هيئة الدواء المصرية

IN THIS ISSUE

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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

December 2023

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Safety Notification ! : Antidepressant withdrawal: taper antidepressants slowly

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

- Withdrawal symptoms can occur when stopping antidepressants. These can be severe in some people.
- Slowly tapering antidepressants reduces the risk of withdrawal symptoms developing.
- Healthcare professionals should provide their patients with information on antidepressant withdrawal and monitored for withdrawal symptoms.

What is antidepressant withdrawal?

Antidepressant withdrawal comprises one or more adverse effects that can occur when people discontinue antidepressants. In some people, withdrawal symptoms can be severe and protracted.2

Symptoms of antidepressant withdrawal

Antidepressant withdrawal can be associated with a wide range of symptoms.

Most common: Dizziness , Fatigue , Headache, Nausea

Common: Sleep difficulties , Anxiety , Irritability , Tremor

Less common: Suicidal thoughts, Sexual dysfunction, Cognitive dysfunction, Loss of coordination

Risk factors for antidepressant withdrawal

Antidepressant withdrawal can happen any time an antidepressant is reduced or stopped, but is more likely when:

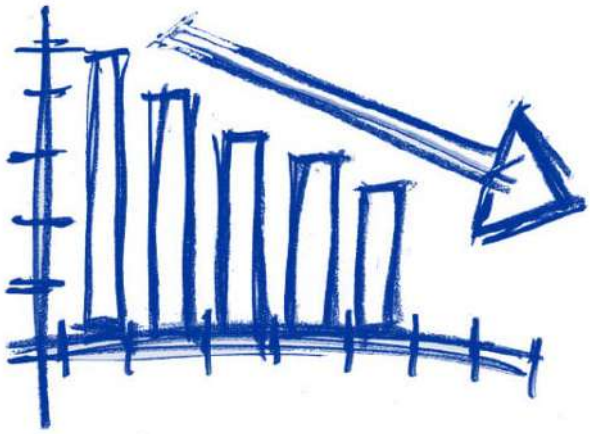
- Antidepressants are stopped abruptly
- Antidepressants are tapered too quickly
- Patients on high dose of antidepressants and patients using antidepressants for long time
- Someone has been on antidepressants for a long time.
- All antidepressants can cause withdrawal symptoms, but some are associated with a higher risk (eg, venlafaxine and paroxetine).

Dose tapering

To reduce the risk of antidepressant withdrawal, slowly taper the patient's dose before stopping it completely. Provide the patient with information on antidepressant withdrawal and monitor them for withdrawal symptoms.

Patient information

Patients should speak to their healthcare provider if they are thinking about stopping or reducing their antidepressant, or if they are having withdrawal symptoms.



References:

MedSafe : *(Click Here)*

" Cytarabine may induce tumor lysis syndrome in acute myeloid leukemia cases."

The regional center in Cairo received one case that developed tumor lysis syndrome after the administration of the antineoplastic agent (Cytrabine) 40 mg subcutaneously once daily.

One female patient of 62 years old was administering Cytrabine for acute myeloid leukemia (AML) for 5 days. After 2 days from Cytrabine administration, she was admitted to hospital with diarrhea, nausea, vomiting and irregular heartbeats (mild symptoms of Tumor lysis syndrome TLS).

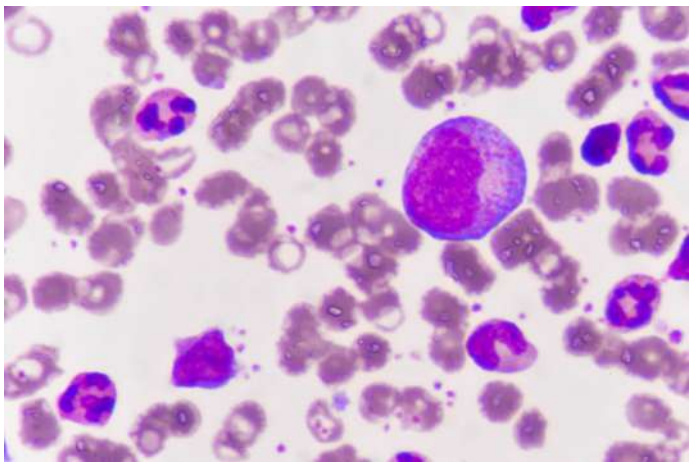
She received 3 more doses of Cytrabine then her laboratory tests results revealed hypocalcemia, hyperuricemia, hyperkalemia and hyperphosphatemia and she was diagnosed with tumor lysis syndrome. Unfortunately, the patient died afterwards of tumor lysis syndrome.

Background:

Tumor lysis syndrome (TLS): Tumor lysis syndrome (TLS) is an oncologic emergency that is caused by massive tumor cell lysis with the release of large amounts of potassium, phosphate, and nucleic acids into the systemic circulation. Catabolism of the nucleic acids to uric acid leads to hyperuricemia, and the marked increase in uric acid excretion can result in the precipitation of uric acid in the renal tubules and can also induce renal vasoconstriction, impaired autoregulation, decreased renal blood flow, and inflammation, resulting in acute kidney injury. Hyperphosphatemia with calcium phosphate deposition in the renal tubules can also cause acute kidney injury and in the cardiac conduction system can result in arrhythmias.[2]

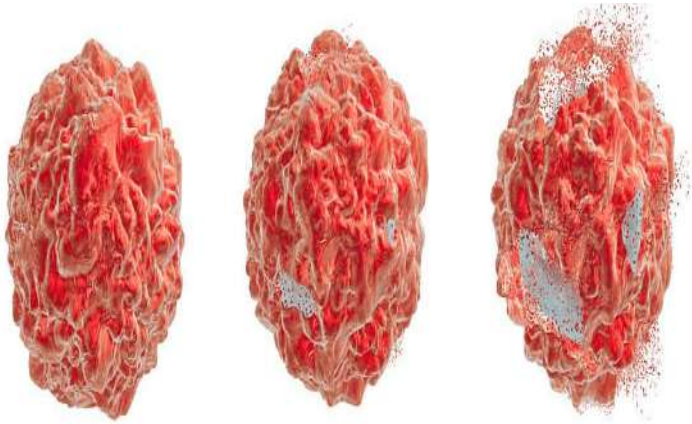
Risk factors for developing tumour lysis syndrome include:

- High tumour cell proliferation rate
- Bulky disease (greater than 10 cm)
- Increased WCC (greater than 25 x 109/L)
- increased LDH (greater than 2 x ULN)
- Chemosensitive malignancies
- High intensity or highly potent therapy
- Novel or targeted therapy, used alone or in conjunction with conventional anticancer agents, even in patients with low-grade disease.3, 4



Malignancies associated with a higher risk of TLS include:

- Burkitt lymphoma/leukaemia.
- Acute lymphoblastic leukaemia.
- Lymphoblastic lymphoma.
- Acute myeloid leukemia AML.
- Diffuse large cell lymphoma.
- Solid tumors with high proliferative rate and rapid response to therapy.



Local Case Report (Continued)

" Cytarabine may induce tumor lysis syndrome in acute myeloid leukemia cases."

Additional conditions that may predispose patients to developing TLS:

- Renal insufficiency or renal failure
- Dehydration
- Decreased urinary flow.
- Pre-existing uraemia or hyperuricaemia
- Pre-existing hyperphosphataemia

Clinical impact of tumor lysis syndrome

- Patients who are at high or moderate risk for TLS should take preventive measures because of the possible severity of the complication. In the event that TLS does occur, patients should receive treatment immediately.
- The major causes of death in patients with clinical TLS were cardiac arrhythmias and acute kidney injury.

Cytarabine: inhibits DNA synthesis. Cytarabine enters cells through a carrier mechanism and needs to be changed into aracytidine triphosphate, which is its active component. DNA incorporates the pyrimidine analogue cytarabine, but its main effect is to inhibit DNA polymerase, which reduces DNA synthesis and repair. Since the degree of cytotoxicity and incorporation into DNA correspond linearly, pharmacological activity and toxicity are caused by incorporation into DNA. Cytarabine only affects the S phase of the cell cycle; it prevents the G1 phase from progressing into the S phase.

Labeled information:

- According to Cytrabine Injection Summary of product Characteristics (SmPC) it was stated under General precautions section that like other cytotoxic drugs Cytarabine Injection may induce hyperuricemia secondary to rapid lysis of neoplastic cells.

Recommendations for Healthcare professionals:

- Based on what was stated in the report, the following was recommended:
- For patients who do not have established TLS, they should receive the prophylactic measures of TLS.
- Intravenous (IV) hydration and the use of hypouricemic medications, such as rasburicase and allopurinol, are the primary preventive strategies.
- Pay attention for the initial mild probable symptoms of TLS.
- The most important factors to monitor in individuals who are at risk for TLS are urine output and repeated electrolyte and serum uric acid serial assays. It is important to regularly measure and record urine production and fluid balance

References:

Tumor lysis syndrome (TLS): *(Click Here)*

Tumor lysis syndrome (TLS): *(Click Here)*

Potential signal of Necrotizing soft tissue infections with vincristine

EPVC has recently published a poster for potential signal of Necrotizing soft tissue infections with vincristine in ISOP, Nov 2023, Bali, Indonesia.

Introduction

Vincristine is an antitumour medication given to the patient as part of polychemotherapy. Necrotising soft tissue infections (NSTIs) are serious life-threatening medical conditions starting in the dermis and epidermis, which then damage the deeper layers of adipose tissue, fascia, or muscle. NSTIs progress rapidly with severe morbidity and have fatality rates of 25%–35%, even with appropriate therapy. Vincristine-associated NSTIs was identified as a potential signal of disproportionate reporting on both the Egyptian and global level.

Objectives

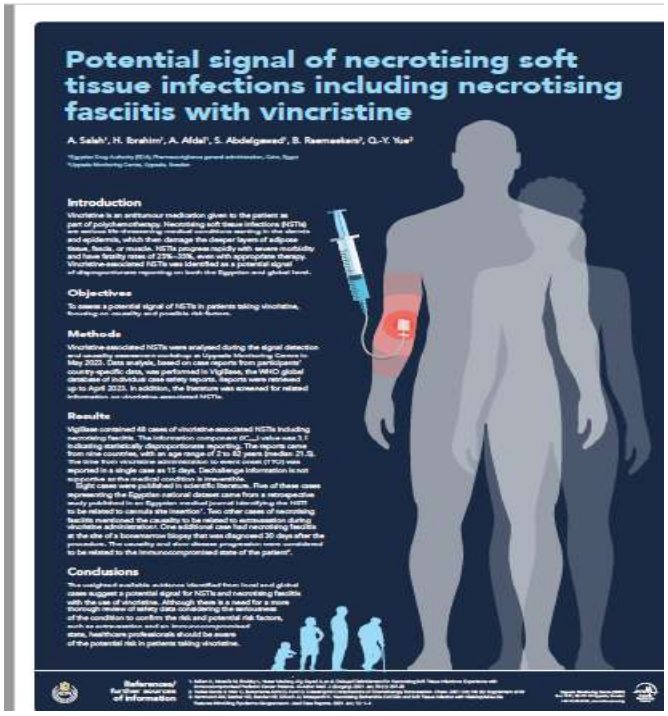
To assess a potential signal of NSTIs in patients taking vincristine, focusing on causality and possible risk factors.

Methods

Vincristine-associated NSTIs were analysed during the signal detection and causality assessment workshop at Uppsala Monitoring Centre in May 2023. Data analysis, based on case reports from participants' country-specific data, was performed in VigiBase, the WHO global database of individual case safety reports. Reports were retrieved up to April 2023. In addition, the literature was screened for related information on vincristine-associated NSTIs

Results

VigiBase contained 48 cases of vincristine-associated NSTIs including necrotising fasciitis. The information component (IC025) value was 3.1 indicating statistically disproportionate reporting. The reports came from nine countries, with an age range of 2 to 82 years (median 21.5). The time from vincristine administration to event onset (TTO) was reported in a single case as 15 days. Dechallenge information is not supportive as the medical condition is irreversible. Eight cases were published in scientific literature. Five of these cases representing the Egyptian national dataset came from a retrospective study published in an Egyptian medical journal identifying the NSTI to be related to cannula site insertion Two other cases of necrotising fasciitis mentioned the causality to be related to extravasation during vincristine administration2 . One additional case had necrotising fasciitis at the site of a bonemarrow biopsy that was diagnosed 30 days after the procedure. The causality and slow disease progression were considered to be related to the immunocompromised state of the patient3 .



Conclusions

The weighted available evidence identified from local and global cases suggest a potential signal for NSTIs and necrotising fasciitis with the use of vincristine. Although there is a need for a more thorough review of safety data considering the seriousness of the condition to confirm the risk and potential risk factors, such as extravasation and an immunocompromised state, healthcare professionals should be aware of the potential risk in patients taking vincristine.

Potential signal (2)

Adverse outcomes of uncompleted pregnancy following insulin exposure: What the analysis of Egyptian postmarketing pharmacovigilance data tells us

EPVC has recently published a poster for potential signal of Adverse outcomes of uncompleted pregnancy following insulin exposure in ISOP, Nov 2023, Bali, Indonesia.

Introduction

Diabetes mellitus is a major public health burden particularly in developing countries. Egypt is one of the leading countries in terms of prevalence of the disease1 . Insulin products are widely used in diabetic patients and may be used as the first line of treatment in pregnant women.

Objective

To analyse and characterise Egyptian case reports of foetal death/abortion events in pregnant women following insulin exposure.

Methods

These combinations were analysed during the Signal Detection and Causality Assessment Workshop organised by Uppsala Monitoring Centre in May 2023. Data analysis, based on case reports from participants' country-specific data, was performed in VigiBase, WHO's global database of reported potential side effects of medicinal products. Case series were analysed using the Bradford Hill criteria for causation. A literature search was performed and product information reviewed.

Results & Discussion

Cumulatively through 16 April 2023, 74 unique cases were retrieved in VigiBase, with insulin as a suspect or interacting drug and relevant MedDRA preferred terms including foetal death/stillbirth/abortion relatedadverse events. After in-depth assessment no well -documented cases were found. Age ranges between 18 and 49 (median 33) years, with the highest percentage of cases (n=56, 76%) in the age group below 40 years. Time-to-onset was reported in 20 cases (27%) with no consistent pattern identified. Reported concomitant medications represented drugs routinely used during pregnancy.

Many of the cases indicated poor control of diabetes during pregnancy with or without a medical history of couldn't be determined using the available dataset since the needed insulin doses differ among trimesters2 . As a result, most Bradford Hill criteria did not support causality in the underlying case series. A review of the literature didn't identify any relevant article correlating events of uncompleted pregnancy with insulin use. Rather, numerous studies associate diabetes with risks of congenital anomalies, maternal and foetal adverse pregnancy outcomes, including uncompleted pregnancy events. A recent prevalence study conducted in 449 Egyptian diabetic patients has shown poor control of diabetes in the general population

Conclusions

The weighted cumulative evidence isn't sufficient to support a causal association between insulin use and events of uncompleted pregnancy. Rather, confounding by indication and poor diabetes management in pregnancy among Egyptian women were implied. Accordingly, communicating the importance of proper diabetes control during pregnancy and a call for expanding the national pregnancy registry for medication safety monitoring are recommended.

Egyptian Pharmaceutical Vigilance Center (EPVC) Vigiflow expansion project

The Egyptian Pharmaceutical Vigilance Center (EPVC) is pleased to announce the continued advancement of the Vigiflow Expansion program. In line with our ongoing commitment to pharmacovigilance, we recently hosted a virtual training webinar titled "How to be an Effective Focal Point In Your Facility and VigiFlow Data Entry Pitfalls" in collaboration with the Egyptian Healthcare Authority (EHA). The primary objective of this webinar was to strengthen the pharmacovigilance system across diverse facilities, with a focus on enhancing the quality of cases recorded in the database and elevating the overall reporting system.

Concurrently, as we conduct these trainings, EPVC is actively receiving cases through the national database, reviewing them, and offering valuable feedback to coordinating organizations. This strategic approach is anticipated to establish a more robust and reliable method for tracking and addressing pharmaceutical safety concerns.

"Together for Safe Medicine" Initiative News:

The shared pharmacists from first three waves of the Initiative "Together for Safe Medicine "had made a lot of valuable activities concerning sharing in **Med safety week** from 6 November 2023 till 12 November 2023 as they made posts on social media, banners, videos, and preparing training materials (PowerPoint, word, and PDF) aiming to improve their role 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 through Cooperation with different non HCP institutions like schools, medical associations and universities.

Acknowledgment

The Egyptian Pharmacovigilance Center is Extremely thankful to all participating pharmacists from the 1st,2nd and 3rd waves of the Initiative "Together for Safe Medicine "for their important role in sharing in international events related to drug and patient safety **Med safety week** resulted in reporting **26** adverse drug reaction reports with continuous improvement in reports quality to the Pharmacovigilance national database, As pharmacists made PV awareness sessions for **400** patients and had made pharmacovigilance awareness lectures for **206** HCPs members in governmental hospitals during Med safety week starting from 6 November 2023 till 12 November 2023.

The Egyptian Pharmaceutical Vigilance Center (EPVC) expresses sincere gratitude to the Egyptian HealthCare Authority- Port Said Hospitals and Swiss Canal University Hospital for their proactive interventions in the management of hypersensitivity cases resulting from contrast dyes injection which demonstrate a strong commitment in improving patient safety. Your dedicated efforts have a substantial impact on healthcare safety, and we truly appreciate your unwavering commitment.

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EPVC Tips

On Pharmacovigilance

Recognition of signs of a serious ADR (Adverse Drug Reaction):

A serious adverse reaction is any untoward medical occurrence associated with the use of a medical product at any dose in a patient

the outcome is one of the following:

1. Death (Direct outcome of the adverse reaction).
2. Life-Threatening (Risk of dying at the time of the adverse reaction or it is suspected that the use or continued use of the product would result in the patient's death).

3. Hospitalization (Initial or prolonged).
4. Disability (Significant, persistent, or permanent disability e.g.: change, impairment, damage, or disruption in the patient's body function / structure, physical activities, or quality of life).
5. Congenital Anomaly.
6. Medically important event or reaction (The patient might require intervention to prevent one of the other outcomes listed above).

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.

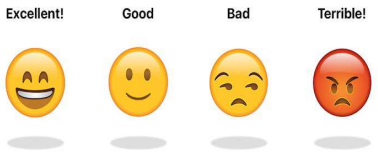
What is the Egyptian Pharmaceutical Vigilance Center?

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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