هيئة الدواء المصرية

IN THIS ISSUE

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مركز اليقظة الصيدلية المصري

EPVC Mission

Pharmaceutical Vigilance administration is the way through which the processes for authorizing, regulating, monitoring and evaluating the safety of any pharmaceutical product or medical device take place, in addition to disseminating any safety information for public health programs, healthcare professionals, and the Egyptian citizen.

The Pharmaceutical vigilance administration is an integral part of the Central Administration of Pharmaceutical Care that works on the enhancement of the pharmaceutical services to guarantee safe and effective use of medications in Egypt, under the patronage of the Egyptian Drug Authority.

Newsletter

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Safety Notification ! : Infusion-related reactions – not all allergy related

The Regulatory Authority in New Zealand has published the following safety notification:

Key messages

- Infusion-related reactions may be allergic or pseudo-allergic.
- Overlapping clinical presentations may make distinguishing between these different infusion-related reactions challenging.
- If signs and symptoms of anaphylaxis are present, immediately discontinue the infusion and initiate appropriate management.

The Centre for Adverse Reactions Monitoring (CARM) in New Zealand received a report of a vancomycin infusion-related reaction where the patient developed redness and itch .(Previously called 'Red Man Syndrome', the clinical presentation of severe vancomycin infusion reaction may mimic that of anaphylaxis.

What are infusion-related reactions?

Infusion-related reactions are potentially serious adverse events associated with parenteral administration of medicines and may have different underlying causes

Infusion-related reactions may be allergic or pseudo-allergic.

Allergic type or hypersensitivity reactions can be classified into types I to IV, depending on the mechanism. Anaphylaxis is the most severe presentation of an immunoglobulin E (IgE)-mediated (type I) medicine reaction

Pseudo-allergic type or nonimmune hypersensitivity reactions are rare, unpredictable reactions to a medicine. The mechanisms underlying most pseudo allergic

reactions are not known. With vancomycin infusion reaction, mast cells are activated independent of IgE and the clinical presentation can mimic an IgE mediated allergic reaction.

It may be difficult to distinguish clinically between allergic and pseudo-allergic reactions. However, both types of reaction can be potentially life threatening. If signs

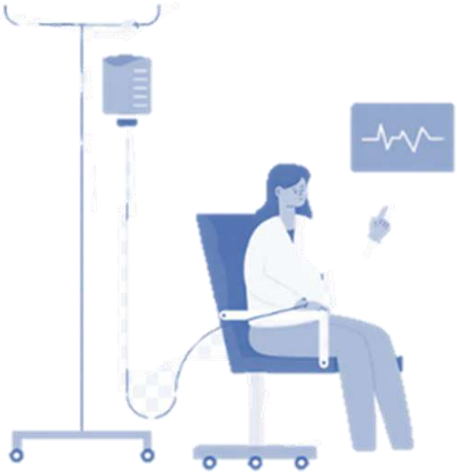
and symptoms of anaphylaxis are present, immediately discontinue the infusion and initiate appropriate management.

Administer medicines with potential for infusion-related reactions in a suitable environment with adequately trained personnel and resuscitation equipment.

Examples of medicines associated with infusion-related reactions

Vancomycin, intravenous iron and monoclonal antibodies are examples of medicines associated with infusion-related reactions (not an exhaustive list).

Vancomycin



Rapid administration of vancomycin may cause vancomycin infusion reaction, a pseudo-allergic reaction.

To minimize the risk of vancomycin infusion reaction, administer vancomycin at a rate of 500mg/ hour or slower, and at an appropriate dilution.3

Symptoms of vancomycin infusion reaction may include hypotension (low blood pressure), flushing, erythema (skin redness), urticaria (skin welts), pruritis (itchiness), or pain and muscle spasm of the chest and back. Stopping the infusion usually stops the symptoms. Rule out other causes such as anaphylaxis

Safety Notification ! : Infusion-related reactions – not all allergy related (Continued)

Depending on the severity of the vancomycin infusion reaction, it may be possible to restart the infusion at a reduced rate after the symptoms have resolved. Monitor the patient closely for further reactions.

Intravenous iron

For intravenous administration of iron polymaltose, use a slow infusion rate initially and observe the patient. Increase the rate if the infusion is well tolerated. The approximate infusion time is 5 hours.

Ferric carboxylates can be administered via slow intravenous undiluted injection or as a diluted infusion. For 500mg–1,000mg doses, the minimum infusion time should be 15 minutes.

Monitor patients during and after iron administration. If an infusion-related reaction occurs, stop the infusion and take appropriate action.

Mild infusion-related reactions with intravenous iron may include symptoms such as itching, flushing, sensation of heat, slight chest tightness, hypertension or back/joint pains. The reaction may be related to the rate of the infusion, rather than an allergic reaction.

Following resolution of mild symptoms, restart the infusion at a slower rate if clinically appropriate.

Rarely, serious allergic reactions, including anaphylaxis, can occur with intravenous iron.

Monoclonal Antibodies

Infusion-related reactions can occur with monoclonal antibodies, with potential to cause a wide spectrum of symptoms.

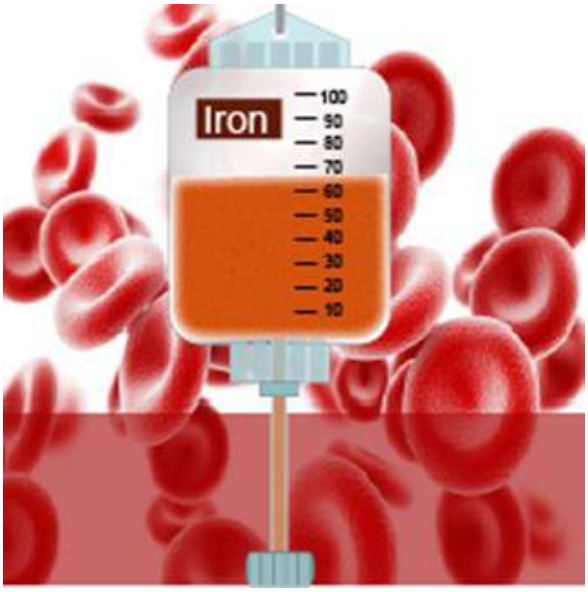
Rituximab is a monoclonal antibody associated with a high incidence of pseudo allergic infusion reactions. To reduce this risk, premedicate the patient and administer

the first rituximab dose at a slower rate (refer to the data sheet and/or clinical guidelines for premedication recommendations). Patients who have elevated white

blood cells are more likely to have severe infusion-related reactions.

Symptoms of rituximab infusion reactions may include fever, chills, rigors, hypotension, urticaria and angioedema and features of cytokine release syndrome. Symptoms are usually reversible with interruption of the infusion. Decision for retreatment depends on the severity and nature of the reaction.

data sheet for further information about administration and infusion-related reactions.



References:

MedSafe : *(Click Here)*

Local Case Report

" Adverse events following administration of Phyto menadione (Vitamin K) intravenous infusion."

The regional center in Cairo received 4 cases that suffered from a number of adverse events including Chest tightness, Back pain, Redness, and Shortness of breath after the administration of Phyto menadione 10 mg reconstituted on normal saline for slow intravenous infusion over 30 minutes.

All the cases have been recovered after drug withdrawal and corrective treatment was given on the form of Avil injection.

Although the adverse events are non-serious and are all stated in the Smpc of Vitamin K products administered by intravenous rout but what draws attention to those cases is the detected cluster.

After following up with the reporter it was found that after replacing the suspect drug with other Phyto menadione trade name the reaction did not recur although using the same concentration and infusion rate.

Trade names for vitamin K vary in what their recommended administration routes are, by following the accurate dose, route of administration and adequate preparation for each brand; the frequency of the adverse event can be reduced.

Background:

Phyto menadione, or vitamin K1, is a water-insoluble vitamin that is indicated for the treatment of various coagulation disorders due to a lack of or a decrease in factors II, VII, IX, and X. The interplay of these factors in the coagulation cascade leads to formation of thrombin and then fibrin that is responsible for clot stabilization (1).

Administration

Route-Specific Administration

Phytomenadione is available for oral, intravenous (IV), subcutaneous and intramuscular (IM) administration.

Oral Administration

Oral absorption requires the presence of adequate bile salts. Bile salts must be given with the tablets when the endogenous supply of bile to the gastrointestinal tract is deficient.

Guidelines recommend oral over subcutaneous administration for the treatment of supratherapeutic INR when no significant bleeding is present.

Phyto menadione injection has been administered orally and is typically used when lower oral doses (e.g., 1 mg) are needed and no oral product is commercially available.

Injectable Administration

Phyto menadione can be administered intramuscularly (IM), subcutaneously, or intravenously (IV) by slow IV infusion.

In general, IM and IV routes should be avoided; however, the IV route is the preferred route for rapid reversal of warfarin.

IV and IM administration are associated with an increased risk of anaphylactoid reactions.

Anaphylactoid reactions have occurred during the first infusion and in patients receiving IV Phytomenadione that has been diluted and injected by slow IV infusion.

Similar reactions have been reported with IM administration.

Therefore, restrict IV and IM administration to those situations where another route is not feasible, and the increased risk involved is considered justified.

Subcutaneous administration is the preferred parenteral route. However, subcutaneous administration often results in delayed and erratic absorption.

Visually inspect parenteral products for particulate matter and discoloration prior to administration.

Local Case Report (Continued)

" Adverse events following administration of Phyto menadione (Vitamin K) intravenous infusion."

Intravenous Administration

Dilute the Phytomenadione injection with preservative-free 5% Dextrose Injection, 0.9% Sodium Chloride Injection, or 5% Dextrose and 0.9% Sodium Chloride Injection only; other diluents should not be used.

Infuse slowly at a rate not exceeding 1 mg/minute.

Intramuscular Administration

If IM injection is necessary, inject deeply into a large muscle mass (e.g., anterolateral thigh or deltoid [children and adolescents only]).

Subcutaneous Administration

Inject subcutaneously taking care not to inject intradermally.

Adverse Effects

Adverse effects have not been reported for individuals ingesting higher amounts of dietary vitamin K orally; tolerable upper intake levels have not been established.

During intravenous administration of phytonadione, serious hypersensitivity reactions or anaphylaxis can occur.

Typically, these reactions occur upon first-time administration of phytonadione.

Severe hypersensitivity/anaphylactoid reactions including anaphylactic shock, cardiac arrest and/or respiratory arrest, and death have occurred during and immediately after intravenous injection of phytonadione.

Other effects associated with these reactions include transient flushing, "peculiar" sensations of taste (dysgeusia), dizziness, rapid and weak pulse, profuse sweating (hyperhidrosis), hypotension, weakness, sinus tachycardia, chest pain (unspecified), dyspnea, and cyanosis.

An injection site reaction consisting of pain, swelling, and tenderness at the site may occur.

Skin hypersensitivity reactions, including rash and vesicular rash, have been reported with Phytomenadione injections.

Cutaneous reactions, including eczematous reactions, scleroderma-like patches, urticaria, and delayed-type hypersensitivity reactions, have also been associated with parenteral phytonadione.

Recommendations:

Based on what was stated in the report, the following must be taken in consideration:

Follow the dose , route of administration and method of preparation stated in each product insert.

The difference in Vitamin K products formulations may contribute to the observed ADR, as stated in the preparations with polyoxyethylated castor oil as a solubilizer.

Adverse reactions are more likely with higher doses, inadequate dilution, and rapid infusion of vitamin K1.

The American College of Clinical Pharmacy ACCP guidelines advocate the use of the lowest effective dose (ie, 5-10 mg), dilution in at least 50 mL of fluid, and infusing over a minimum of 20 minutes (5).

References:

[1] Phytomenadione background: *(Click Here)*

[2] Phytomenadione safety and efficacy: *(Click Here)*

[3] Vitamin K different formulation safety: *(Click Here)*

[4] Phytomenadione SPC: *(Click Here)*

[5] ACCP guidelines: *(Click Here)*

Egyptian Pharmaceutical Vigilance Center (EPVC) Vigiflow expansion project Trainings for Raising Reporting Awareness

The Egyptian Pharmaceutical Vigilance Center (EPVC) is delighted to continue vigiflow expansion training in collaboration with **SCUMIN "Supreme Council Of Universities Medicines Information Network"**

The program's objective is to train pharmacists employed by the institutions how to integrate with the EPVC efforts using the national database reporting system. It will give the organization access to a robust reporting system. Furthermore, it will raise the quality of cases added to the database and improve the reporting system as a whole.

In order to improve the quality of the cases entered into the national database, EPVC works in tandem with the training sessions to receive cases through the database, review them, give insightful feedback to the coordinating organizations, and find out if more training is required. It is anticipated that this strategy will produce a more strong and dependable way to monitor and handle safety risks related to pharmaceuticals.

In a related context, EPVC would like to express its appreciation to the Mansoura University - Oncology Center, Alexandria University, and Kasr Eleiny Hospital for their commitment and hope they continue to have success in their endeavors.

"Together for Safe Medicine" Initiative News:

We are happy to announce the start of registration for the 4th wave of the Initiative "Together for Safe Medicine after the success of the previous three waves with the help of Egyptian pharmacists all over Egypt governments as they had made a lot of valuable efforts in applying, practicing, and spreading the science of Pharmacovigilance between HCPs in the hospital pharmacies and public where they succeeded in spreading the meaning and aim of Pharmacovigilance to children and adults by making creative, attractive and simplified videos and by good communication with the public through their community pharmacies and governmental pharmacies. We can't wait for starting the complete successful journey of the Initiative "Together for Safe Medicine with the members who will participate with us in the fourth wave.

EPVC Tips

On Pharmacovigilance

Avoid self-medication:

Self-medication has traditionally been defined as "the taking of drugs, herbs or home remedies on one's own initiative, or on the advice of another person, without consulting a doctor.

Potential risks of Self-medication

* Incorrect self-diagnosis
* Failure to seek appropriate medical advice promptly.
* Incorrect choice of therapy
* Failure to recognize special pharmacological risks.
* Rare but severe adverse effects
* Failure to recognize or self-diagnosis contraindications, interactions, warnings and precautions.
* Failure to recognize that the same active substance is already being taken under a different name.
* Failure to report current self-medication to the prescribing physician (double medication/harmful interaction)
* Failure to recognize or report adverse drug reactions.
* Incorrect route of administration
* Inadequate or excessive dosage
* Excessively prolonged use
* Food and drug interaction
* Risk of dependence and abuse
* Storage in incorrect conditions or beyond the recommended shelf life.

Improved knowledge and understanding about self-medication may result in rationale use of all medications.

Visit EDA website to find all medicine- related news, updates and alerts *Click here*

You will find all EPVC Newsletters and DHPCs here

You will also find all alerts regarding counterfeited and falsified products released by Central Administration of Operations *here*

The Egyptian Pharmaceutical Vigilance center
مركز اليقظة الصيدلية المصري

One report counts

A call for reporting

Please remember that you can report safety information of medicines to EPVC using the following communication information:

What is Pharmacovigilance

Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug- related problem.

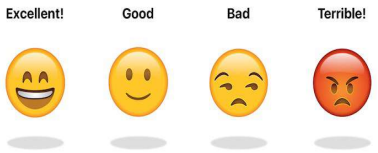
What is the Egyptian Pharmaceutical Vigilance Center?

With the increasing demand for patient's safety which is becoming more stringent, . The Egyptian Pharmaceutical Vigilance Center was established to be responsible for the safety monitoring of the pharmaceutical products throughout its lifecycle and it is the regulatory authority regarding Pharmacovigilance and its applications .

EPVC monitors the safety of all types of pharmaceutical products, including human medicines, biological products, supplements, cosmetics, veterinary medicines, medical devices, Biocides and pesticides

Participate with us

We invite you to take a quick survey on how much our communication with you is effective
We value your feedback! Help us enhance our communication by taking a quick survey. Your insights are crucial in ensuring we meet your expectations.
Survey Link: (Click Here)



Thank you for your valuable input

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