



The VAM-IHCA Trial

Key Article

Andersen LW, et al. *Effect of vasopressin and methylprednisolone vs placebo on return of spontaneous circulation in patients with in-hospital cardiac arrest.* JAMA. 2021. Published online September 29, 2021.

Background

- In-hospital cardiac arrest (IHCA) occurs in approximately 290,000 patients per year in the US.
- Though improved when compared to OHCA, survival to hospital DC for IHCA is still low at approximately 25%.
- Similar to OHCA, best practice for IHCA resuscitation centers on immediate recognition, high-quality chest compressions, early defibrillation, and post-cardiac arrest care.
- Medications commonly used in IHCA include epinephrine, amiodarone, and lidocaine.
- In 2009 and 2013, Mentzelopoulos and colleagues published two studies that demonstrated improved ROSC and survival to hospital DC for IHCA patients that received vasopressin and methylprednisolone.
- Though these two trials were positive, both the AHA and European resuscitation guidelines have not recommended this drug combination for IHCA due to lack of additional evidence.
- The current trial was performed to essentially validate the results of these two prior trials.

Objective

- To determine whether the combination of vasopressin and methylprednisolone administered during in-hospital cardiac arrest improve return of spontaneous circulation.

Study

- Randomized, placebo-controlled, parallel group, double-blind, superiority trial
- 10 hospitals in Denmark
- Patients
 - Included
 - 18 years of age or older
 - IHCA
 - Received at least 1 dose of epinephrine during cardiac arrest
 - Excluded
 - OHCA
 - DNR order prior to arrest
 - Receiving ECMO or had an LVAD at the time of arrest
 - Pregnancy
- Intervention
 - Patients randomized in a 1:1 ratio
 - Vasopressin / Methylprednisolone Group
 - 20 IU vasopressin
 - 40 mg of methylprednisolone

- Given as soon as possible after the first dose of epinephrine
 - Additional doses could be administered after each epi dose for a max of 4 doses
 - Placebo Group
 - Ampules of sodium chloride
- Primary Outcome
 - Return of spontaneous circulation for at least 20 minutes
- Secondary Outcomes
 - Survival at 30 days
 - Favorable neurologic outcome at 30 days
- Adverse Events
 - Hyperglycemia
 - Hyponatremia
 - Infections
 - GI bleeding
 - Mesenteric and peripheral ischemia

Results

- Overall, 2632 patients with IHCA were screened during the trial period.
- A total of 501 patients were included in the analysis
 - Vasopressin / Methylprednisolone Group: 237 patients
 - Placebo Group: 264 patients
- Baseline characteristics were similar between the groups
 - Mean age: 71 years
 - 64% were men
 - 66% occurred on a general medical or surgical ward
 - 90% of patients had an initial non-shockable rhythm
 - Median time from arrest to first epi and trial drug administration was 5 minutes and 8 minutes, respectively
- Primary Outcome - ROSC
 - Vasopressin / Methylprednisolone Group: 42%
 - Placebo Group: 33%
 - Risk Ratio of 1.30 (95% CI 1.03-1.63; p=0.03)
 - Fragility Index = 3
- Secondary Outcomes
 - 30-day Survival
 - Vasopressin / Methylprednisolone Group: 9.7%
 - Placebo Group: 12%
 - Not statistically significant
 - Favorable neurologic outcome
 - Vasopressin / Methylprednisolone Group: 7.6%
 - Placebo Group: 7.6%
 - Not statistically significant
 - Favorable neurologic outcome at 30 days
 - Vasopressin / Methylprednisolone Group: 4.6%
 - Placebo Group: 7.2%
 - Not statistically significant
- Adverse Events

- Hyperglycemia
 - Vasopressin / Methylprednisolone Group: 77%
 - Placebo Group: 63%
- Hypernatremia
 - Vasopressin / Methylprednisolone Group: 28%
 - Placebo Group: 31%

Limitations

- Large number of patients screened, but only 501 patients ultimately included
- Though multicenter, took place only in Denmark
- Primary outcome was ROSC, not favorable neurologic survival at discharge
- Some differences occurred between patients in the post-resuscitation period. For those that survived at least 24 hours:
 - 46% of placebo vs 24% of intervention got steroids
 - 30% of placebo vs. 14% of intervention patients were placed on ECMO
 - Could these differences have attenuated a survival difference?
 - TTM used in only about 25% of patients in each group
- 90% of patients had an initial nonshockable rhythm

Take Home Points

- Among IHCA patients, the administration of vasopressin and methylprednisolone resulted in a significant increase in ROSC, however did NOT improve survival at 30 days and survival with favorable neurologic outcome.
- The use of vasopressin and steroid for patients with IHCA, and OHCA, requires further study and is not ready for standard care.