DRUG UPDATE

Centhaquine: The New Paradigm in Hypovolemic Shock Management

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INTRODUCTION:

2-[2-[4-(3-Methylphenyl) piperazin-1-yl] ethyl] quinoline citrate, or, Centhaquine.

Indian scientist found in earlier animal model studies that drug has paradoxical effect. The drug with higher doses decreased blood pressure, lower doses in fact increased blood pressure in rats with blood loss. This led to studies which revealed that centhaquine is a highly effective resuscitative agent for the hypovolemic shock.

Centhaquine is indicated as a newer resuscitative agent for the treatment of patients with hypovolemic shock as an adjuvant of care. Centhaquine uniquely stimulates alpha 2β-adrenergic receptors to increase venous blood return and cardiac out put ; and on alpha 2α-

adrenergic receptors to decrease vascular resistance, thereby enhancing tissue blood perfusion.

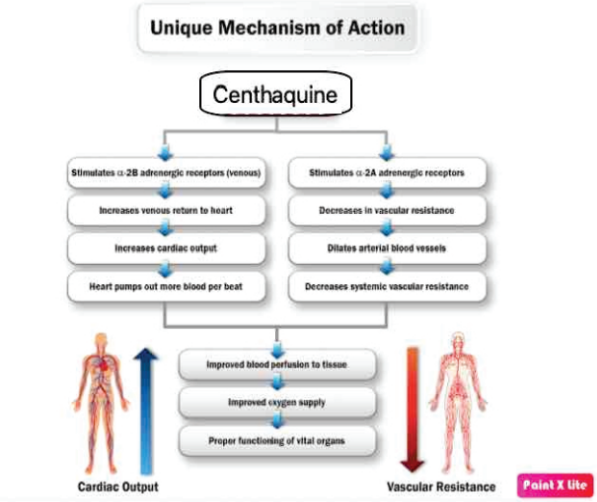

Diagram 1: adopted from lyfaquin.com

Enhancing tissue blood perfusion has a significant advantage in reducing the volume of resuscitation and preventing extravasation of fluids, fluid over load. Centhaquine does not act on beta-adrenergic receptors and therefore the risk of arrhythmia is mitigated.

Preclinical studies :

In a rabbit blood loss model, a pig and a rat model centhaquine significantly reduced the amount of fluid and norepinephrine needed to maintain a target mean arterial pressure.

Serum lactate levels were also lower in the centhaquine group an hour after resuscitation. This is noteworthy, as hypovolemic shock increases serum or blood lactate, which characterised into a poor prognosis that is high risk of mortality and poor patient outcomes.

Clinical studies in humans:

In a phase 1 trial to determine safety and tolerability, intravenous centhaquine was found to be safe and well tolerated. The adverse events happened only at a dose ten times the normal therapeutic dose of 0.01 mg/kg. However, they were mild and resolved within an hour without medical interventions.

Phase 2 trail of Centhaquine's safety and efficacy as a resuscitative agent alongside the standard treatment for hypovolemic shock from blood loss; When given 0.01 mg/kg centhaquine, patients had improved blood pressure, lactate levels, required less vasopressors, and had reduced mortality. Any adverse events in this trial were unrelated to the study.

After promising out-come of phase 1 and 2 trials; a phase 3 trial took place in multiple emergency rooms and ICU units within India. Patients with a mean arterial blood pressure (MAP) of 65 mmHg or less and lactate levels indicative of shock, and who were receiving standard care for hypovolemic shock were intravenously given 0.01 mg/kg centhaquine or a control. 71 patients were given centhaquine, and 34 were given a control dose of normal saline, all of whom had lost a similar amount of blood. If systolic blood pressure remained below 90 mmHg after four hours, another dose was given. The minimum number of doses given over 48 hours was one , and the maximum was six.

After twenty days, the mortality in the group given centhaquine was 2.94%, versus 11.76% in the

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control group. The serum lactate levels after three days were also significantly higher in the control group, with only 46.88% having a level of 1.5 mmol or less, compared to 69.35% of the group given centhaquine. Patients given centhaquine also showed an increase in pulse pressure and mean arterial blood pressure.

SOFA score were improved in patients given centhaquine. Contrastingly, the control group had no change in acute respiratory distress syndrome scores, and actually saw worsening multiple organ dysfunction.

Method of Preparation:

Therapeutic dose: 0.01mg/kg body weight

Safety and Contraindications:

Hypersensitivity to Centhaquine or to any of the excipients.

Special warnings and precautions for use:

Centhaquine should be administered with precautions in hepatic failure, renal failure and decompensated heart failure patients as safety and efficacy of Centhaquinehas not been established in the same cases

The safety and efficacy of Centhaquine is also not established in pregnancy, lactating women, paediatric and geriatric population.

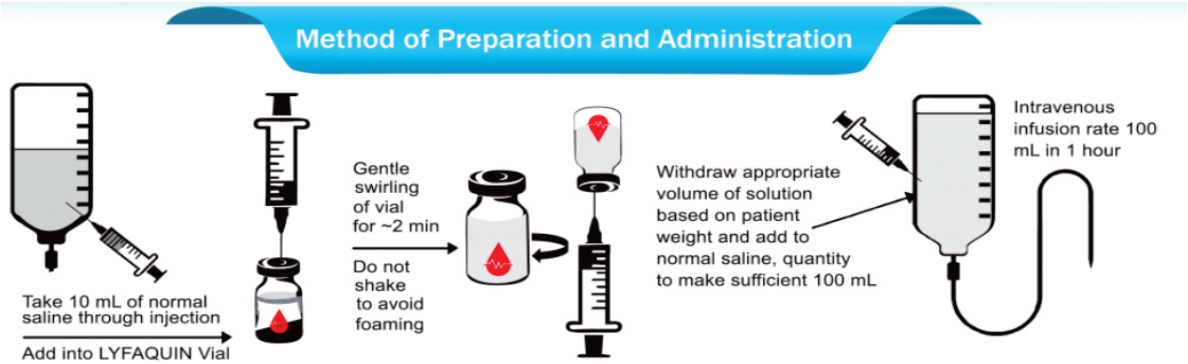

Diagram 2: adopted from lyfaquin.com

Drugs interactions:

No drug-drug interaction or drug-food interaction has been observed.

Together, these preclinical and clinical results show that centhaquine is an effective and safe resuscitative agent for hypovolemic shock, improving patient outcomes and saving lives. Centhaquine is now approved for use by the Drug Controller General of India as an additional resuscitative agent for hypovolemic shock.

REFERENCE : On line access on 28/07/21 from following links

1. https://researchoutreach.org/articles/ centhaquine-new-resuscitative-agent-haemorrhagic-shock
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