Statin use following rhabdomyolysis in the Veteran Affairs Health Care System

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Abstract

Cholesterol lowering medications such as statins are recommended for the prevention and treatment of cardiovascular disease. Rarely patients experience a serious muscle-affecting adverse effect known as rhabdomyolysis. This diagnosis results in acute kidney injury and warrants hospitalization. In patients who have experienced rhabdomyolysis, little is known about the prescribing rates of statins following diagnosis. This was an observational, retrospective, descriptive data collection using VA data from June 1999 to November 2016. A total of 7,148 patients with a previous diagnosis of rhabdomyolysis were identified with nearly 70% of patients re-prescribed statin therapy within one year of index date. If re-initiation is considered, the benefits and risks should be considered as the safety of this practice is not known. However, following diagnoses of rhabdomyolysis, use of statins appears to be common.
Background

• Statins reduce cholesterol levels by inhibiting HMG-CoA reductase
  • Key enzyme in cholesterol synthesis

• Statins are the among the most effective medication classes to prevent cardiovascular disease¹

• Adverse effects include a spectrum of muscle disorders ranging from subjective muscle pain to rhabdomyolysis

Rhabdomyolysis\textsuperscript{2}

- Muscle pain and/or weakness associated with evidence of myoglobinuria and creatinine kinase (CK) 10x ULN (often exceeding 10,000 IU/L) and/or acute increases in serum creatinine $\geq 0.5$ mg/dl
- Results in hospitalization, acute kidney injury and may lead to other complications resulting in death
- **General prevalence:** fewer than 200,000 US cases per year
- **Prevalence among statin users:** 1.5 cases per 100,000 people

Clinical Problem and Objective

• Clinical Problem:
  • Following an episode of rhabdomyolysis there is limited
guidance if patients should be restarted on statin therapy
with unclear prescribing patterns

• Objective:
  • To describe the prescribing rates of statins (among
users of statins) following a diagnosis of
rhabdomyolysis
Methods

• Non-experimental retrospective descriptive data analysis

• Inclusive dates from 6/1/1999 - 11/1/2016

• Data was accessed from the VA corporate data warehouse (CDW) through the VA Informatics and Computing Infrastructure (VINCI)

• Among users of statins as defined by previous medication fills, the International Classification of Diseases (ICD-9/10) codes for rhabdomyolysis were used to identify subjects
Methods

• Corresponding lab values for serum creatinine and CK as well as demographic data was obtained
  • Pre-Values taken immediately prior to index date
  • Post-Values taken immediately following index date

• Calculated days to first prescription fill following diagnosis
  • Date of prescription – index date of diagnosis

• Informed consent not deemed necessary based on limited patient risk

• Approved by University of Iowa Institutional Review Board (IRB) and VA Research and Development Committee
### Results

- 7,148 subjects identified as being a recent user of statins with subsequent diagnosis of rhabdomyolysis

<table>
<thead>
<tr>
<th>Demographic and lab information</th>
<th>Result (mean)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>66</td>
<td>22-101</td>
</tr>
<tr>
<td>Sex Male %</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>Pre-diagnosis Serum creatinine (mg/dl)</td>
<td>1.90</td>
<td>0.5-18</td>
</tr>
<tr>
<td>Post-diagnosis Serum creatinine (mg/dl)</td>
<td>2.03</td>
<td>0.3-16.9</td>
</tr>
<tr>
<td>Pre-diagnosis Creatine Kinase (IU/L)</td>
<td>5,153</td>
<td>7-195,302</td>
</tr>
<tr>
<td>Post-diagnosis Creatine Kinase (IU/L)</td>
<td>4,299</td>
<td>10-227,327</td>
</tr>
</tbody>
</table>
Results

- Among 7,148 users of statins with a diagnosis of rhabdomyolysis:

<table>
<thead>
<tr>
<th>First statin fill following diagnosis of rhabdomyolysis</th>
<th>&lt;30 days</th>
<th>30-365</th>
<th>&gt;365 days</th>
<th>No statin use</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,129 (43.8%)</td>
<td>4,358 (60.9%)</td>
<td>4,986 (69.7%)</td>
<td>2,162 (30.2%)</td>
<td></td>
</tr>
</tbody>
</table>
Discussion

• Among statin users the majority of patients with a diagnosis of rhabdomyolysis are eventually prescribed a statin within the first year
  • Many within the first 30 days

• Approximately 1 out of 3 patients are not prescribed statin therapy following rhabdomyolysis

• The relative safety of this practice is not known

• Cumulative statin use did increase which may suggest that patients remain on therapy following re-initiation without further incident
Strengths and Limitations

**Strengths**
- National VA data used to identify a rare adverse effect
- Accuracy of data used to identify index dates and fill dates

**Limitations**
- Misclassification of diagnosis
- Unable to tell if medication fills were erroneous or if patients actually took medication
- Many patients likely had diagnosis entered after labs ordered thereby not reflecting true pre-diagnosis values for serum creatinine or CK
- Unable to comment on the relative safety of statin use following diagnosis
- Other etiologies of rhabdomyolysis possible
Conclusions

• Despite occurrence of serious side effects, our data show the majority of patients and prescribers are willing to re-initiate statin therapy following a diagnosis of rhabdomyolysis.

• The relative safety of this practice is not known.

• The decision to restart or defer statin therapy following a diagnosis of rhabdomyolysis should be based on the anticipated benefits and risks.
  • Reversible causes of muscle injury or risk factors for rhabdomyolysis have been corrected.
References


Survey link