Spironolactone: The Missing Drug in the Treatment of Patients Hospitalized with Congestive Heart Failure

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Abstract

- **Objective:** To assess the impact of interventions to increase the use of spironolactone in patients with congestive heart failure (CHF) due to ventricular systolic dysfunction.

- **Methods:** Charts of patients admitted to the medicine department of a single hospital with a primary diagnosis of class IV CHF and left ventricular ejection fraction of 40% or less were randomly selected and reviewed. Data were obtained for 30 preintervention and 30 postintervention patients. Measures included rates of use of spironolactone, β blockers, and angiotensin-converting enzyme (ACE) inhibitors/angiotensin-receptor blockers (ARBs) and documentation of contraindications to these therapies.

- **Interventions:** Interventions consisted of adding a clinical decision support reminder to the physician order entry system that alerted physicians ordering ACE inhibitors/ARBs for CHF to consider adding β blockers and spironolactone, an educational program to raise awareness of guideline recommendations, and multidisciplinary efforts to identify patients with CHF on admission and communicate appropriate recommendations to the medical team.

- **Results:** The rate of spironolactone use was 0% in the preintervention sample and 40% in the postintervention sample. Use of ACE inhibitors/ARBs and β blockers did not differ between the preintervention group (73% and 66%) and postintervention group (67% and 60%). Documentation of contraindications to ACE inhibitors/ARBs and β blockers increased from 40% and 0% preintervention, respectively, to 100% and 60% postintervention.

- **Conclusion:** There was a substantial increase in the utilization of spironolactone in patients with systolic dysfunction after the implementation of relatively inexpensive interventions. We continue to look for systems improvements to further increase appropriate use of spironolactone and other evidence-based therapies.
lags in the appropriate adoption of guideline recommendations. In a survey of more than 1500 patient office visits for heart failure, the prevalence of ACE inhibitor use was only 31%, and the doses used were often lower than those used in the clinical trials [12]. Efforts have been undertaken to maximize the use of ACE inhibitors/ARBs and β blockers, the 2 primary drugs in CHF treatment. However, less has been done to increase the use of spironolactone. In our hospital, we implemented a quality improvement initiative to improve the medical treatment of CHF, particularly with regard to spironolactone therapy. We considered any increase in the use of medications or documentation of contraindications to their use to be an improvement.

**Methods**

**Project Goals and Team Members**

The goal of this project was to improve the medical treatment of patients hospitalized with CHF due to left ventricular systolic dysfunction with a focus on the use of spironolactone. The project had 3 objectives: to determine baseline hospital adherence to the national heart failure guidelines, to identify barriers that prevented the hospital from meeting those guidelines, and to create systems changes in the delivery of care to patients with CHF. A multidisciplinary quality improvement team supervised the project. The team consisted of a quality improvement coordinator, an internist, a cardiologist, a care management supervisor, a registered nurse, an information technology specialist, and a clinical pharmacist. The team’s responsibilities were to evaluate the current hospital practices, identify the barriers that impede the adoption of the national guidelines, recommend system changes to facilitate application of these guidelines, and remeasure outcomes to assess improvement. The quality improvement team met once every 2 months to review the results and monitor the progress of the study. It also took the lead in creating program materials and developing corrective tools.

**Evaluation of Hospital Practice**

To assess the current hospital practice of the pharmacologic treatment of CHF, we performed a retrospective review of 65 charts randomly selected from all admissions to the medicine department with a primary diagnosis of class IV CHF between 1 January 2001 and 31 December 2001. The following ICD-9-CM codes were used to identify patients: 428.0, 428.1, and 428.9 for CHF and 786.05 for shortness of breath. Only patients with NYHA class IV heart failure documented by history were included in the review. Heart failure was considered to be secondary to systolic dysfunction if the ejection fraction was 40% or less as determined by echocardiogram, angiographic ventriculography, or radionuclide angiography. Thirty-five patients had an ejection fraction greater than 40% and therefore were excluded from the study. We collected demographic information and recorded the discharge medications, comorbid diseases, laboratory findings, physician’s specialty, physician’s documentation of side effects/contraindications, and the admission ward for all patients. The percentages of patients receiving ACE inhibitors or ARBs, β blockers, and spironolactone on discharge were calculated. Other medications such as digoxin and loop diuretics were not included because of lack of mortality benefit and to simplify the study.

**Identification of Barriers and System Improvements**

After reviewing the initial results, the quality improvement team made several recommendations and system changes based on identified barriers. Efforts were focused on improving the use of spironolactone. A major barrier identified was a lack of knowledge among health care providers regarding CHF guidelines. Therefore, an educational program involving residents, attending physicians, physician assistants, and nurses was undertaken to raise the awareness of health care professionals regarding CHF guidelines. The program included organized lectures in grand rounds, conferences, house-staff meetings, and nurses seminars as well as printed material published in the hospital periodicals and pharmacy pamphlets.

Another factor resulting in suboptimal use of medical therapy was the “memory factor”: health care providers would occasionally forget to add recommended therapies when testing patients receiving multiple medications. To address this issue, a clinical decision support reminder was added to the physician order entry system (Ulricare, NOASavannah, GA). The reminder was a pop-up message that appeared when a physician entered an order for an ACE inhibitor or an ARB and that prompted the physician to consider adding β blockers and/or spironolactone when indicated (Figure). The reminder structured
specifically asked to physician whether the treatment was being ordered for CHF as opposed to diabetes or hypertension. With this process, ACE inhibitors and ARBs were used as identifiers of CHF patients.

The third limiting factor was difficulty with identifying patients with CHF. When patients without a previous diagnosis of CHF were admitted to the hospital with dyspnea or lower extremity edema, the final diagnosis of heart failure was not added to the computer record as an ICD-9 code until discharge. This made identification of the CHF patients on admission a challenge. Therefore, the nurse coordinator or clinical pharmacist assigned to medical wards was charged with identifying patients admitted with CHF. The medication list of patients with an ejection fraction of 40% or less and without contraindications to the use of spironolactone was reviewed by these individuals, and appropriate recommendations were added to the front of the chart or directly communicated to the medical team. We followed the laboratory contraindications for spironolactone used in the RALES study (ie, a serum creatinine concentration > 2.5 mg/dL and a serum potassium concentration > 5 mmol/L).

All 3 interventions took place concurrently and their implementation was closely monitored by the quality improvement team.

Evaluation of Interventions
The new system changes were implemented in October 2002.

Outcomes were measured again in April 2003, 6 months after the introduction of the new system. For the postintervention measurement, 30 charts were randomly selected from the population of patients admitted to the hospital with a primary diagnosis of CHF due to systolic dysfunction during the preceding 6 months. Patient characteristics, rates of use of CHF medications, and rates of documentation of contraindications were collected and compared with the first group using Fisher’s exact test for small samples and t test. Both tests were performed using GraphPad InStat version 3.00 (GraphPad Software, San Diego, CA). Data collection was confidential and access was password protected and restricted to involved researchers.

Results
There were no significant differences between the preintervention group and postintervention group in regard to gender, age, ethnic distribution, ejection fraction, or severity of disease (Table). In the postintervention group, 22 patients (73%) were on ACE inhibitors or ARBs. In the remaining 8 patients (27%), 5 had contraindications to the use of ACE inhibitors/ARBs documented, and of these 5, only 1 was on the combination hydralazine and nitrates. Twenty patients (67%) were on β blockers at discharge. Of the 10 patients who did not receive β blockers, only 4 (40%) had documentation of contraindications. None of the 30 patients were taking spironolactone or other aldosterone inhibitor, nor was

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Preintervention Sample</th>
<th>Postintervention Sample</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (interquartile range), yr</td>
<td>79 (49–96)</td>
<td>76 (39–94)</td>
<td>0.29</td>
</tr>
<tr>
<td>Female, %</td>
<td>47</td>
<td>40</td>
<td>0.79</td>
</tr>
<tr>
<td>Race/ethnic group, n (%)</td>
<td></td>
<td></td>
<td>0.73</td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>25 (84)</td>
<td>23 (77)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>4 (13)</td>
<td>6 (20)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Median ejection fraction, % (range)</td>
<td>30 (10–40)</td>
<td>30 (15–40)</td>
<td>0.94</td>
</tr>
<tr>
<td>Severity of disease, n (%)</td>
<td>19 (63)</td>
<td>21 (70)</td>
<td>0.78</td>
</tr>
<tr>
<td>Admitted to the intensive care unit</td>
<td>10 (33)</td>
<td>12 (40)</td>
<td>0.79</td>
</tr>
<tr>
<td>Drug utilization, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On ACE inhibitor</td>
<td>22 (73)</td>
<td>20 (67)</td>
<td>0.24</td>
</tr>
<tr>
<td>Not on ACE inhibitor/ARB with documented contraindication</td>
<td>5 (63)</td>
<td>10 (100)</td>
<td>0.06</td>
</tr>
<tr>
<td>On β blocker</td>
<td>20 (66)</td>
<td>18 (60)</td>
<td>0.88</td>
</tr>
<tr>
<td>Not on β blocker with documented contraindication</td>
<td>4 (40)</td>
<td>7 (60)</td>
<td>0.007</td>
</tr>
<tr>
<td>On spironolactone</td>
<td>0 (0)</td>
<td>12 (40)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker.
there documentation of contraindications to their use in the charts.

Of the 30 patients in the postintervention group, 20 (67%) were on an ACE inhibitor or ARB, 18 (60%) were on β blockers, and 12 (40%) were on spironolactone upon discharge. Contraindications were documented in all the patients who were not treated with ACE inhibitors/ARBs and 60% of those not treated with β blockers. Contraindications to spironolactone were not collected because in one of the interventions the clinical pharmacists identified only patients who were eligible for its use.

Discussion

Medical treatment remains the mainstay of CHF therapy. Multiple randomized clinical trials have demonstrated the efficacy of several pharmacologic treatments in improving CHF morbidity and mortality and in decreasing hospitalization [3–5,10]. Despite the clinical evidence, these medications remain underutilized [13,14]. Underutilization may vary with age [15,16], presence of comorbidities [16,17], medical specialty [12,18], region, sex, and insurance [12]. Even when appropriate medications are used, optimal dosage frequency is not attained [19]. In our study, the use of ACE inhibitors and β blockers, albeit suboptimal, was comparable to rates reported in other studies [12–14]. On the other hand, spironolactone use was completely absent prior to the system changes and clearly improved following the quality improvement intervention.

Spironolactone is an aldosterone antagonist that has been used for many years as a potassium-sparing diuretic and antihypertensive. It inhibits aldosterone by competing with it for receptor sites in the distal renal tubule. It increases water and sodium excretion without depleting potassium. The RALES study demonstrated the effectiveness of adding spironolactone to standard treatment of severe CHF [7]. The study was terminated early after a 30% reduction in the risk of death was observed among patients receiving spironolactone in conjunction with an ACE inhibitor. This reduction was attributed to lower risks of death from progressive heart failure and from sudden cardiac death, which may have been due to a reduction in myocardial and vascular fibrosis caused by the spironolactone. More recently, a trial using the selective aldosterone blocker eplerenone demonstrated a significant reduction in morbidity and mortality in patients hospitalized with acute myocardial infarction complicated by left ventricular dysfunction [8].

Despite the published data, spironolactone continues to be underutilized in patients with heart failure. In a recent survey conducted at a university hospital in the United Kingdom, only 13% of eligible patients received spironolactone [20]. In our preintervention sample, spironolactone was not used at all. Multiple factors could have accounted for its underuse. A major factor is lack of awareness of or familiarity with the guidelines. Another possible factor is concern over side effects. Many physicians avoid the use of spironolactone due to concerns about severe hyperkalemia in patients taking ACE inhibitors or ARBs. However, it has been demonstrated that ACE inhibitors and low-dose (25 mg) spironolactone raise the potassium level only minimally and that the use of these agents together is safe [7]. Finally, the presence of comorbidities, such as renal failure or diabetes, may discourage health care providers from adding drugs that can potentially worsen the condition. In fact, renal failure appears to be more common in patients treated with spironolactone [21,22].

Additional potential factors that may have contributed to the low rate of adherence to the guidelines include lack of facilities or resources, physicians’ perception of the guidelines as being too complicated or difficult to apply in a routine manner, concerns over adding more drugs to an already complex list of heart failure medications, and the perception that spironolactone should be prescribed only in the outpatient setting. We tried to address these issues with a number of strategies to facilitate the increasingly complex management of patients hospitalized with CHF. Increasing health care providers’ awareness of guidelines through education and checklists, adding clinical decision support reminders to the physician order entry system by using other well prescribed CHF medications as identifiers, and applying a multidisciplinary approach involving pharmacists, nurses, and the medical team were some of the actions undertaken to enhance the treatment of CHF. However, it is unclear which intervention contributed most to the increase in spironolactone use. We suspect that the clinical decision support reminders may have played a major role. In a study published in 2000, physician order entry and clinical decision support systems were shown to increase and/or change the use of several medications [23]. On the other hand, studies have failed to show a difference in clinicians’ practice behavior through improvement of their knowledge by educational interventions [24,25]. Nonetheless, the interventions we employed are easy to implement and relatively inexpensive and have led to a significant improvement in spironolactone use in our hospital.

Increased use of ACE inhibitors/ARBs or β blockers was not observed. In fact, one would not expect a change in ACE inhibitor/ARB use since all untreated patients postintervention had documented contraindications to ACE inhibitors and ARBs. Therefore, excluding patients with contraindications, the percentage of use was a 100%. Similarly, use of β blockers did not increase, possibly because their use was limited by the more frequent contraindications documented in the postintervention group and because efforts were mainly concentrated on the utilization of spironolactone, the most glaring deficiency.
SPIRONOLACTONE AND CHF

One may argue that spironolactone is primarily an outpatient drug and should only be started when the patient’s condition is deemed stable to avoid side effects and drug interactions. However, patients are more likely to continue medications initiated prior to hospital discharge than those started in the outpatient setting [26]. Furthermore, in the EPHESUS trial, eplerenone was initiated during hospitalization of patients admitted with myocardial infarction and ventricular dysfunction without major side effects [8].

This study has several limitations, including a small sample size, absence of control groups, and the involvement of only one hospital. These limitations may affect its internal and external validity. However, in quality improvement projects, the study design becomes secondary to the processes investigated, and the information learned is used to improve the quality of care and close the gap between desired and actual performance.

Pharmacologic treatment of CHF remains suboptimal, particularly with regard to the use of spironolactone. A quality improvement project can increase the use of spironolactone in hospitalized patients. We achieved improvements through a computerized clinical decision support system using other CHF medications as patient identifiers, an educational program to raise awareness of guideline recommendations, and multidisciplinary efforts to identify patients with CHF. These interventions can be adapted to any institution at minimal cost. As we continue to refine the different modalities of our process, we aim toward greater compliance with spironolactone as well as other recommended CHF therapies.

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References


