هيئة الدواء المصرية

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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

September 2025

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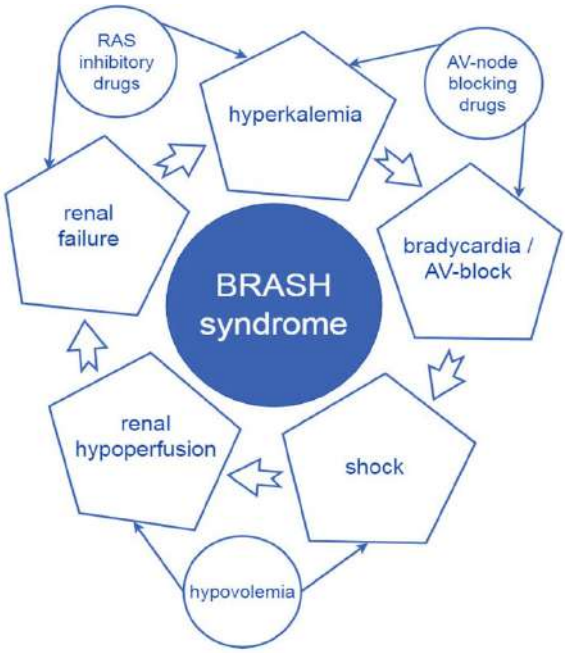
Prescriber Update : Hyperkaliemia or BRASH syndrome?

Summary

Patients with BRASH syndrome may present with a range of symptoms from asymptomatic bradycardia to multiorgan failure. The main differential diagnosis to consider is isolated hyperkalaemia. BRASH syndrome involves the synergistic effects of atrioventricular (AV) node blockers with hyperkalaemia, causing profound bradycardia. • Triggers include hypovolaemia due to illness and starting or increasing the dose of medicines such as AV blockers. Medicines that cause acute kidney injury, hyperkalaemia or reduced cardiac output may also contribute to the development of BRASH. The New Zealand Pharmacovigilance database recently received a case report of BRASH syndrome in a patient taking propranolol and diltiazem. As this was the first report of BRASH syndrome, we have included this article to explain the symptoms and encourage reporting of any further cases.

What is BRASH syndrome?



BRASH syndrome is an increasingly recognised clinical entity. The acronym describes the signs of this syndrome: bradycardia, renal failure, atrioventricular (AV) nodal blockade, shock and hyperkalaemia.

In BRASH syndrome, the synergistic effects of AV node blockers with hyperkalaemia result in profound bradycardia that is greater than expected from either factor alone. Areduced cardiacoutput leads to worsening renal dysfunction that exacerbates the hyperkalaemia, creating a vicious cycle that can progress to multiorgan failure. Triggers include hypovolaemia due to illness and starting or increasing the dose of medicines such as AV blockers. Older people with underlying cardiac or renal impairment, especially those taking multiple AV blockers, are at greater risk.

Clinical presentation and evaluation

Patients with BRASH syndrome may present with a range of symptoms from asymptomatic bradycardia to multiorgan failure. The main differential diagnosis to consider is isolated hyperkalaemia. In patients with isolated hyperkalaemia, bradycardia generally results from severe hyperkalaemia. However in BRASH syndrome, bradycardia often occurs with moderate hyperkalaemia. In addition, an electrocardiogram (ECG) may show bradycardia without other features of hyperkalaemia. Similarly, in patients experiencing BRASH syndrome, the bradycardia is not explained by supratherapeutic levels of AV node blockers. Patients are generally taking their medicines at the correct dose. Healthcare professionals should consider BRASH syndrome in patients taking AV blocking medicines who present with signs of bradycardia and/or hyperkalaemia, even if they seem relatively well.

Which medicines are associated with BRASH syndrome?

Calcium channel blockers and beta-blockers depress AV node conduction and are most often associated with BRASH syndrome. Renally-cleared beta-blockers may increase the risk, as accumulation can occur as renal function worsens.

Other medicines that are associated with precipitating factors such as acute kidney injury, hyperkalaemia or reduced cardiac output may also contribute to the development of BRASH syndrome. Examples include angiotensin-converting enzyme(ACE) inhibitors, angiotensin II receptor blockers (ARBs), spironolactone, digoxin and amiodarone.

References

1. Medsafe : (click here)

Local Case Safety Report: Case of Pancytopenia /Shock /Drug toxicity / Diarrhea / Vomiting / Abdominal pain and Drug toxicity induced by incorrect dose administration of Methotrexate

Reason for publishing

On 20 July 2025, the Cairo Regional Center for Pharmacovigilance received a serious adverse drug reaction (ADR) report concerning an elderly female patient treated with Methotrexate for Rheumatoid Arthritis (RA).

Medication error: Patient was prescribed Methotrexate 50 mg/2 ml, to be given once daily intramuscularly, instead of the correct regimen (once weekly). On23 July 2025: The patient presented to the Emergency Room with acute gastrointestinal (GI) toxicity (vomiting, diarrhea, abdominal pain), later confirmed as Methotrexate toxicity.

Clinical course:

- Developed dehydration, metabolic acidosis.
- Day 2: Severe pancytopenia detected on CBC (anemia, leukopenia, thrombocytopenia).
- Deteriorated further with hemodynamic instability, required ICU admission and mechanical ventilation.

Background

Methotrexate

Indications: Used as an antineoplastic and immunosuppressant in cancers, severe psoriasis, and autoimmune diseases such as RA.

Mechanism of Action:

- Folate antagonist that inhibits key enzymes in nucleotide synthesis (e.g., dihydrofolate reductase, thymidylate synthase, AICART).
- Prevents immune cell proliferation (T-cells, macrophages).
- Decreases pro-inflammatory cytokines (TNF-α).
- Increases anti-inflammatory cytokines (IL-10).

Rheumatoid Arthritis

A chronic autoimmune disease characterized by joint inflammation, pain, swelling, and stiffness, with systemic involvement.

Methotrexate Toxicity

1. Risk Factors & Triggers
   - High doses (≥ 500 mg/m²).
   - Incorrect administration frequency (e.g., daily instead of weekly).
   - Comorbidities (renal/hepatic impairment).
   - Drug interactions.
2. Clinical Manifestations
   - Acute: GI disturbances (nausea, vomiting, diarrhea), CNS symptoms.
   - Chronic: Mucosal ulcers, skin lesions, pancytopenia.
   - Systemic effects:
     - Hematologic: Myelosuppression, pancytopenia.
     - Renal: AKI (due to crystallization or tubular toxicity).
     - GI: Ulceration, mucositis, diarrhea.
     - Hepatic/Pulmonary: Hepatitis, rare fibrosis or pneumonitis.

Management of Toxicity

1. Immediate cessation of Methotrexate.
2. Folinic acid (Leucovorin) rescue:
   - Restores folate pools.
   - Dose guided by serum Methotrexate levels.
3. Hydration & urinary alkalinization:
   - Maintain urine output >2 L/m²/day.
   - Keep urine pH >7.0 ($NaHCO_3$ infusion).
4. Supportive care:
   - ICU admission if severe.
   - G-CSF for bone marrow recovery.
   - Transfusions and infection prophylaxis.
   - Dialysis (high-flux) if renal clearance impaired.

Local Case Safety Report: Case of Pancytopenia /Shock /Drug toxicity / Diarrhea / Vomiting / Abdominal pain and Drug toxicity induced by incorrect dose administration of Methotrexate

Labeled Safety Information (SmPC)

Warnings:
Methotrexate must be prescribed once weekly; daily dosing errors have led to fatal toxicity.
Requires close monitoring of CBC.
Undesirable effects: Ulcerative stomatitis, leukopenia, GI distress.
Overdose:
Reported with erroneous daily use.
Management: Calcium folinate rescue, transfusion, dialysis if required.

Recommendations for Healthcare Professionals

Prescribers:
Explicitly state "once weekly" on all Methotrexate prescriptions.
Reinforce patient education on correct dosing schedule.

Pharmacists:
Provide counseling at dispensing to prevent overdose errors.
Highlight weekly schedule clearly on packaging/labels.

Prevention of Toxicity:
Co-prescribe folic acid/folinic acid to reduce GI/hepatic effects.
Advise patients to take folic acid on a different day than Methotrexate.

Patient Safety:
Educate patients on early warning signs (mouth ulcers, fever, fatigue, bleeding, severe GI upset).
Urgently report symptoms to physician/pharmacist.

Key Learning Point:

Methotrexate toxicity is often due to **medication errors in dosing frequency (daily instead of weekly)**. Such errors can rapidly result in **life-threatening pancytopenia and multi-organ failure**

References

1. ***Methotrexate SmPC:*** (click here)
2. ***Methotrexate drug information :*** (click here)
3. ***PubMed :*** (click here)
4. ***labeled information :*** (click here)

Together For Safer Medicine Initiative:

The Egyptian Pharmacovigilance Center (EPVC) is extremely proud of the 7th wave participants of the "Together for Safe Medicine" initiative.

- 47 participants from governmental and community pharmacies have successfully completed the required assignments and have now advanced to the executive phase, which will extend over the next three months, applying pharmacovigilance science in their workplaces.
- EPVC also extends sincere gratitude to all participants who made remarkable efforts in spreading pharmacovigilance awareness — whether through social media activities or by delivering educational lectures for healthcare professionals and the public.

Together, we continue our mission toward safe and effective medicine use in Egypt.

VigiTest Competition: The Journey of Challenge Continues!

Pharmacovigilance champions – the excitement isn't over yet!
The VigiTest Competition returns for another round, and it's your chance to sharpen your skills and showcase your knowledge in the field of pharmacovigilance.

•After an impressive past 3 rounds filled with enthusiastic participation and bright minds, the journey continues! Each month, we'll bring you updated and new questions in pharmacovigilance science and principles. Are you ready to rise to the challenge?
How to Join: It's simple. Scan the QR code provided in the newsletter or tap the link below to access the competition questions. Answer the questions correctly with your knowledge and skill, to secure your spot among the top performers.
Monthly Winners: Every month, we'll recognize the top participants.
Annual Winners: At the end of the year, the top consistent winners will be recognized for their performance throughout the year and win certificate of appreciation for their participation.
Stay tuned for updates, results, and upcoming challenges in the next release.
The competition is ongoing — and the next challenge is waiting for YOU!
Scan the QR code or tap the link below, follow the instruction and answer the questions.
https://forms.gle/MrdUPNQHsMwtFmvK8

Scan me!

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BE-Vigilant Initiative News

The Egyptian Drug Authority (EDA) has officially launched the **BE-Vigilant Initiative** for 2025–2026, under the theme "**Expand the Learning More**…". This initiative is designed to support pharmacovigilance focal points across healthcare facilities and enhance the skills of users of the national database, particularly in managing and utilizing Vigiflow effectively.

The objectives of this national initiative are to:

1. Strengthen pharmacovigilance practices across healthcare institutions in Egypt.
2. Foster capacity building for focal points and broaden their learning journey.
3. Collaborate with healthcare providers to promote timely reporting of adverse drug reactions (ADRs) and ensure the safe use of medicines.
4. Enhance patient safety through continuous awareness and education by focal points.

The approaches of Be-Vigilant initiative:

EPVC is pleased to welcome the **Supreme Council of University Hospitals (SCOUH**) as a valued participant in the BE-Vigilant Initiative – Cohort 1. A total of 40 focal points from various university hospitals have participated, reflecting SCOUH's strong commitment to advancing pharmacovigilance. Their active involvement in the initiative's learning journey aims to enhance pharmacovigilance activities, and to improve the collection and reporting of adverse drug reactions (ADRs) in a more efficient and systematic manner.

EPVC extends its sincere appreciation to Mansoura International Hospital, affiliated with Secretariat of **Specialized Medical Centers (SMC),** for its active and outstanding contribution to pharmacovigilance efforts. The hospital's dedication to detecting and reporting special cases of adverse drug reactions (ADRs) has been truly commendable. These valuable reports have not only supported national drug safety monitoring but have also been featured in the EPVC newsletter, serving as exemplary cases that highlight the critical role of vigilant healthcare professionals in safeguarding patient safety.

The latest case published in the former EDA Newsletter was about Fournier's Gangrene.

EPVC would like to extend sincere appreciation to the Ismailia and Luxor Governorates at the General Authority for Healthcare (EHA), for their efforts in enhancing pharmacovigilance practices through various tools of patient education and awareness about the importance of pharmacovigilance.

Ismailia Medical Complex, Ismailia: The PV coordinator published an awareness video addressing recent safety alerts for certain medicines issued by the EDA.

Zarnekh Family Medicine, Luxor: The PV coordinator conducted an in-person awareness campaign at outpatient clinics, focusing on the importance of reporting ADRs and the available reporting channels.

EPVC Tips On Pharmacovigilance

A Message from the Expanded Program on Immunization (EPI)

The Expanded Program on Immunization (EPI) emphasizes the importance of vaccine safety and high-quality adverse event reporting. All stakeholders are encouraged to adhere to the following key clinical and reporting recommendations:

1. Clinical Management of Skin Reactions

Although vaccines are generally considered safe and have a favorable benefit–risk profile, adverse reactions may occur in a small proportion of vaccine recipients. Accordingly, the following recommendations are provided to minimize the occurrence and severity of such reactions and to ensure their appropriate management.

- Post-Immunization Inflammation

When a child develops skin inflammation or an injection-site reaction following a previous vaccine dose, the child should also be referred promptly to a dermatologist for specialized assessment and management.

- Continuation of Vaccination Following Allergic Reactions: Benefit–Risk Considerations

Certain vaccine-preventable diseases, such as rabies, are associated with an extremely high risk of mortality if left untreated. In contrast, allergic reactions that may occur following vaccination are generally manageable and treatable. Therefore, completion of the vaccination series remains essential. When clinically appropriate, prophylactic anti-allergic medication may be considered before administering subsequent vaccine doses.

2. Strengthening AEFI Reporting Practices

- Comprehensive Data Collection

To facilitate accurate assessment of serious adverse events following immunization (AEFIs), healthcare providers should ensure that all relevant clinical information is thoroughly documented and included in AEFI reports, thereby improving the quality and reliability of investigations.

- Documentation

Healthcare providers are encouraged to maintain a high level of vigilance and ensure complete documentation and follow-up of all suspected AEFI cases.

The commitment of healthcare professionals to these recommendations is essential for safeguarding public health, maintaining confidence in immunization programs, and supporting the continued success of the national vaccination program. All stakeholders are strongly encouraged to actively monitor, document, and report any AEFI in a timely manner.

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

You will find all EPVC Newsletters and DHPCs here

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.

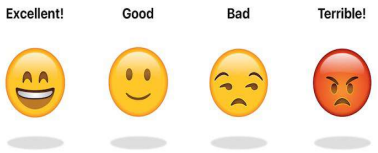
What is the Egyptian Pharmaceutical Vigilance Center?

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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