
Tocilizumab	It is an antagonist of the IL-6 receptor and inhibits IL-6-mediated signalling, resulting in a reduction in inflammatory mediator production.	IV: Initial dose 4 mg/kg once every 4 weeks; may be increased to 8 mg/kg once every 4 weeks based on clinical response. Max dose: 800 mg. SC:<100 kg: 162 mg once every other week; increase to 162 mg once every week based on clinical response. ≥100 kg: 162 mg once every week.	Neutropenia, thrombocytopenia, diarrhoea, nausea, abdominal pain, mouth ulceration, gastritis.
Rituximab	Binds to the CD20 antigen, thereby activating complement-dependent B-cell cytotoxicity, which recruits immune effector functions to mediate B-cell lysis.	Initial: 1 g once every 2 weeks for 2 doses.	Dysphagia, stomatitis, constipation, dyspepsia, throat irritation, rash, pruritus, alopecia.

PHARMACOLOGICAL TREATMENT : OTHERS [1,2,3]

Corticosteroids

Drug	Mechanism of Action	Dose	Possible Side Effects
Prednisolone	Reduces inflammation by suppressing the migration of polymorphonuclear leukocytes and reversing the increased capillary permeability.	Initially 10-15 mg daily.	Osteoporosis, Weight gain, Hypersensitivity, Abdominal pain, peptic ulceration.
Hydrocortisone		IM/IV: Initial: 100 to 500 mg/dose at intervals of 2, 4, or 6 hours. Oral: Initial 20-240 mg/day.	Visual disturbances, blurred vision, insomnia, anaphylactoid reactions, Cushing syndrome.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Drug	Mechanism of Action	Dose	Possible Side Effects
•Ibuprofen •Diclofenac •Naproxen	Reversibly inhibits COX-1 and COX-2 enzymes, thus resulting in decreased formation of prostaglandin precursors.	Ibuprofen: 200 to 400 mg every 4 to 6 hours as needed. Max dose: 3.2 g/day Diclofenac: 50 mg tds Naproxen: 550-1100 mg in 2 divided doses	Headache, Drowsiness, dizziness, allergic reaction, stomach ulcer, diarrhoea.
•Meloxicam •Etoricoxib •Celecoxib	Selectively inhibit COX-2 enzymes primarily responsible for inhibition of prostaglandin synthesis.	Celecoxib: 100 or 200 mg bid. Max: 400 mg daily. Etoricoxib: 60 mg once daily, may increase to 90 mg once daily as necessary. Meloxicam: 15 mg daily. May be reduced to 7.5 mg daily.	Insomnia, abdominal pain. flatulence, headache, nausea, diarrhoea, rhinitis.

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COVID-19 Vaccine: Immunization Stress-Related Response (ISRR)

by: Farid Mohd Jamil

Introduction

Since the introduction of the National COVID-19 Vaccination Programme up to 31st December 2021, 24,042 Adverse Event Following Immunization (AEFI) reports have been received by National Pharmaceutical Regulatory Agency (NPRA). This is equivalent to 0.42 reports per 1,000 doses administered. 93.1% of the report s received were not serious, short-term, and did not pose any potential risk to the health of the vaccine recipients [1]

An AEFI is defined as any untoward medical occurrence that follows the administration of a vaccine and may not necessarily be causally related to the vaccine itself.[2] Hence, it is inaccurate to assume that all AEFIs reported in this summary report are directly caused by the vaccine.

Apart from vaccines, the reported adverse events can also be caused by **fear of injections, or the immunization process**, previously undiagnosed illness, underlying diseases, or medications being taken concurrently by the vaccine recipients. These events may also be coincidental, happen to occur shortly after a vaccine was administered. [1]

Immunization Stress-Related Response (ISRR)

According to World Health Organization (WHO) in 2019, immunization stress-related response (ISRR) is defined as "a response to the stress that some people may experience upon receiving an injection, and it encompasses a wide range of symptoms". ISRR is manifested with signs and symptoms of vasovagal-mediated, hyperventilation-mediated, or stress-related neurological and psychiatric reactions.[3] There are various aspects of the immunization procedure that can cause people to feel stress about vaccination such as injection pain, dread of seeing a needle and blood, previous traumatic needle experiences, and negative information regarding immunization in the media.

While other AEFIs occur only after immunization, an ISRR can occur immediately before, during or after immunization

It is inaccurate to assume ISRR as a vaccine-related AEFI.

Table 1: Classification of stress responses and reactions[3]

Immunization stress-related response
Acute stress response (fight or flight response) • Occur before, during or immediately after vaccination (usually within 5 mins) • Transient and resolves spontaneously • Sign & Symptoms include mild worry “butterflies in the stomach” to moderate level of worry , headache/dizziness, nausea, severe responses include difficulty in breathing or hyperventilation, tingling in the fingers and toes, increased heart rate, palpitations
Vasovagal reaction • Manifested as symptoms mild dizziness or a brief loss of consciousness (due to insufficient blood flow to the brain) • An acute stress response may lead to physiological overcompensation & a vasovagal reaction • Sign & Symptoms include nausea, sweating or pallor, dizziness, blurred vision and syncope (loss of consciousness usually last less than 20 seconds)
Dissociative neurological symptom reaction (with or without non-epileptic seizures) • Occurs after vaccination • Characterized by neurological symptoms with no physical finding • The current evidence suggests that DNSRs result from complex multifactorial etiologies. • These reactions occur most commonly in stress events other than vaccination • Sign & symptoms include non-epileptic seizure, difficulty walking or moving limb, weakness, tingling sensations in the muscles

Managing ISRR

The role of a vaccinator is very important in managing ISRR. Vaccinators should clearly explain that the reaction was not related to the vaccine, program or procedure error. Symptoms of ISRR are not harmful and will resolve spontaneously. Vaccinations are advised to be held in a calm, private, planned ambient environment, even during administration to a large group, such as in a school. Syncope can be avoided by measures such as vaccinating the individual while he or she is seated or in the supine position and encouraging muscle tension.[4]

Differentiating of Anaphylaxis and Acute Stress Response

It is very important to be able to differentiate between anaphylaxis and acute stress response. While acute stress response may resolve spontaneously, anaphylaxis reaction is a life threating event if left untreated. Anaphylaxis is a serious systemic hypersensitivity reaction which may compromise in airway, breathing and/or circulation and may present without the classical skin features or circulatory shock. It is usually acute in onset and may result in death.[5] However, the incidence of anaphylaxis following COVID-19 vaccination is generally rare. NPRA had received a total of 100 AEFI reports for anaphylaxis with Covid-19 vaccines equivalent to 1.8 reports per million doses administered.[1]

Table 2: Differences between Anaphylaxis & Acute Response Rate

	Anaphylaxis	Acute Response Rate	
		General Vasovagal reaction with syncope	General Vasovagal reaction with syncope
Onset	Usually, 5 minutes after immunization but may be delayed up to 60 min	Sudden, occurs before, during or shortly after (<5min) immunization	Sudden, occurs before, during or shortly after (<5min) immunization. May present after 5 min if the individual stands suddenly
Symptoms			
Skin	Urticaria, general erythema, angioedema, general pruritus with or without skin rash	Pale, sweat, cold & Clammy	Pale, sweat, cold & Clammy
Respiratory	Persistent cough, noisy breathing and airway constriction : wheeze, stridor. If very severe, respiratory arrest.	Hyperventilation (rapid, deep breathing)	Normal to deep breath
Cardiovascular	Increase heart rate, reduce blood pressure, circulatory arrest	Increase heart rate, normal or systolic blood pressure	Increase heart rate with or without transient reduce in blood pressure
Gastrointestinal	Nausea, vomiting, abdominal cramps	Nausea	Nausea, Vomiting
Neurological	Uneasiness, restlessness, agitation, loss of consciousness, little response when supine or lying flat	Fearfulness, light-headedness, dizziness, numbness, weakness, tingling around the lips, spasms in hands, feet	Transient loss of consciousness, good response once supine or lying flat, with or without tonic-clonic seizure

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3. World Health Organization. https://vaccine-safety-training.org/immunization-anxiety-related-reactions.html
4. World Health Organization. Immunization Stress-related Responses; A Synopsis. A synopsis of the manual for program managers and health professionals to prevent, identify and respond to stress-related responses following immunization, 2019
5. CLINICAL GUIDELINES ON COVID-19 VACCINATION IN MALAYSIA 4 th Edition,2021

DRUG UPDATES

Tablet Abacavir Sulphate 300mg

A. DESCRIPTION

Abacavir is an antiviral nucleoside reverse transcriptase inhibitor used in combination with other antiretrovirals for the treatment of Human Immunodeficiency Virus (HIV).

B. REGISTRATION NUMBER

MAL20001015ARZ

C. PRICE

RM 131.25/pack of 60's

D. DEPARTMENT

Medical (Infectious Disease)

E. PRESCRIBER CATEGORY

A* - (Consultant/ Specialist for specific indications only)

F. PREGNANCY CATEGORY

Category C (MIMS)

G. MECHANISM OF ACTION

Abacavir sulphate, a synthetic carbocyclic nucleoside analogue, is converted to the active metabolite carbovir triphosphate by cellular enzymes.

This metabolite which is an analogue of deoxyguanosine 5' triphosphate (dGTP) competes with natural substrate dGTP and is incorporated into the viral DNA, thereby inhibiting the activity of HIV-1 reverse transcriptase (RT).

The incorporated nucleoside that lacks the 3'-OH group terminates viral DNA growth by preventing the formation of the 5' to 3' phosphodiester linkage needed for elongation of DNA chain.

H. INDICATION IN FUKKM

Antiretroviral combination therapy of HIV infection in adults and adolescents from 12 years of age.

I. DOSE AND ADMINISTRATION

Adult

- 300mg twice daily or 600mg daily.

Children

i. (14-19kg): one-half of a scored abacavir tablet twice daily.
ii. (20-24kg): one-half of a scored abacavir tablet in the morning & one whole tablet in the evening.
iii. (≥25kg): according to adult dose.

J. ADVERSE REACTIONS

Common

- **Dermatologic**: Rash (7%).
- **Gastrointestinal:** Nausea (7% - 19%).
- **Neurologic:** Headache (7% - 13%), Sleep disorder (10%).

Serious

- **Cardiovascular:** Disorder for cardiovascular system, Myocardial Infarction.
- **Hepatic:** Hepatomegaly, Hepatotoxicity, Steatosis of liver.
- **Dermatologic:** Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis.
- **Immunologic:** Hypersensitivity reaction.

K. USE IN SPECIFIC POPULATION

- **Paediatric:**
  - Use in adolescent above 12 years old with dosage adjustment if weight less than 25kg.
  - Insufficient data for the safety in children below age of 12 years old.
- **Geriatric:**
  - The pharmacokinetics of abacavir have not been studied in patients over 65 years of age.
- **Patients with renal impairment:**
  - There is no dosage reduction required in patients with renal impairment.
- **Patients with hepatic impairment:**
  - Mild hepatic impairment: 200mg twice daily.
  - Moderate to severe impairment: not recommended in these patients.
- **Pregnancy:**
  - Pharmacokinetics of abacavir are not significantly changed by pregnancy and dose adjustments are not needed for patients who are pregnant.
- **Breastfeeding:**
  - Abacavir is present in breastmilk and was detected in serum of infant exposure to breastmilk.
  - HIV guidelines do not recommend breastfeeding for patients who are living with HIV.

L. PRECAUTIONS

- **Cardiovascular:** Myocardial infarction may occur. Consider underlying risk of coronary heart disease.
- **Endocrine & metabolic:** Lactic acidosis including fatalities has been reported with an increased risk in women and obesity, discontinue if suspected.
- **Hepatic:** Severe hepatomegaly with steatosis including fatalities has been reported with an increased risk in women and obesity, discontinue if suspected. For mild hepatic impairment, dosage adjustment necessary.
- **Immunologic:** Immune reconstitution has been reported. Further evaluation may be necessary. Autoimmune disorders have been reported in the setting of immune reconstitution syndrome.

M. CONTRAINDICATIONS

- HLA-B*5701 allele positive patient.
- Hypersensitivity to abacavir or any other component of the product.
- Moderate or severe hepatic impairment.

N. STORAGE

- Store in room temperature
- Do not store above 30°C

O. PHARMACIST ROLE

- Reinforce the importance of proper timing & implications of non-adherence including occurrence of drug resistance.
- Provide medication administration schedule & suggest adherence tools to increase adherence.
- Counsel patient/caregiver on hypersensitivity syndrome (usually occur in 1st 6 weeks of therapy) which can be characterised by fever, rash, progressive nausea, malaise, diarrhoea & respiratory symptoms such as sore throat, cough & shortness of breath.
- Monitor sign & symptoms of withdrawal in patient who are receiving concomitant methadone therapy since there are drug interaction.
- Educate on healthy lifestyle such as eat only fully cooked meat, vegetables and boiled water as bacteria may be present in half cooked meals.
- Counsel patient knowledge on HIV/AIDS, CD4, viral load & the association of CD4 & viral load to the disease.

P. REFERENCE

Product information leaflet, FUKKM, QUEST3+, MIMS, UpToDate, IBM Micromedex

By: Luqman Hakim Sofian Sauri

DRUG UPDATES

Ibuprofen 100mg/5ml Suspension

A. DESCRIPTION

Ibuprofen is a propionic acid derivative of non-steroidal anti-inflammatory drug (NSAIDS) that show anti-inflammatory, analgesic and antipyretic activity. This contributes to symptomatic relief of pain and inflammation.

B. REGISTRATION NUMBER

MAL08042445AZ

C. PRICE

RM 3.50/bottle of 60ml

D. DEPARTMENT

General Surgery

E. PRESCRIBER CATEGORY

B – Medical Officers

F. PREGNANCY CATEGORY

Category B, D in 3rd trimester or near delivery (MIMS MALAYSIA)

G. MECHANISM OF ACTION

Ibuprofen acts by inhibiting cyclooxygenase-1 and cyclooxygenase-2 isoenzymes which are responsible for converting arachidonic acid to the prostaglandin precursor. This will inhibit synthesis of prostaglandins in body tissues and reduce inflammation.

Other proposed mechanisms which lead to its anti-inflammatory effect include inhibition of chemotaxis, alteration of lymphocyte activity, reduction in pro-inflammatory cytokines and blockade of neutrophil aggregation. However, these mechanisms are not fully elucidated.

H. INDICATION IN FUKKM

a) Anti-inflammatory for rheumatic disease.
b) Analgesic for treatment of mild to moderate pain.

I. DOSE AND ADMINISTRATION

Children: 5 - 10 mg/kg/dose (max 2.4 gm/day) every 6 - 8 hourly. Not recommended for <7kg body weight.

Prescribing Restrictions: Not indicated in fever due to infection.

J. ADVERSE REACTIONS

Common:

- **Gastrointestinal:** Heartburn (3 – 9%), nausea (3 – 9%), vomiting (1 – 3%), constipation (1 – 3%).
- **Neurologic:** Dizziness (3 – 9%), headache (1 – 3%).
- **Dermatologic:** Skin rash (3 – 9%), pruritus (1 – 3%).

Serious:

- **Cardiovascular:** Congestive heart failure (<1%), Myocardial infarction (<1%), Hypertension (<1%).
- **Dermatology:** Steven-Johnson Syndrome (<1%).
- **Gastrointestinal:** Gastrointestinal hemorrhage (<1%), Gastrointestinal perforation (<1%), Pancreatitis (<1%).
- **Hematologic:** Agranulocytosis (<1%), Aplastic anemia (<1%).

DRUG UPDATES

K. CONTRAINDICATIONS

- Hypersensitivity (including asthma) to ibuprofen or other NSAIDs.
- History of gastrointestinal bleeding, perforation or ulceration related to NSAID therapy.
- Gastrointestinal ulceration, perforation or hemorrhage.
- Severe cardiac failure or patients undergoing coronary artery bypass graft surgery.
- Severe renal or hepatic impairment.
- Pregnancy (3rd trimester).

L. USE IN SPECIFIC POPULATIONS

- **Pediatric use:** Ibuprofen is not recommended for children weighing less than 7kg.
- **Geriatric use:** Patients ≥65 years old are at increased risk for serious GI events. Use with caution.
- **Pregnancy**: Fetal risk cannot be ruled out. Ibuprofen can be used during the first 2 trimesters of pregnancy. Use in the third trimester is not recommended. If necessary, use should be limited to lowest effective dose & shortest duration possible.
- **Breastfeeding:** Infant risk cannot be ruled out. Limited studies showed ibuprofen appears in very low concentration in the breast milk. Use is not recommended.
- **Patients with renal impairment:** Ibuprofen use in patients with advance kidney disease should be avoided unless the benefits outweigh the risks.
- **Patients with hepatic impairment:** Use with caution in patients with hepatic impairment.

M. PRECAUTIONS

- **Cardiovascular:** NSAIDs cause an increased risk of serious adverse thrombotic events such as, fatal MI and stroke. Risk may occur early during treatment and may increase with duration of use.
- **Gastrointestinal:** Patients with a history of peptic ulceration and other gastrointestinal disease should use ibuprofen in caution as their conditions may be exacerbated.
- **Respiratory:** Bronchospasm has been reported with use of NSAIDs in patients with bronchial asthma, thus caution is required in such patients.

N. STORAGE

Store below 30°C

O. PHARMACIST ROLE

- Counsel patient/caregiver on the proper way to administer, store and discard the medication.
- Monitor any incidence of side effects after starting the medication such as, heartburn, dizziness, rash or fluid retention.
- Advise patient to inform the doctor if planning to have children before taking the medication
- Advise patient/caregiver to avoid additional use of NSAIDs during ibuprofen therapy unless consulted with a doctor.
- Counsel patient/caregiver to take ibuprofen with food or milk to minimize gastrointestinal irritation.
- Remind patient to not smoke or drink alcohol while taking ibuprofen because it may increase risk of gastrointestinal bleeding.

P. REFERENCES

Product information leaflet, FUKKM, QUEST3+, MIMSGateway, Micromedex, Medscape, UpToDate

By: Muhammad Hazim bin Jamal

TOTAL DAILY INSULIN DOSE (TDID) REQUIREMENT AMONG UNCONTROLLED TYPE 2 DIABETIC PATIENTS IN MEDICATION THERAPY ADHERENCE CLINIC (MTAC) IN A PUBLIC HOSPITAL, MALAYSIA.

AUTHORS Zamani N, Kwan EW, Ng SY, Toh KY, Roslan NI, Ahmad Tamezi AM

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) has emerged as one of the main health problems in Malaysia. Insulin therapy was highly used for the treatment of T2DM in addition to oral agents. However, to determine the optimum dose of insulin is mostly a challenge as the insulin titration approach needs to be individualized. This is due to different demographic and clinical characteristics of each patient. In addition, there is limited studies done in Malaysia regarding the total dose of insulin required for individual patients.

OBJECTIVE

The objectives of this study were to investigate the TDID per body weight among uncontrolled T2DM patients and to determine the factors associated with the TDID.

METHODOLOGY

A retrospective, cross sectional and observational study was conducted among T2DM patients of Hospital Tengku Ampuan Afzan who were recruited under Diabetic Medication Therapy Adherence Clinic (DMTAC) service from January 2017 to December 2018. A total of 155 patients were included. Simple and multiple linear regressions were used to determine the factors associated with TDID.

RESULTS

The mean TDID was 57.9 ± 26.2u/day. The mean TDID per body weight was 0.79 ±0.33u/kg/day. There was no significant difference of TDID per body weight reported among patients who were prescribed with or without metformin (p=0.818) . Analysis by multiple linear regression (MLR) showed that only gender was significantly associated with TDID per body weight. Being female, a patient will require an increase in TDID per body weight of 0.124 unit/kg/day compared to male patient (95% CI 0.017, 0.231, p = 0.024) . This may possibly be due to the fact that females have higher BMI, adiposity, easily gain weight and low tendency of experiencing hypoglycaemia. Age, race, HbA1c, duration of DM and duration of insulin were not significantly associated with TDID per body weight.

CONCLUSION

Mean TDID among uncontrolled DMTAC patients in HTAA was 57.9u/day and the mean TDID per kg was 0.79u/kg/day. Only gender was significantly associated with TDID per body weight. Other factors such as insulin technique and BMI which may influence TDID were not included in this study and further prospective study may further increase our understanding on TDID and factors that affect it to guide on the insulin dosing better among Malaysian population.

THE OUTCOMES OF THREE-FACTOR PROTHROMBIN COMPLEX CONCENTRATE (3F-PCC) IN WARFARIN ANTICOAGULATION REVERSAL: A PROSPECTIVE, SINGLE-ARM, OPEN-LABEL, MULTICENTRE STUDY

AUTHORS Koh HK, Jagan N, George D, Mazlan-Kepli W, Mohamed S, Lim HT, Ross NT, Mazlan AM

INTRODUCTION There is a wide variation on the efcacy of three-factor Prothrombin Complex Concentrate (3F-PCC) in warfarin reversal.

OBJECTIVE We aimed to determine the efficacy and safety of 3F-PCC in warfarin reversal.

METHODOLOGY This multicentre prospective study analysed data from adult patients on warfarin who received 3F-PCC (Prothrombinex-VF®) for anticoagulation reversal between June 2019 to October 2020. Purposive sampling was used in this study. Study endpoints included target INR achievement, adverse drug reactions (ADRs), and in-hospital all-cause mortality. Logistic regression analyses were used to assess independent predictors of study endpoints.

RESULTS One-hundred thirty-seven patients with a median age of 68 (59–76) years were recruited, who were predominantly male (59.9%, n=82). A total of 102 patients required 3F-PCC for life-threatening (40.9%, n=56) and clinically signifcant bleeding (33.6%, n=46). Initial INRs ranged from 1.55 to undetectable high (>26). All patients had INR reduction, of which 62% (n=85) achieved target INR, whereas 12.4% (n=17) achieved INR below the target range. Median INR was reduced from 4.76 (3.14–8.32) to 1.54 (1.27–1.88) post-3F-PCC (p<0.001). The use of adjunctive reversal agents and initial INR<3.6 were the signifcant predictors for target INR achievement. Six (4.4%) ADRs were observed. Two (1.5%) cases with the suspected acute coronary syndrome were associated with mortality. Ischemic stroke occurred in one (0.7%) patient. The incidence of in-hospital all-cause mortality was 21.2% (n=29).

CONCLUSION The rate of INR achievement was 62% in our study without apparent increased risk of thromboembolic events and in-hospital all-cause mortality.

PAEDIATRIC THALASSEMIA COUNSELING REFRESHMENT COURSE 2022

16 February 2022

Bilik Mesyuarat Topaz, UFL

Participants of the day

Participants listening to a talk by paediatric specialist, Dr Noor Azmi

PAEDIATRIC THALASSEMIA COUNSELING REFRESHMENT COURSE 2022

> Talk on Dietary Intake in Thalassemia Patients given by dietitian Puan Hasme Anim

Token of appreciation for the speakers

PharmCare
Hospital Tengku Ampuan Afzan

PHARMBOWL 2022

26 FEBRUARY 2022
MEGALANES, BERJAYA MEGAMALL

THE PARTICIPANTS

PharmCare
Hospital Tengku Ampuan Afzan

PHARMBOWL 2022

PRIZE-WINNERS (MALE)

PharmCare
Hospital Tengku Ampuan Afzan

PHARMBOWL 2022

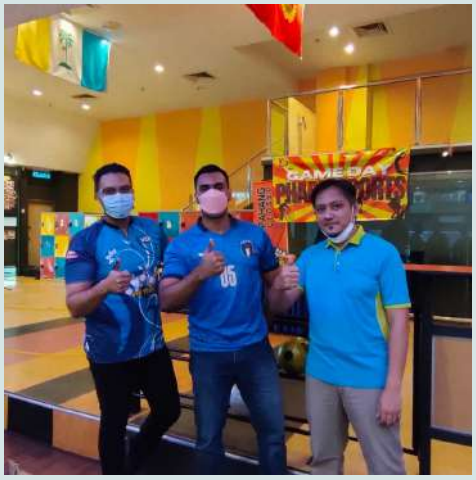
PRIZE-WINNERS (FEMALE)

PharmCare
Hospital Tengku Ampuan Afzan

HIGHLIGHTS OF THE DAY






PharmCare
Hospital Tengku Ampuan Afzan

BEST PLAYER

MALE

En. Muhammad Muhaimin bin Zainuddin

FEMALE

Pn. Aida Roziana binti Ramlan

KEMENTERIAN KESIHATAN MALAYSIA

KENALI UBAT PAXLOVID

Paxlovid adalah ubat antivirus untuk rawatan penyakit COVID-19 tahap ringan hingga sederhana.

Paxlovid merupakan kombinasi ubat nirmatrelvir (juga dikenali sebagai PF-07321332) dan ubat ritonavir.

Paxlovid hanya digunakan oleh pesakit yang memenuhi semua kriteria berikut:

- berumur 18 tahun ke atas,
- dijangkiti COVID-19 tahap ringan hingga sederhana, dan
- jangkitan COVID-19 yang dialaminya berisiko tinggi untuk menyebabkan kemasukan ke hospital atau kematian.

KEMENTERIAN KESIHATAN MALAYSIA

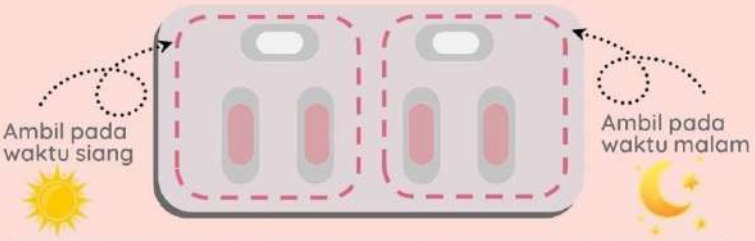
SEBELUM AMBIL PAXLOVID ...

Maklumkan kepada doktor dan ahli farmasi sekiranya anda :

- Mempunyai sebarang alergi
- Menghidapi sebarang penyakit terutamanya penyakit hati atau buah pinggang
- Mengambil sebarang ubat seperti lovastatin, alfuzosin atau phenytoin
- Sedang hamil atau merancang untuk hamil
- Sedang menyusukan bayi

KEMENTERIAN KESIHATAN MALAYSIA

CARA PENGAMBILAN PAXLOVID



Ambil 1 biji ritonavir berwarna putih dan 2 biji nirmatrelvir berwarna merah jambu,

2 kali sehari, selama 5 hari .

- Telan keseluruhan tablet. Jangan kunyah, potong atau hancurkan tablet.
- Ambil kesemua tiga tablet secara serentak bagi setiap dos.
- Habiskan dos seperti yang diarahkan oleh doktor dan ahli farmasi.

KEMENTERIAN KESIHATAN MALAYSIA

KESAN SAMPINGAN PAXLOVID

Penggunaan Paxlovid sentiasa dipantau secara berterusan.

Laporkan sebarang kesan sampingan melalui borang *Consumers Reporting Side Effects to Medicines (ConSERF)* di www.npra.gov.my.

KEMENTERIAN KESIHATAN MALAYSIA

JIKA TERLUPA AMBIL DOS PAXLOVID

KEMENTERIAN KESIHATAN MALAYSIA

CARA PENYIMPANAN PAXLOVID

Simpan ubat Paxlovid dengan cara penyimpanan yang betul.

PHARMACY BULLETIN
BIL 1/2022

THANK YOU FOR READING!

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