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

May 2023

Volume 14 **Issue 5**

Safety Alert !!

Buproprion: unmasking of Brugada syndrome

Buproprion may cause unmasking of Brugada syndrome, which may lead to cardiac arrest or sudden death

Bupropion hydrochloride is licensed for use in various forms and indications, including for the treatment of major

depressive disorder (MDD), the treatment of nicotine dependence as an aid to smoking cessation, and for weight

management in specific patients.

• Product information for bupropion containing medicines is to be updated to advise that use may unmask Brugada

syndrome. Brugada syndrome is a rare hereditary disease of the cardiac sodium channel with characteristic ECG

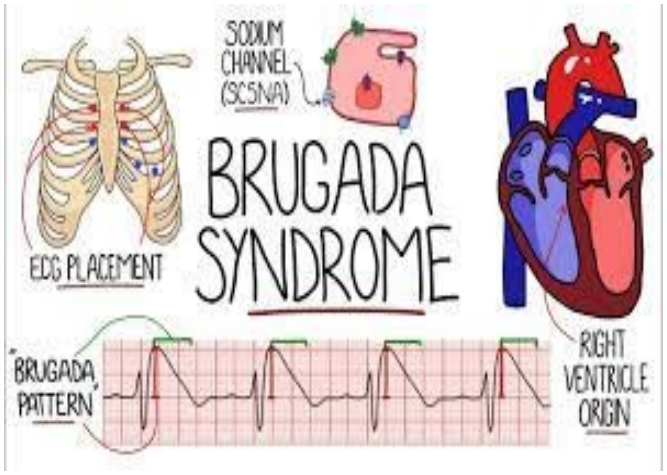
changes (right bundle branch block and ST segment elevation in right precordial leads).

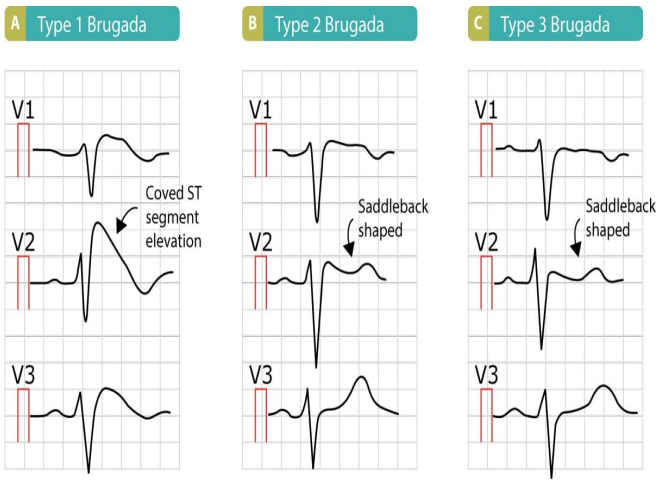
• Treatment with bupropion, in patients with Brugada syndrome may lead to cardiac arrest or sudden death and

caution is advised in these patients or in patients with a family history of cardiac arrest or sudden death.

• Patients are advised to talk to their doctor before taking bupropion if they have pre-existing Brugada syndrome

or if there is a family history of cardiac arrest or sudden death.





References:

HPRA: *(Click here)*

The Egyptian Pharmaceutical Vigilance center
مركز اليقظة الصيدلية المصري

EPVC Investigation reports

Aflibercept induced endophthalmitis and vitreous detachment

Introduction

Between January, 2023 and May, 2023, the Egyptian Pharmaceutical Vigilance Administration received 8 individual case safety reports of ophthalmology cases experienced Endophthalmitis and/or Vitrectomy after receiving Aflibercept Intravitreal injection.

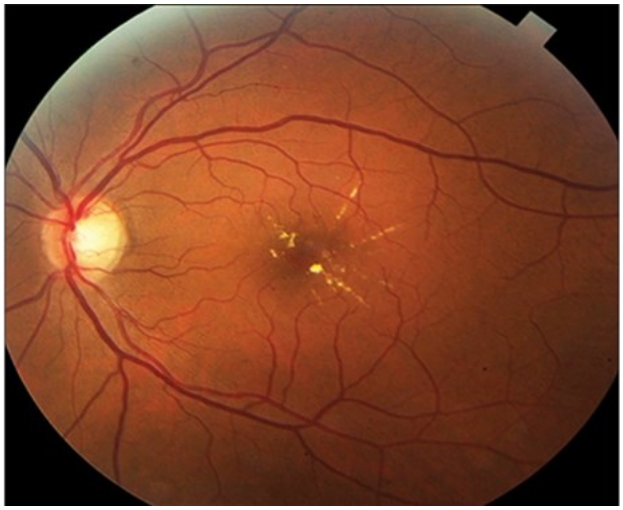
Background:

A. Ophthalmic-related issues

1. Macular Edema

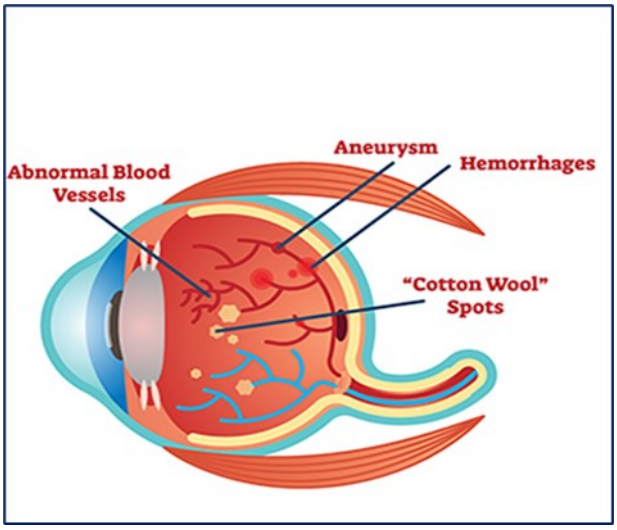
Macular edema is swelling in part of the retina (the light-sensitive layer of tissue at the back of your eye). People with macular edema may have blurry vision, but treatment can reduce swelling and prevent vision loss.

Causes of macular edema:



Macular edema happens when blood vessels leak into a part of the retina called the macula. This makes the macula swell, causing blurry vision.

- Diabetic macular edema (DME): When diabetic retinopathy causes macular edema.
- Age-related macular degeneration (AMD): In a certain type of AMD called wet (or neovascular) AMD, abnormal blood vessels in the macula leak fluid into or under the retina, which can cause swelling in the macula.



- Retinitis pigmentosa (RP):RP is a genetic disease. Some people with RP can also have swelling in the macula.

- Uveitis: Uveitis is inflammation inside the eye that happens when the immune system attacks eye tissue. It can cause swelling in any part of the eye, including the macula.
- Blocked veins in the retina (retinal vein occlusion). When veins in the retina are blocked, blood can't drain the way it should, and it leaks into the macula which can cause swelling.

2. Diabetic Retinopathy

Diabetic retinopathy is a serious sight-threatening complication of diabetes. Diabetes interferes with the body's ability to use and store sugar (glucose). The disease is characterized by too much sugar in the blood, which can cause damage throughout the body, including the eyes.

Over time, diabetes damages small blood vessels throughout the body, including the retina. Diabetic retinopathy occurs when these tiny blood vessels leak blood and other fluids. This causes the retinal tissue to swell, resulting in cloudy or blurred vision.

Aflibercept induced endophthalmitis and vitreous detachment (continued)

3. Endophthalmitis

Endophthalmitis is an infection of the tissues or fluids inside the eyeball. It is an urgent medical emergency. Endophthalmitis can blind the case if it's not treated quickly.

There are two main types of endophthalmitis:

Exogenous Endophthalmitis: This is the most common type of endophthalmitis. With this type, the source of the infection comes from outside the body. Bacteria or fungi gets inside the eye from surgery, an injection into the eyeball or an eye injury.

Symptoms usually begin within only a few days of an eye procedure or injury. When symptoms begin quickly like this, it is acute endophthalmitis.

The infection can also develop more slowly. When symptoms take longer to emerge, it is chronic endophthalmitis. This happens when specific types of bacteria or fungi enter the eye.

Endogenous Endophthalmitis: This is the second main type of endophthalmitis. It starts as an infection in another part of the body and spreads to the eye. For example, this can happen with a urinary tract infection or blood infection.

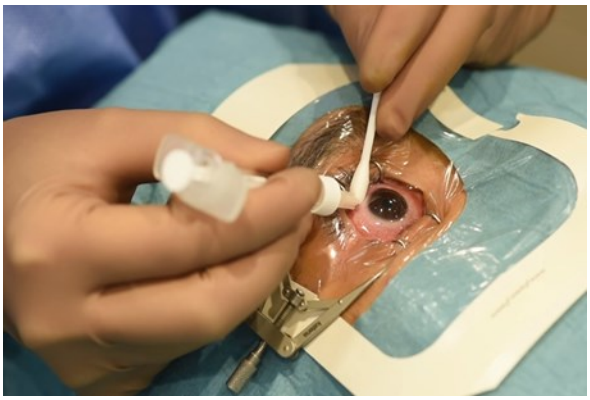
Endophthalmitis another classification: Infectious endophthalmitis and non- infectious endophthalmitis:

More Common Features	Infectious	Noninfectious
Pain	Moderate to severe pain	Usually mild pain
Vision loss	Severe	Mild to moderate
Fibrin	Always present	Rare
Hypopyon	Very common	Usually absent
Vitreous opacity	Usually prominent	Usually mild
Conjunctival/vascular congestion	Very common	Often absent
Less Common Features	**Infectious**	**Noninfectious**
Retinal infiltrates	Occasionally present	Absent
Intraretinal hemorrhages	Common	Rare
Whitening of retinal vessels	May be present	Absent
Clinical Course	**Rapidly progressive**	**Slow improvement**

3.Intravitreal injection

Intravitreal injections are the fastest growing procedure in ophthalmology and their expanding use represents one of the most dynamic areas of innovation over the past decade in the treatment of eye disease. IVT drug delivery considerably minimizes systemic exposure and directly bypasses the eye's natural barriers allowing for intraocular levels of drug not obtainable with systemic or even topical administration.

Intravitreal injections involve injecting therapeutic agents inside the vitreous cavity through pars plana under aseptic precautions.



4.Vitrectomy

Vitrectomy is an eye surgery used to treat problems of the eye's retina and vitreous. In this surgery, an ophthalmologist:

- Remove blood or other substance keeping light from focusing properly on the retina
- Remove scar tissue that is wrinkling or tearing the retina and causing poor vision
- Help repair a retina that has detached (pulled away) from the eye wall

- Remove a foreign object stuck inside the eye from an injury
- During vitrectomy, the ophthalmologist removes some or all the vitreous from the middle of the eye. This vitreous is replaced with either a salt water (saline) solution or a bubble made of gas or oil.
- During healing after surgery, the eye replaces the saline solution or the bubble with the natural fluid the eye makes called aqueous humor.

Aflibercept induced endophthalmitis and vitreous detachment (continued)

Vitrectomy indications:

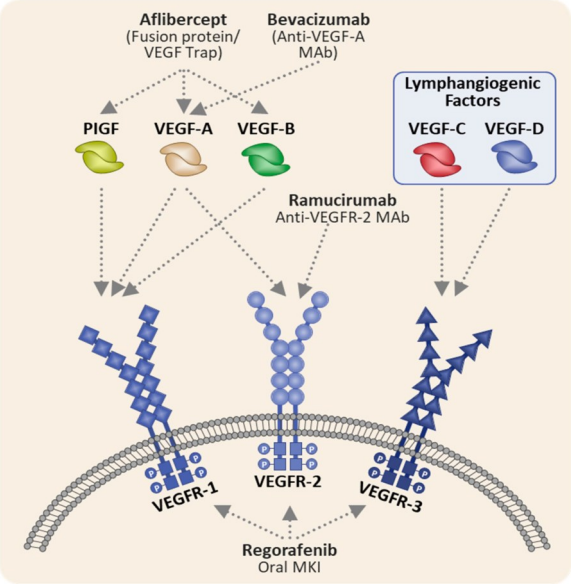
- Diabetic retinopathy, with bleeding or scar tissue affecting the retina or vitreous gel
- some forms of retinal detachment (when the retina lifts away from the back of the eye)
- macular hole (a hole or tear in the macula)
- macular pucker (wrinkles or creases in the macula).
- Endophthalmitis
- Severe eye injury
- Certain problems during cataract surgery

Aflibercept Dose

-Aflibercept 40 mg/mL solution for Intravitreal injection in a single-use vial)

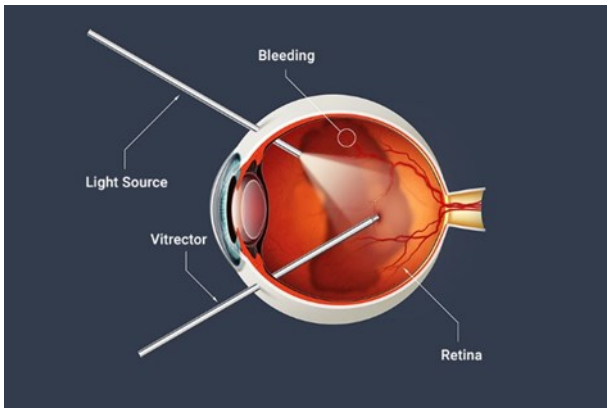
Aflibercept Mechanism of Action:

Aflibercept is a recombinant fusion protein that acts as a decoy receptor for vascular endothelial growth factor-A (VEGF-A) and placental growth factor (PLGF). Aflibercept binds to VEGF-A and PLGF and inhibits binding and activating of endothelial cell receptors, thereby suppressing neovascularization and slowing vision loss.



Aflibercept Indications

1. Age-related wet macular degeneration
2. Diabetic macular edema and retinopathy
3. Macular edema following retinal vein occlusion.
4. Retinopathy of prematurity



The risk of Endophthalmitis with Aflibercept is already described in the product information: The FDA reported that Endophthalmitis occurs in <0.1% of Intravitreal injections with Aflibercept. According to the EMA's summary of product characteristics (SPCs), Endophthalmitis is un - common side effect for Aflibercept. While Lexicomp concluded that Aflibercept induced Endophthalmitis is less than 1%. Regarding Vitreous detachment: vitreous detachment (2% to 8%), vitreous opacity (1% to 8%)

Aflibercept induced endophthalmitis and vitreous detachment (continued)

RECOMMENDATIONS

To the ophthalmologist and HCPs:

Prevention is key to reducing the incidence of infectious endophthalmitis. An outbreak of post-intravitreal endophthalmitis resulted from poor aseptic technique.

Povidone-iodine: Recommended for all intravitreal injections

The use of sterile gloves is recommended as part of universal precautions.

Avoid the lash and lid touch.

Use of a sterile lid speculum is recommended during the injection to prevent needle contact with the lids or lashes.

Face masks are recommended and talking should be limited as much as possible.

The vial is for single use in one eye only.

The vial contains more than the recommended dose of 2 mg aflibercept (equivalent to 0.05 mL). The excess volume must be discarded prior to administration.

The solution should be inspected visually for any foreign particulate matter and/or discoloration or any variation in physical appearance prior to administration. In the event of either being observed, discard the medicinal product.

For the intravitreal injection, a 30 G x ½ inch injection needle should be used.

Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry. If required, sterile equipment for paracentesis should be available.

Following intravitreal injection patients should be instructed to report any symptoms suggestive of endophthalmitis (e.g. eye pain, redness of the eye, photophobia, blurring of vision) without delay.

Each vial should only be used for the treatment of a single eye. Extraction of multiple doses from a single vial may increase the risk of contamination and subsequent infection.

Key signs and symptoms of intravitreal injection related adverse events including endophthalmitis, intraocular inflammation, increased intraocular pressure, retinal pigment epithelial tear and cataract.

Traceability:

To improve the traceability of Aflibercept (biological medicinal product), the name and the batch number of the administered product should be clearly recorded.

Patient counseling points:

You may experience temporary visual disturbances after an Intravitreal injection with AFLIBERCEPT and the associated eye examinations.

Not to drive or use machinery until visual function has recovered sufficiently.

In the days following AFLIBERCEPT administration, you are at risk of developing endophthalmitis, or retinal detachment.

If your eye becomes red, sensitive to light, painful, or develops a change in vision, the patient should seek immediate care from an ophthalmologist.

References:

1. Intro : (Click here)

2.FDA: (Click here)

3. EMA: (Click here)

4.Vitrectomy: (Click here)

5. Eye Problems:(Click here)

6. Eye conditions:(Click here)

7.Intravitreal-injection: (Click here)

8.Intravitreal-injection Complication: (Click here)

9. Intravitreal-injection Complication: (Click here)

Two cases from Cairo : Atracurium besilate- Isoflurane caused cardiac arrest and bronchospasm due to inappropriate dose adjustment (Medication error)

Introduction Paragraph:

The regional center in Cairo received two fatal cases following the administration of Atracurium besilate and Isoflurane together:

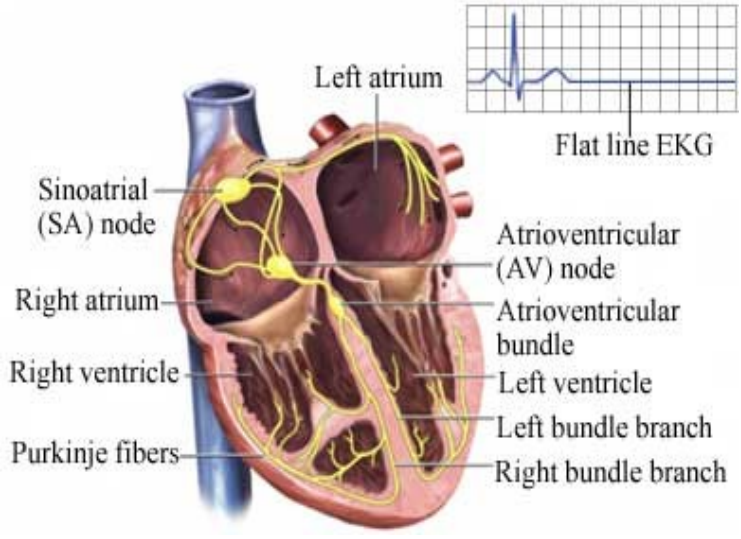
The first case is concerning a 12 years old male child weighing 30 Kg who was admitted to the hospital for tonsillectomy. The patient was administered Atracurium besilate with a dose of 20 mg (the calculated accurate dose according to the patient's weight is 12-18 mg) [1] as an intravenous injection, and isoflurane 1.5 %, with a dose 1.5 % (the accurate dose according to the patient weight ranges from 1.5% to 3 %) [2], as inhalation.

After administration, the patient developed cardiac arrest.

Corrective treatment was given in the form of corticosteroid and adrenaline injections.

Concomitant drugs were administered include: Propofol 150 mg and alfentanil with dose 25 mcg intravenously.

The second case is concerning a 10 year old male child weighing 30 Kg, was admitted to the hospital for Appendectomy. On 23/1/2023 the patient was administered Atracurium besilate with a dose 15 mg (the accurate dose according to the patient's weight is 12-18 mg) [1] as an intravenous injection, and Isoflurane 1.5 %, with dose 1.5 % (the accurate dose according to the patient weight ranges from 1.5% to 3 %) [2] as inhalation.



After administration, the patient developed severe bronchospasm following the intubation.

Which resulted in intensive care unit (ICU) admission.

Concomitant drugs which were administered include: Propofol 60 mg and alfentanil with a dose of 30 mcg intravenously.

According to the Summary of Product Characteristics (SmPC) of Atracurium besilate, in case of concomitant administration of both atracurium and isoflurane dose adjustment is required as Isoflurane and Enflurane increase the potency of atracurium and prolong neuromuscular block by approximately by 35%. [3]

Two cases from Cairo : Atracurium besilate- Isoflurane caused cardiac arrest and bronchospasm due to inappropriate dose adjustment (Medication error) (Continued)

Background:

Atracurium besilate is a non-depolarizing neuromuscular blocking agent with a short duration of action. Its lack of significant cardiovascular effects and its lack of dependence on good kidney function for elimination provide a clinical advantage over alternate non-depolarizing neuromuscular blocking agents. [4]

Labeled information:

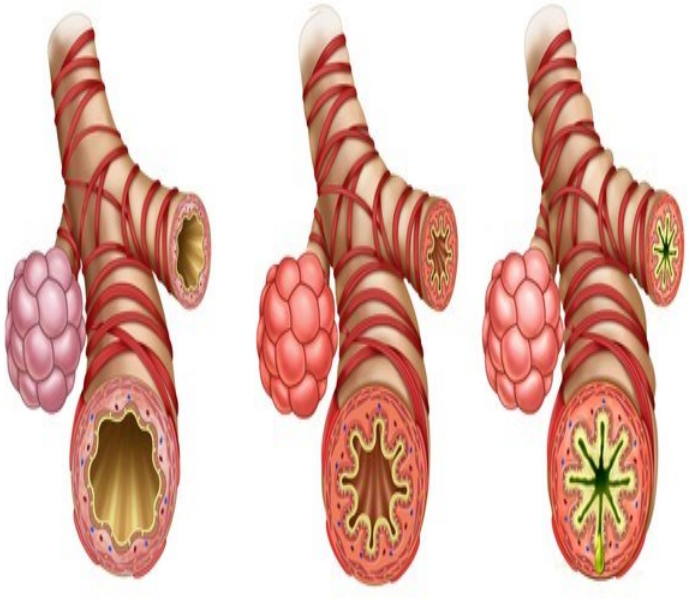
According to Atracurium besilate SmPC [5] it was stated under Interaction with other medicinal products and other forms of interaction section; Concomitant use of inhalation anaesthetics such as halothane, isoflurane or enflurane may increase the neuromuscular block produced by atracurium besilate.

Dosage and Administration:

The usual dose for adults ranges from 0.3 to 0.6 mg/kg of body weight (depending on the required duration of full block) and provides adequate relaxation for 15 to 35 minutes. (The dosage based on body weight in children over the age 1 month is the same as in adults).

Recommendations for Healthcare Professionals:

Moderate interaction was found between Atracurium and Isoflurane as isoflurane can prolong the effects of atracurium. Close monitoring for prolonged breathing cessation and respiratory paralysis after use of isoflurane is required [6].



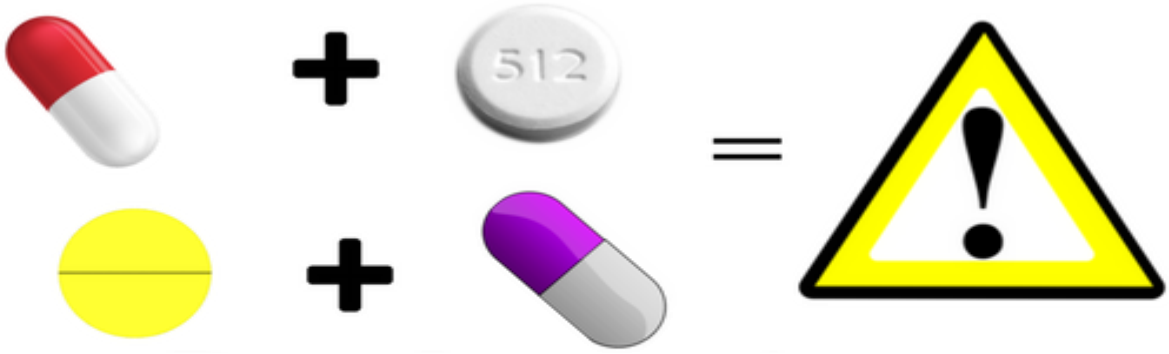
Bronchospasm

Dose adjustment for atracurium besilate must be performed during the concomitant use of inhalation anaesthetics such as halothane, isoflurane or enflurane that may increase the neuromuscular block produced by atracurium besilate. (Isoflurane and enflurane increase the potency of atracurium and prolong neuromuscular block by approximately 35%) [3].

Atracurium besilate should be administered only in a unit with adequate facilities for endotracheal intubation and artificial ventilation.

Two cases from Cairo : Atracurium besilate- Isoflurane caused cardiac arrest and bronchospasm due to inappropriate dose adjustment (Medication error) (Continued)

- Accurate dose of atracurium besilate must be calculated based on the patient body weight as stated in the SmPC of Atracurium as follows; The usual dose for adults ranges from 0.3 to 0.6 mg/kg of body weight (depending on the required duration of full block) and provides adequate relaxation for 15 to 35 minutes. (The dosage based on body weight in children over the age 1 month is the same as in adults) [5].
- atracurium besilate Interaction with other medicinal products must be taken in consideration as stated in the SmPC of the drug (As with all non-depolarizing neuromuscular blocking agents, non-depolarizing neuromuscular block may be increased and/or extended by interaction with inhalation anesthetics, antibiotics, antiarrhythmic agents, diuretics, magnesium sulfate, ketamine) [5].



References:

1. Atracurium besilate dose(Click here)
2. Isoflurane dose (Click here)
3. Atracurium besilate SPMC (Click here)
4. Atracurium besilate background(Click here)
5. Atracurium besilate Interaction with other medicnal products (Click here)
6. Atracurium besilate and isoflurane drug interaction (Click here)

Together for Safe Medicine Initiative Progress

The Egyptian pharmacovigilance center Keeps on thanking all participating pharmacists in the first three waves of the Initiative "Together for Safe Medicine "for their important role in practicing and spreading pharmacovigilance science in their Community and governmental pharmacies which lead to an increase in the ADRs reporting rate with continuous improvement in reports quality to the Pharmacovigilance national database where the first three waves activities started from 20 September 2022 till January 2023 and ended with receiving a badge. The Received badge is to be hung in shared pharmacies indicating their valuable sharing and practicing of Pharmacovigilance will be renewed after two years provided that the shared pharmacies keeping in practicing Pharmacovigilance activity and sending ADRs reports to the national database through E-reporting Link so EPVC encourages all shared pharmacists too keep on and never stop sharing and sending ADRs reports because it is our honor to keep Sharing with us in EPVC Community Club and to keep in saving patients lives through practicing pharmacovigilance.

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

As the Vigiflow expansion project continued, The Egyptian Pharmaceutical Vigilance Centre (EPVC) is pleased to announce that the number of received individual case safety reports (ICSRs) through the national database has increased significantly.

To enhance the quality of the received ICSRs submitted through the national database, EPVC is delighted to review them and give comments to the coordinating organizations, asking if any extra training is needed.

As one of the most cooperative organizations, EPVC would like to express its appreciation to the Egyptian Healthcare Authority (EHA), particularly the Port Said organizations that recently joined the Vigiflow expansion project. The EPVC would like to express its gratitude for their effort and wish them well in the future.

EPCV would like to thank the participating institutes for their great effort in Vigiflow expansion project specially :

1. **Qena Oncology Centre**
2. **Meet Ghamr Oncology Centre**
3. **Damanhour Oncology Centre**

Looking foreword for more fruitful collaborations

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EPVC Tips On Pharmacovigilance

Medication-Overuse Headaches

The Big Catch-up

Vaccines reduce risks of getting a disease by working with your body's natural defenses to build protection. When you get a vaccine, your immune system responds. Nowadays we have vaccines to prevent more than 20 life-threatening diseases, helping people of all ages live longer, healthier lives.

'The Big Catch-up' is an extended effort to lift vaccination levels among children to at least pre-pandemic levels and endeavors to exceed those, as During the pandemic, essential immunization rates declined in over 100 countries.

This effort is Led by a broad range of national and global health organizations, also it aims to ensure stronger primary health care services for essential immunization in the future.

Visit EDA website to find all any 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
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One report counts

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

A call for reporting

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

Communication information

The Egyptian Drug Authority (EDA)
Pharmaceutical Care Administration
The Egyptian Pharmaceutical Vigilance Center (EPVC)

Address: 21 Abd El Aziz AlSoud Street. El-Manial, Cairo, Egypt, PO Box: 11451
Hotline: 15301
Fax: +202 – 23610497
Email: pv.followup@edaegypt.gov.eg
Reporting link: www.edaegypt.gov.eg
https://sites.google.com/view/epvc-reporting/healthcare-professional-public-adverse-drug-event-reporting/reporting-other-adverse-drug-event-cases

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