A Review on Nitroglycerin: Present and Future
Department of Anesthesia, Intensive Care and Pain management,
Faculty of Medicine, Zagazig University, Egypt
*Corresponding author: Ahmed Ezzat Attia Mostafa, Mobile: (+20)01020427065, E-mail: midozewil@gmail.com

ABSTRACT
Nitroglycerin, a vasodilator, is typically used to treat anginal chest discomfort. The FDA currently approves it for the acute prophylaxis of angina pectoris owing to coronary artery disease (CAD) as well as the acute alleviation of an episode. The treatment of hypertensive urgency/emergency, coronary artery spasm, cocaine-related angina, congestive heart failure (CHF), and chronic anal fissures are a few of the unapproved, off-label uses for this medication. In order for medical professionals to successfully direct patient therapy in circumstances where nitroglycerin is advantageous to patient care, the present review describes the indications, mechanism of action, routes of administration, significant adverse effects, contraindications, monitoring, and toxicity of nitroglycerin.

Keywords: Nitroglycerin, Angina pectoris, Chronic anal fissure, Review, Zagazig University.

INDICATIONS OF NITROGLYCERIN
Nitroglycerin, a vasodilator, is commonly employed to treat anginal chest pain. Nitroglycerin, which Pfizer first offered for sale under the trade name Nitrostat, has been recognized by the FDA since 2000. The FDA currently approves it for the acute prophylaxis of angina pectoris owing to coronary artery disease as well as the acute alleviation of an episode. The treatment of hypertensive urgency or emergency, coronary artery spasm, cocaine-induced angina, congestive heart failure (CHF), and chronic anal fissures are only a few examples of off-label, unauthorized usage (1,2).

The powerful intended effects of nitroglycerin are predominantly brought on by venodilation, despite the fact that it has a vasodilatory effect in both arteries and veins. Blood pools in the venous system as a result of venodilation, which diminishes demand ischemia-related angina symptoms and lowers the preload on the heart. Vasodilation of the blood vessels still happens and helps to relieve anginal symptoms, but the results won't be as noticeable. Increased blood flow to the heart through the coronary arteries will improve perfusion, however this benefit is minor compared to venodilation's effects (3,4).

MECHANISM OF ACTION
Nitroglycerin transforms into nitric oxide (NO) in the body, just like other nitrates used to alleviate anginal chest discomfort. Guanosine is activated by NO and then converted by the enzyme guanylyl cyclase. Guanosine 3',5'-triphosphate (GTP) is converted to vascular smooth muscle and other tissues produce guanosine 3',5'-monophosphate (cGMP).

Following the activation of numerous protein kinase-dependent phosphorylations, myosin light chains within smooth muscle fibers are ultimately dephosphorylated by cGMP. This activity results in the desired vasodilatory effect by relaxing the smooth muscle in blood vessels (5,6).

ADMINISTRATION
Most frequently, nitroglycerin is given as a tablet to be swallowed sublingually. It is prescribed for outpatient use and given at medical facilities. Patients may be administered nitroglycerin as a preventative measure for anginal chest discomfort prior to an event that could potentially trigger anginal symptoms. They need to be told to wait for the nitroglycerin to completely dissolve in their mouths and for the drug to permeate the mucosa of their oral cavities. There are three different doses: 0.3 mg, 0.4 mg, and 0.6 mg. Every five minutes until relief is noticed, repeat the dose. After three doses, if anginal pain still exists, immediate medical intervention is necessary. Within 1 to 3 minutes after administration, vasodilatory effects start to show up, peaking in 5 minutes. The liver is where nitroglycerin is primarily metabolized, and its half-life is typically 2 to 3 minutes (2).

The most common way to deliver nitroglycerin in intensive care units (ICU) and emergency rooms is intravenously (IV). When sublingual nitroglycerin has not worked to ease symptoms or when prompt, continuous symptom alleviation is needed, it is administered. It is given as a drip of 5% dextrose in water with a starting IV infusion dose of 5 mcg/min. In order to treat acute coronary syndromes, the drip is routinely employed hypertensive emergencies, and exacerbations of congestive heart failure (CHF). Its impact requires thorough observation after delivery (3).

Nitroglycerin is routinely administered transdermally to treat acute angina episodes in emergency rooms. The patient's skin is treated with a 2% ointment before being let to soak. It is mostly utilized for individuals who are unable to tolerate sublingual nitroglycerin administration or who have previously had a negative the sublingual tablet's response. Absorption is followed by full impact in 5 to 10 minutes. Since hair can prevent absorption, it is preferable to apply on a surface with little to no hair. If additional dosages are required, care must be taken to prevent applying to the same region again. Dermatitis
and skin irritation might result from frequently applying the ointment to the same area. There are further transdermal patches available in doses of 0.1 mg, 0.2 mg, 0.4 mg, and 0.6 mg every hour, although these are only employed for the prevention of angina. The same application precautions for the ointment and patches are used (7).

SIDE EFFECTS

The majority of the harmful side effects of nitroglycerin are caused by the drug’s vasodilatory properties. These properties consist of:

- Dizziness
- Weakness
- Palpitations
- Vertigo
- Headaches
- Nausea
- Vomiting
- Diaphoresis
- Syncope

Numerous of these negative effects are a result of nitroglycerin’s hypotensive effects. Patients may experience dizziness, weakness, palpitations, and vertigo as symptoms of orthostatic hypotension. Patients with conditions that depend on preload may experience severe hypotension. Even at therapeutic levels, Nitrate-induced hypotension, which can cause nausea, vomiting, diaphoresis, pallor, and collapse in some patients, may be more common. Headaches can be really bad, throbbing, chronic, and they can happen right away. The most harmful side effect, syncope, can cause falls and the injuries they bring. When an inhibitor of phosphodiesterase-5 (PDE-5) is utilized concurrently, the risk of syncope greatly rises (8). Additionally, some patients taking nitroglycerin have been reported to experience drug rash, flushing, and exfoliative dermatitis (7).

CONTRAINICATIONS

Although reports are extremely rare, nitroglycerin allergies do exist. Patients who have complained of allergic reactions to the drug should not take nitroglycerin.

Nitroglycerin therapy is not recommended if there is documented history nitroglycerin hypersensitivity, severe anemia, a right-sided myocardial infarction, or increased intracranial pressure.

Nitroglycerin and PDE-5 inhibitors like sildenafil citrate, vardenafil hydroxide, or tadalafl shouldn’t be used together. It has been demonstrated that PDE-5 inhibitors exacerbate the hypotensive effects of nitrates and hasten syncopal episodes (8).

MONITORING

Nitroglycerin is quickly metabolized by the body and has a half-life of 2 to 3 minutes no testing is currently done to keep track of its levels. Its effects are frequently closely watched when given for measuring blood pressure in real-time as a drip in the intensive care unit or emergency room. The efficiency of the drip must be maximized in order to provide timely input on the patient’s health. The effectiveness of nitroglycerin when given sublingually is often evaluated on the basis of the disappearance of symptoms, including angina, hypertension, and heart failure (CHF), among others.

Monitoring vital signs may be important in the event of an overdose in order to track the hemodynamic effects of the nitroglycerin. It is advised to continuously monitor your oxygen saturation, heart rate, breathing rate, and blood pressure.

Both nitroglycerin and its hepatic metabolism are characteristics of a medication that is protein-bound. As a result, there are several medication interactions. Providers should ascertain whether before prescription, Verify that the patient is not taking any drugs that might interact with nitroglycerin. Tricyclic antidepressants, Heparin, alteplase, and several anticholinergic medications are among those that frequently interact. Limiting alcohol consumption is also advised.

Because nitroglycerin is in pregnancy category C, breastfeeding mothers should exercise caution when using it. The possibility of nitroglycerin excretion in breast milk is currently unknown (13).

TOXICITY

Nitroglycerin overdose toxicity is primarily caused by an augmented vasodilatory reaction. In these patients, it is normal to anticipate hypotension, venous pooling, increased vasodilation, and decreased cardiac output. Also possible are compensatory effects like tachycardia and palpitations. In addition to unpleasant headaches, vasodilation and venous pooling can increase the volume of blood in the cranial space, raising intracranial pressures and triggering other symptoms like confusion, fever, vertigo, nausea, and vomiting. The symptoms will worsen as intracranial pressure rises, finally resulting in dyspnea caused by decreased respiratory effort, heart block, bradycardia, paralysis, seizures, coma, and death (20).

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REFERENCES
