Considerations on Phasing Out Medications In the Treatment of Peripartum Cardiomyopathy After Full Recovery

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Background

- There are currently no guidelines concerning the duration of treatment for peripartum cardiomyopathy (PPCM).
- Evidence-based guidelines for the initial treatment of heart failure with reduced LVEF include diuretics, beta-blockers (BB) and ACE-inhibitors or angiotensin receptor blockers (ACEI/ARB) in tolerable dosages as “Class I (“should use”) recommendations.
- There is evidence that “fully recovered” PPCM subjects can safely have withdrawal of treatment if some conditions are met. This investigation seeks to provide data relative to the safety of phasing out treatment following recovery.
Echocardiographic followup, 82 PPCM patients, Hôpital Albert Schweitzer, Haiti, 2000-2004

Discontinuation of Heart Failure Medications:

- Curr Treat Options Cardiovasc Med. 2001 Dec;3(6):469-480. Peripartum Cardiomyopathy. Baughman KL. Author information. Division of Cardiology, Department of Medicine, The Johns Hopkins Hospital, 600 North Wolfe Street, Blalock 536, Baltimore, MD 21287, USA. kbaughma@jhmi.edu

Abstract: It is critical that the diagnosis of peripartum cardiomyopathy is limited to women with congestive heart failure and decreased systolic function of the left ventricle in the last month of pregnancy or within 5 months after delivery. Patients must have no pre-existing cardiac disease and no other cause for current cardiac dysfunction. The inclusion of patients before the last month of pregnancy or after 5 months postpartum introduces a large number of patients with cardiac disorders due to causes other than peripartum cardiomyopathy. Ventricular performance at rest and with exertion determines the type of management, its intensity, and duration. Patients whose ventricular function is normal at rest and with exercise or dobutamine can have their heart failure therapy tapered and ultimately discontinued after 6 to 12 months of standard treatment. Those with normal resting but abnormal stress cardiac function should continue some form of medical therapy (afterload reduction or beta-blocker) for longer periods of time, if not for life. Those with persistently abnormal ventricular function must receive optimal heart failure therapy forever and face the same relatively poor prognosis as patients with dilated cardiomyopathy from any cause. Options for management include standard heart failure therapy (digoxin, diuretics, afterload reduction, and anticoagulation), Swan-Ganz catheter monitoring and use of inotropic agents, intra-aortic balloon counterpulsation, and left ventricular assist device. Patients with peripartum cardiomyopathy are candidates for heart transplantation, assuming they meet all other criteria.
Discontinuation of Heart Failure Medications:

[Improved outcomes in peripartum cardiomyopathy with contemporary. Amos AM, et al, Am Heart J 2006;152:509213.] Division of Cardiology, Duke University Medical Center, Durham, NC, USA.

• Results Fifty-five patients were identified with an average follow-up of 43 months. Their mean initial ejection fraction (EF) was 20%. Compared with their initial EF, 62% of patients improved, 25% were unchanged, and 4% declined. No patients died, and 10% eventually required transplant. At 2 months after diagnosis, 75% of those who eventually recovered had an EF N45%. Factors associated with lack of recovery at initial assessment were a left ventricular (LV) end-diastolic dimension N5.6 cm, the presence of LV thrombus, and African-American race. Recovery of LV function was not predicted by the initial EF. Among patients who recovered, the withdrawal of heart failure medications was not associated with decompensation over a follow-up of 29 months.

• Conclusions The morbidity related to PPCM is less than previously reported. Initial LV end-diastolic dimension and EF at 2 months predict long-term outcomes. The discontinuation of heart failure medications after recovery did not lead to decompensation.
Phased Withdrawal of Pharmaceutical Treatment (developed by JDFett, MD):

**Figure 1: One Approach for Phased Withdrawal of Treatment for PPCM After Restoration of Systolic Heart Function:**

- **Diagnosis of PPCM.** Treatment following AHA Guidelines for Heart Failure with reduced LVEF. Class I recommendations include:
  1. Diuretics as needed for fluid overload.
  2. ACEI/ARB at tolerable dosages.
  3. BB at tolerable dosages when stable circulatory status.

- **Echo Cardiogram for LVEF at:** 2 months, 6 months, 1 year

- **Reached recovery goal of LVEF 0.35 (preferable to 0.50).** Consider if can wean off treatment.

- **Have not reached Recovery Goal.** Continue treatment, optimize dosages of BB + ACEI/ARB.

**Weaning Process (Note: continue BB indefinitely if history of ventricular tachyarrhythmias or if LVEDD continues > 5.5 cm.)**

a) Start with 1/3 to 1/2 reduction of ACEI/ARB. (Some prefer to stop entirely as a first step).
b) Within 3 months do echo for LVEF; if decreased by at least 5 absolute LVEF points, resume previous dosage.
c) If LVEF stable, discontinue ACEI/ARB.
d) Within 3 months do echo for LVEF; if EF decreased to LVEF < 0.50, resume previous dosage.
e) If stable consider start weaning BB in same manner.
f) Do not begin weaning process until after 6 months of treatment.
g) Minimum safe duration of treatment suggested conservatively as one year.
h) Some would do an exercise stress echo to assess adequate contractile reserve (looking for at least 10% increased LVEF from resting to target exercise heart rate) before total discontinuation of Rx.
**WHAT CONSTITUTES “FULL RECOVERY?”**

**RECOVERY OUTCOMES IN THREE STUDIES:**

<table>
<thead>
<tr>
<th>Level of recovery</th>
<th>Internet Study (JDFett, MD)</th>
<th>North American IPAC Study*</th>
<th>European Study**</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF ≥ 0.50</td>
<td>78 % (74/95)</td>
<td>72 % (72/100)</td>
<td>(not reported)</td>
</tr>
<tr>
<td>LVEF ≥ 0.55</td>
<td>44 % (42/95)</td>
<td>52 % (52/100)</td>
<td>47 % (45/96)</td>
</tr>
</tbody>
</table>

Internet Study Results:

74/95 PPCM subjects recovered to LVEF 0.50 or more
Results (continued):

Maintained recovery while continuing treatment

- Maintained recovery (35/36)
- Deteriorated (1/36)
Maintained recovery after phasing out treatment
Weaning Process (Note: continue BB indefinitely if history of ventricular tachyarrhythmias or if LVEDD continues > 5.5 cm.)

a) Start with 1/3 to 1/2 reduction of ACEI/ARB. (Some prefer to stop entirely as a first step).

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Enduring recovery came to almost all subjects who reached recovery level whether phasing out treatment after recovery or staying on some level of treatment.

This lends support to previous reports indicating safety in phasing out treatment after recovery from PPCM.

Each subject is unique and all factors must be considered with respect to continuing or phasing out some treatment.
“I was diagnosed 4 years ago and I too was told that the heart medications would be bad for my infant and had to stop breastfeeding. The cardio they assigned me to in the hospital (I had been taken to the ER days before) also told me about 20 times that I should get my tubes tied immediately (I didn't) because I would probably die if I got pregnant again and yes, he said it just like that. He also was nice enough though to tell me that if it had been 10 years or more earlier, my chances of dying from PPCM were great. I was like..wow...geez....awesome. After a little over a year on meds, I was considered recovered.”

—USA Member, PPCM Survival Support Group, Facebook, 12 November 2015.
I had a very healthy pregnancy and delivery in 2008. Then, 2 weeks after my C-section I was diagnosed with PPCM. I was angry, devastated, sad, worried...the list went on. I was told that I would have to take those meds the rest of my life, that my ejection fraction would stay the same, and absolutely no more babies....I was so broken from hearing and experiencing all of this...I mean this was my FIRST child and I was 27 years old, and my husband and I wanted at least 2 more children. HERE IS THE GOOD NEWS!!!!!.... by 2010, my EF DID go up (despite what I was told), by the end of 2012 my EF remained up and I was taken off the meds and have not taken carvedilol or Furosemide since 2012, I have had great echo's showing nothing but a normal functioning heart since 2010 (despite the fact that I was told "they couldn't make me any promises" as to whether or not my heart would ever get back to where it was prior to my pregnancy)..... and I had to see my cardiologist once a year since 2008.... but as of August 2015, he released me as a patient!!!!! My heart is back to normal and fully functioning with no meds....only diet and exercise!!!!! The entire time after my diagnosis, I refused to accept the specifics....I acknowledged them and watched my diet, and listened to the recovery instructions of my cardiologist...but I said I will NOT be on these meds for the rest of my life....and here I am healthy, recovered, and the only med I take at all is a multi vitamin!!!!!
A 31-year-old gravida 2, para 2 patient was diagnosed with PPCM two weeks postpartum with echocardiographic LVEF at diagnosis of 0.24. She received treatment with lisinopril and carvedilol with improvement to LVEF 0.46.

She phased out all medications, and 3 years later became pregnant (LVEF 0.45 at first trimester).

She delivered a healthy female child but experienced dyspnea on exertion and persistent pedal edema 3 days postpartum. An echocardiogram revealed reduction of LVEF to 0.34. She received treatment with lisinopril and carvedilol with gradual improvement of LVEF to 0.42, where it continues unchanged 3 years later.
Results

- Follow-up from 1 to 12 years, median 4.5 years. Recovery to LVEF ≥0.50 or above took from 3 months to 5 years. [87/95 (92%) known to author by previous communications.]
  - 74/95 (78%) recovered to LVEF ≥50% and above;
  - 37/38 (97%) fully recovered, phased off medications, stayed recovered;
  - 35/36 (97%) fully recovered, continued medications, stayed recovered;
  - 20 (21%) not yet recovered, continued medications;
  - 1 (01%) not yet recovered, no medications.
- There were 10 post-PPCM pregnancies, 2 (20%) with relapse of heart failure.
Methodology

- Use of on-line identification of PPCM subjects, initially through A Mother’s Heart group; and subsequently through its successor, Facebook PPCM Survivor Support Group. A one-day on-line query included:
  1) Have you at some time been diagnosed with PPCM? Date? EF (as indicated on echocardiography report)?
  2) Did you experience full recovery (LVEF at least to 50 %)?
  3) Did you phase out treatment? How soon after diagnosis?
  4) After that, did your EF remain above 50 %?
  5) Are you still taking medications? Which one(s)?

- Each response analyzed for completeness, follow-up when necessary, Included only North American subjects with at least 1-year follow-up.