EGYPTIAN DRUG AUTHORITY

هيئة الدواء المصرية

IN THIS ISSUE

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EPVC
The Egyptian Pharmaceutical Vigilance center
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

July 2024

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Safety Notification ! : Medicine-induced hyponatremia: increased risks in older people

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

Key messages

- Hyponatremia (low serum sodium levels) is a common electrolyte disturbance in older people.
- Medicine use is a common cause of hyponatremia.
- Due to a combination of risk factors, older people are more susceptible to hyponatremia. Use medicines that may cause hyponatremia with caution in older people

Hyponatremia may be asymptomatic

Hyponatremia (low levels of serum sodium) is a common electrolyte disturbance, especially in older people. It is defined as a serum sodium concentration of less than 135 mmol/L. Hyponatremia signs and symptoms range from mild and nonspecific (such as weakness or nausea) to severe and life-threatening (such as seizures or coma) .Hyponatremia may also be asymptomatic.3 In older people, hyponatremia can be associated with cognitive impairment, gait disturbances and falls and fractures.

How ageing contributes to an increased risk of hyponatremia

Age-related decline in renal function, urinary concentrating ability and changes to homeostatic mechanisms can contribute to the development of hyponatraemia.3 However, there are usually multiple factors implicated in the development of hyponatremia in older people.

Comorbidities: Many conditions that are known to cause hyponatremia are prevalent in the older population including congestive heart failure, chronic kidney disease, neurological disease, diabetes, hypothyroidism and malignancy.

Medicines: Medicines that cause hyponatremia are often prescribed to older people, such as diuretics, selective serotonin reuptake inhibitors (SSRIs), antipsychotics and carbamazepine.

Polypharmacy: Use of higher doses or multiple medicines increases the risk of medicine-induced hyponatremia. Other risk factors in older people include female gender, low body mass and low baseline serum sodium.

This table outlines the most frequently reported suspect medicines (by medicine class) for the hyponatraemia reports in people aged over 65 years.

Medicine class	Suspect medicine
Diuretics	Bendroflumethiazide
	Chlortalidone
Proton pump inhibitor	Omeprazole
Antidepressants	Citalopram
	Fluoxetine
	Paroxetine
	Escitalopram
	Venlafaxine
Antiepileptic	Carbamazepine
Angiotensin II receptor inhibitors	Cilazapril
Antibiotics	Trimethoprim
Other	Colecalciferol

Prescribing considerations

Use with caution.

If using a combination of medicines that cause hyponatremia, consider lower doses or use alternative treatment options.

Most cases of medicine-induced hyponatremia occur within the first few weeks. However, hyponatremia may also occur later in treatment if other risk factors for hyponatremia develop or during concurrent illness.

Check plasma sodium levels before and shortly after starting treatment. Continue to monitor plasma sodium levels closely throughout treatment as clinically indicated.

If medicine-induced hyponatremia occurs, manage the patient's sodium levels and stop the suspected medicine if clinically indicated.

References:

Medsafe : *(Click Here)*

Safety Notification ! Intravenous Rituximab and Infusion-related reactions

The EPVC regional centre received an ICSR of a female patient, 31 years old, who suffered from non-Hodgkin lymphoma and a history of cardiovascular disease.

The patient is in her first cycle and receiving a protocol of R-CVP Rituximab- (cyclophosphamide, vincristine, and prednisone). After 5 minutes of Rituximab 600 mg infusion, she experienced a rituximab-related infusion reaction that presented as severe dyspnea and redness, hot flushes, and laryngeal spasm. She hasn't yet received any of the other protocol medications.

Infusion has stopped, and 1 ampoule of Avil, and solucortef vial were given. She was placed on an oxygen mask. The clinical pharmacist recommended close monitoring and the addition of Perelman 1000 mg before re-challenge of rituximab infusion.

After 45 mins her symptoms have resolved completely. Rituximab has been re-infused using an infusion pump of rate 50mg/hr after 1st hr and as no signs of reaction occurred the rate has escalated to 100mg/hr. Concomitant medications include spironolactone 25mg, torsemide 5mg, and Bisoprolol 2.5

Background

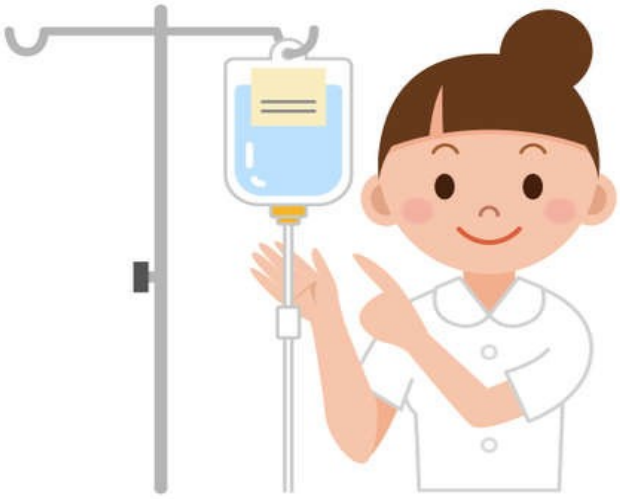
Infusion-related reactions (IRRs) are predictable, occurring in 77% of patients with the first infusion, 30% with the 4th infusion, and 14% with the 8th infusion. Reactions occur within 30 to 120 minutes of the first exposure in over 50% of patients. The mechanism is thought to be an antibody-antigen interaction between rituximab (the antibody) and CD20 (the antigen) on lymphocytes, resulting in cytokine release from cells.

Symptoms include hypotension, fever, chills, rigours, urticaria, bronchospasm, sensation of tongue or throat swelling, nausea, fatigue, headache, pruritis, dyspnea, rhinitis, vomiting, and flushing. Symptoms may progress in severity and include acute respiratory distress syndrome and angioedema. Severe, potentially fatal, infusion-related reactions (0.04-0.07%) may occur within 24 hours of the first infusion and may be clinically indistinguishable from anaphylactic reactions.

Rituximab Infusion Rates

Initial infusion: The recommended initial rate for infusion is 50 mg/hour; after the first 30 minutes, it can be escalated in 50 mg/hour increments every 30 minutes, to a maximum of 400 mg/hr.

Subsequent infusion: The infusion rate can subsequently be infused at an initial rate of 100 mg/hour, and increased by 100 mg/hour increments at 30-minute intervals, to a maximum of 400 mg/hr.



Rapid infusion protocol

The rapid infusion regimen is ONLY to be used in patients who meet the following criteria:

Receiving their second or subsequent infusion of rituximab

Previous infusions received without grade 3 or 4 infusion-related toxicities

Circulating lymphocyte count < 5.0 x 109/L

Safety Notification ! Intravenous Rituximab and Infusion-related reactions

The protocol is as follows:

Initiate at a rate of 20% of the total dose given in the first 30 minutes and the remaining 80% of the total dose given over the next 60 minutes.

If the 90-minute infusion is tolerated in Cycle 2, the same rate can be used when administering the remainder of the treatment regimen (through Cycle 6 or 8).

Patients who have clinically significant cardiovascular disease or who have a circulating lymphocyte count ≥5000 cells/mm3 before Cycle 2 should not be administered the 90-minute infusion.

For mild to moderate infusion reactions, interrupt the infusion or slow the infusion rate for infusion reactions. Continue the infusion at one-half the previous rate upon improvement of symptoms.

Infusion time	First 30 mins	30 min - 1 hr	1 - 1.5 hrs	1.5 - 2 hrs	2 - 2.5 hrs	2.5 - 3 hrs	3 - 3.5 hrs	3.5 hrs onwards
First infusion	50 mg/hr	100 mg/hr	150 mg/hr	200 mg/hr	250 mg/hr	300 mg/hr	350 mg/hr	400 mg/hr (MAX rate)
Subsequent infusions - if nil adverse events during first infusion	100 mg/hr	200 mg/hr	300 mg/hr	400 mg/hr (MAX rate)	→			
Rapid infusion protocol[#] - second or subsequent infusions (see Note) Administer over 90 minutes (approx.)	20% of dose (i.e. 200 mL/hr for dose loaded in 500 mL bag)	Remaining 80% of dose to be given over approx. 60 mins (i.e. 400 mL/hr (MAX rate) for dose loaded in 500 mL bag)						

Special concerns related to biological medicines

- Biological medicines are made by living organisms, which are naturally variable. Thus, the active substance in the final biological medicine can have an inherent degree of minor variability ('microheterogeneity).
- In the context of pharmacovigilance of biologics (reference products and biosimilars), batch numbers are important.
- Monitoring and documenting our Egyptian experience with biologics (Reference products and Biosimilars) are a critical issue.
- Qualified Pharmacists are a real guarantee for good pharmacovigilance practices (GVP), they have great responsibilities to promote safety, and carefully follow up with patients in the era of biologics.

References:

1. ***Drug Monograph :*** *(Click Here)*
2. ***Product SMPC :*** *(Click Here)*
3. ***Clinical info :*** *(Click Here)*

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

The Egyptian Pharmaceutical Vigilance Center (EPVC) is delighted to provide Vigiflow expansion training (advanced level) in coordination with “The Central Administration of Pharmaceutical Affairs”, SMC “Secretariat of Specialized Medical Centers"), and SCUMIN (Supreme Council of Universities Medicines Information Network). 1025 attendees of focal points from “Directorates of Health Affairs at the Egyptian Ministry of Health”, SMC “Secretariat of Specialized Medical Centers” and Kafr El-sheikh University Hospitals received additional two training sessions titled: "Vigiflow and ICSRs common pitfalls, completeness score and Case quality" These training sessions will help to improve the quality of cases being entered into the national database. By providing training to the focal points of various organizations, the hope is that data entry on the national database reporting system will be strengthened on an advanced level. This will ultimately lead to better case's data quality and more accurate reporting. In the midst of these training sessions, EPVC is actively retrieving cases from the national database, revising them, and giving the coordinating organizations constructive criticism. It is anticipated that this approach will lead to a more strong and dependable way of monitoring and controlling pharmaceutical safety threats.

EPVC would like to express its appreciation to Damnhour Oncology, Qena Oncology Center for their high quality in entering ICSRs on vigiflow. To all the organizations who Co-opperated with EPVC to expand the Vigiflow system, EPVC would like to thank you for submitting cases to the national database reporting system. We hope they continue to succeed in their endeavors and appreciate their dedication and maturity in moving forward with more advanced stages for case quality as well as their monthly entry cases, which are substantial, in the national database.

“Together for Safe Medicine“ Initiative News:

Egyptian Drug Authority (EDA) announces the launching of registration for the fifth wave of the Central Administration of Pharmaceutical Care pharmacovigilance Initiative “Together for Safe Medicine". Where pharmacists of a community pharmacy in Egypt , or outpatient pharmacies of any governmental hospital , any private institution can register for the fifth wave of the initiative and the last registration date is Tuesday, July 30, 2024.

EPVC is extremely thankful for The TOP 20 pharmacists that had been chosen from the fourth-wave community and governmental pharmacies who applied a lot of valuable activities as they used the most advanced tools in spreading Pharmacovigilance science and activities Between HCPs and the public as Pharmacovigilance Artificial intelligence videos, PODCAST recent tool in Social media and the pharmacists have shared PV awareness and educational videos through their YouTube Channels.

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EPVC Tips

On Pharmacovigilance

Instructions For Use for reusable and re-sterilizable Medical Devices

If the device is reusable, the information for use (IFU) must provide "Information on the appropriate processes to allow reuse", including cleaning, disinfection, packaging and, where appropriate, the method of sterilization of the device to be reserialized. Examples: Surgical forceps and endoscopes.

In general, reprocessing reusable medical devices involves three steps:

- At the point of use, devices receive initial decontamination and cleaning and steps are taken to prevent drying of blood, tissue, other biological debris and contaminants on the device.
- The device is then transferred to the reprocessing work area where it is thoroughly cleaned.
- Finally, the device is either disinfected or sterilized, depending on the intended use of the device, and the materials from which it is made and it is stored or routed back into use.

References:

Picture : *(Click Here)*

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*

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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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