Title: "Battle over Beta: Concomitant use of Milrinone and Beta Blockers"

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Learning Objectives:

1. Describe mechanisms of action for both milrinone and beta blockers.
2. Discuss the data surrounding concomitant use of beta blockers and milrinone.
3. Recognize whether concomitant use would pose safety risks or offer benefit in various patient populations.

Abstract:

Beta blockers have been shown to significantly reduce mortality in patients with heart failure and is one of the four pillars of current guideline directed medication therapy. As patients progress to advanced heart failure, inotropic agents are enlisted to aid in the augmentation of cardiac output. This can be done as a temporary form of support during episodes of acute decompensated heart failure or as longer-term support for awaiting transplant or even as a palliative measure.

Our most common inotropes (milrinone and dobutamine) exert their action through increasing levels of cyclic adenosine monophosphate (cAMP). Where dobutamine directly stimulates beta-adrenergic G-coupled protein receptors (GCPRs), milrinone circumvents this pathway through inhibition of phosphodiesterase-3, a protein responsible for the breakdown of cAMP. It is a commonly held belief that, due to an opposing mechanism of action, beta blocker use would offset or dampen the cardiac output support that inotropes provide.

Despite advanced heart failure patients being excluded from pivotal randomized control trials that demonstrated the benefits of beta blockers in heart failure, they are commonly continued throughout disease progression and sometimes used in patients who are inotrope dependent. This presentation will review existing literature that analyze the safety and clinical outcomes associated with concomitant use.

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Questions:

1. Which of the following statements is FALSE regarding pharmacotherapy in heart failure?
    a. Milrinone results in increased inotropy and lusitropy
    b. Dobutamine exerts it's action through the same receptor as beta blockers
    c. The use of inotropes have been shown to improve mortality in heart failure
    d. Beta blockers can reverse cardiac remodeling through decreasing myocardial oxygen consumption
2. Which of the following is true regarding beta blocker and concomitant inotrope use? (Select All That Apply)
    a. Prospective trials have shown a trend towards reduction in mortality
    b. May be useful in mitigating arrhythmogenic effects of inotropes
    c. It is indicated as part of guideline directed medication therapy for HFrEF
    d. Retrospective analyses have demonstrated toleration of the combination in certain populations
3. In which of the following patients would it be inappropriate to initiate beta blocker therapy?
    a. 75 YOM on milrinone to assist with volume overload refractory to maximum diuretics approaching euvolemia
    b. 48 YOF continued on home milrinone dose with a beta blocker on outpatient medication list
    c. 39 YOM on dobutamine transferred from OSH with an elevated SCr of 4.2 (BL ~1.4) and hypotension
    d. 61 YOM admitted 2 days ago for STEMI who required support with dobutamine for <24 hours