Tolerability of Conversion from Carvedilol to Metoprolol Succinate in Patients with Heart Failure

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Abstract

- **Objective:** To ascertain the tolerability and safety of changing carvedilol to metoprolol in patients with heart failure.
- **Design:** Observational, retrospective review.
- **Setting:** Outpatient clinic.
- **Participants:** Patients with diagnosis of heart failure or ejection fraction < 40% who were taking carvedilol for at least 6 months before conversion to metoprolol.
- **Measurements:** Blood pressure, heart rate, weight, and percentage of patients requiring urgent care and/or hospitalization for heart failure before and after conversion. Background heart failure drug therapy was recorded before and after conversion.
- **Results:** 142 patients were reviewed. There was no statistical difference in any parameter measured. 108 patients had no problem with the conversion, and 4 patients had evidence of worse heart failure after conversion. 30 other patients changed back to carvedilol, 8 cases due to worsening heart failure.
- **Conclusion:** The majority of patients with heart failure can be switched from carvedilol to metoprolol without adverse sequelae.

Carvedilol is a β-blocking agent with proven benefits in heart failure [1]. In early 2006, there was a national shortage of carvedilol, which posed a clinical dilemma in patients with heart failure. At the time, it was unclear when shipments of carvedilol would resume, meaning that many patients with heart failure might exhaust their supply of the drug. Since stopping β blockers either abruptly or by taper can be dangerous in patients with heart failure, our facility decided to change all patients to metoprolol succinate to circumvent the possibility of β-blocker outage [2]. Since there are no data describing the safety and tolerability of changing β blockers in patients with heart failure, we retrospectively collected outcome data in these patients before and after the conversion.

Methods

The medical records of patients converted from carvedilol to metoprolol in January 2006 were reviewed. To be included in the analysis, all the patients had to have the diagnosis of heart failure and or an ejection fraction less than 40% noted in the medical record. The dose of metoprolol was twice the total daily dose of carvedilol and administered once daily. There was no titration phase when changing to metoprolol. Data collected were the number of urgent care visits and/or hospitalizations (for heart failure–related symptoms) 6 months before and 6 months after the conversion. Patients had to be on carvedilol at least 6 months before conversion to be included in the analysis. The most recent systolic/diastolic blood pressure readings, heart rate, and weight were recorded before and after the conversion. Doses of carvedilol and metoprolol just before and after conversion were noted. Other concomitant heart failure drugs were also recorded while on both β blockers. Noncontinuous variables were compared between groups using a McNemar’s test. Continuous variables were compared between groups using a paired t test. Statistical analysis was performed using SigmaStat 3.0 software (SPSS, Inc, Chicago, IL). Statistical significance was set at an alpha of < 0.05.

Results

The review included 142 patients. All patients were male with a mean age of 73 ± 8 years. The mean dose of carvedilol and metoprolol immediately before and after conversion was 30 mg ± 18 and 60 mg ± 36, respectively. Background drug therapy for heart failure was similar before and after conversion (Table 1 and Table 2). No statistical differences were noted between groups with regard to blood pressure, heart rate, and weight (Table 3). There was no statistical difference between groups in patients requiring an urgent care visit or hospitalization for heart failure; only patients who were on metoprolol were analyzed for this outcome measure.

One hundred eight (76%) patients underwent the conversion with no problems (Figure). Four patients had worsening heart failure on metoprolol but stayed on the drug. The dose ranged from 25 to 100 mg/day and onset was 1 to 3 months after conversion in these patients. Thirty patients were changed back to carvedilol for various reasons.

From the Northern Arizona Veterans Affairs Health Care System, Prescott, AZ.
### Changing β Blockers in Heart Failure

#### Table 1. Percentage of Patients on Other Heart Failure Drugs Before and After Conversion

<table>
<thead>
<tr>
<th>Drug</th>
<th>Carvedilol</th>
<th>Metoprolol</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemide or hydrochlorothiazide</td>
<td>53%</td>
<td>52%</td>
<td>0.60</td>
</tr>
<tr>
<td>Lisinopril or losartan</td>
<td>62%</td>
<td>61%</td>
<td>0.61</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>25%</td>
<td>24%</td>
<td>0.72</td>
</tr>
<tr>
<td>Digoxin</td>
<td>32%</td>
<td>30%</td>
<td>0.68</td>
</tr>
</tbody>
</table>

#### Table 2. Mean Doses of Background Heart Failure Drugs Before and After Conversion

<table>
<thead>
<tr>
<th>Mean Dose (mg/day)</th>
<th>Carvedilol</th>
<th>Metoprolol</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemide</td>
<td>41 ± 33</td>
<td>40 ± 22</td>
<td>0.50</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>23 ± 14</td>
<td>26 ± 13</td>
<td>0.19</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>19 ± 16</td>
<td>17 ± 16</td>
<td>0.06</td>
</tr>
<tr>
<td>Losartan</td>
<td>50 ± 35</td>
<td>58 ± 33</td>
<td>0.29</td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.170 ± 0.07</td>
<td>0.155 ± 0.07</td>
<td>0.10</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>15 ± 14</td>
<td>25</td>
<td>0.17</td>
</tr>
</tbody>
</table>

Although 21% of patients changed back to carvedilol, closer review showed that many of these patients were changed for dubious reasons. One patient had increasing angina, which could have been compensated by increasing the metoprolol dose. Another patient had hypotension, which may have resolved with dose reduction of metoprolol. Four patients reported noncardiac side effects that were unusual and looked suspicious as to real cause and effect (eg, blindness, smell disturbance, rash, arthritis).

Our study is limited in that it was observational and retrospective. To accurately gauge the tolerability of changing carvedilol to metoprolol would involve a randomized blinded study done in a crossover fashion using a relatively large number of patients. Whether such a study will be done is doubtful. Our results do reflect the real-world conversion of carvedilol to metoprolol in patients with heart failure.

Our program to change β blockers could be criticized based on our dose conversion. We used a 2:1 ratio (metoprolol/carvedilol) based on guidelines published by the Veterans Affairs Pharmacy Benefits Management Group. This conversion was somewhat arbitrarily set, based on standard doses for both drugs. One small crossover study compared short-acting metoprolol to carvedilol in patients with heart failure using a dose conversion of approximately 4:1 (metoprolol/carvedilol) [3]. Overall, there was no difference in New York Heart Association functional class or various hemodynamic variables at rest between β blockers. However, 21% of patients developed hypotension, bradycardia, or worsening of symptoms after switching from carvedilol to metoprolol. This suggests that the dose conversion may have been excessive in this series.

Many patients refused to use anything but carvedilol, based either on their own volition or by recommendation of their primary physician. This may be due to the belief that carvedilol is a superior drug to metoprolol for heart failure. The COMET study showed superiority in overall survival in heart failure patients with carvedilol versus metoprolol [4]. However, there have been criticisms of this study, including the relatively low dose of metoprolol used and that a

#### Discussion

This is the first observational study that reports the tolerability and safety of changing β blockers in patients with heart failure. Our results show that the majority of patients can undergo this change without adverse events. Eight percent of patients reported worsening of heart failure with metoprolol. It is not known if this deterioration was due to the change in the β blocker or a reflection of the natural history of heart failure. Our observations suggest that the deterioration was from a natural course, since 4 patients had a continued decline in heart function after the switch back to carvedilol. In addition, we found no difference in urgent care/hospitalizations before and after conversion.
short-acting form was used instead of a long-acting product, like the succinate salt [5]. A long-acting form of metoprolol was used in the MERIT-HF study, which showed a significant mortality benefit versus placebo [6]. These criticisms of COMET may in part explain why the American Heart Association guidelines on heart failure treatment do not advocate carvedilol over metoprolol succinate as the preferred β blocker in heart failure [7]. This was a major reason for our change to metoprolol as the formulary β blocker for heart failure at our facility.

**Figure.** Patient flowchart.

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**References**


