Monitoring Protocol for Clozapine-induced Myocarditis
Agenda

Local Problem

Problem Identification / Importance
Baseline Workflow
Baseline Data

Design and Implementation

Objectives
Solution Selection
Interventions
End-User Involvement

How Health IT was Used

Revised Workflow
Solution Details

Value Derived

Effect of Interventions on Data
Post-Implementation Adherence Data
Post-Implementation Outcome Data
Return on Investment
Overview of Clozapine

- 25-30% of all individuals with schizophrenia meet criteria for treatment resistance (Remington 2010)
- Clozapine is the only antipsychotic with proven efficacy (Remington, Addington et al. 2017)
- Substantial side-effects

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agranulocytosis</td>
<td>Rare (&lt;1%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>60%</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>

- CAMH houses the largest clozapine clinic in North America (~750 patients)
- Goal to double volume over a 5-year period
Problem Identification

• Clinical symptoms of myocarditis noted in patients treated with clozapine
• An expert was consulted who determined that the cause was myocarditis
• Agranulocytosis is the only standard monitoring for clozapine treatment

Why is this Important?

• Clozapine-induced Myocarditis is a potentially fatal yet likely under diagnosed complication of Clozapine therapy
  ➢ Incidence estimated ~ 3%
  ➢ Develops within the first 4 weeks of Clozapine initiation and titration
  ➢ Hypersensitivity reaction with a fatality rate of 10%
Baseline Workflow

Patient presents with TRS → Decision to prescribe Clozapine → Clozapine order(s) entered → Myocarditis symptoms?

Yes → Review and stop treatment → Alternative treatment prescribed → Can re-challenge patient after 1 year

No → Continue treatment
Myocarditis Monitoring

Cardiac Troponin Positive

C-Reactive Protein > 50

Suspected myocarditis
Baseline Data

<table>
<thead>
<tr>
<th>Month</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov-13</td>
<td>0%</td>
</tr>
<tr>
<td>Dec-13</td>
<td>0%</td>
</tr>
<tr>
<td>Jan-14</td>
<td>0%</td>
</tr>
<tr>
<td>Feb-14</td>
<td>0%</td>
</tr>
<tr>
<td>Mar-14</td>
<td>0%</td>
</tr>
<tr>
<td>Apr-14</td>
<td>0%</td>
</tr>
<tr>
<td>May-14</td>
<td>0%</td>
</tr>
<tr>
<td>Jun-14</td>
<td>0%</td>
</tr>
<tr>
<td>Jul-14</td>
<td>0%</td>
</tr>
<tr>
<td>Aug-14</td>
<td>0%</td>
</tr>
<tr>
<td>Sep-14</td>
<td>0%</td>
</tr>
<tr>
<td>Oct-14</td>
<td>0%</td>
</tr>
</tbody>
</table>

Cardiac Specialist

n = 1

Myocarditis Monitoring Protocol

Nov 2013 – Oct 2014

4.2%
Objectives

- Standardize myocarditis monitoring protocol for Clozapine-naïve patients
- Increase compliance to myocarditis monitoring protocol
- Discontinue Clozapine for patients showing warning signs of myocarditis
- Streamline ordering process to save clinician time and prevent errors
Solution Selection

CAMH identified a method to increase myocarditis monitoring for Clozapine patients.

The implementation of I-CARE provided an opportunity to standardize care through order sets.

-Decision to standardize practice through order sets was made through the Hospitalist User Group and the Pharmacy and Therapeutics Committee
Interventions

Policy

• Included Myocarditis monitoring protocol into Clozapine policy (Oct. 2014)

Order Sets

• Integrated Myocarditis monitoring protocol into I-CARE order sets (Nov. 2014)

Mandatory Fields (Locking)

• Reinforced education with cardiology expert (Apr. 2015); monitoring protocol elements made mandatory within I-CARE order sets (Jun. 2015)
End-User Involvement

Integrated Health Record Committee
- Chairs: Dir. Interprofessional Practice, Dir. Medical Informatics
- Includes clinicians and other stakeholders
- Initial approval of need

Hospitalist User Group
- Chair: Medical Head, Hospitalist Services
- Developers and subject matter experts for Clozapine Order Sets
- Representation from physicians, nurses, Pharmacy, Professional practice, and Health Records

Physician User Group
- Chair: Chief Medical Information Officer
- Representation of front-line physicians
- Contains 15 physicians from throughout CAMH

Pharmacy & Therapeutics
- Co-chairs: Appointed Physician and Dir. Pharmacy
- Owners and approvers of Order Set
- Includes a minimum of 6 physicians, 4 pharmacists
Revised Workflow

Patient presents with TRS

Decision to prescribe Clozapine

Pre-Clozapine Initiation Order Set (Baseline)*

Select Clozapine with Titration or Clozapine without Titration Order Set*

Mandatory blood work for 4 weeks*

Can re-challenge patient after 1 year

Alternative treatment prescribed

Review and stop treatment

Abnormal

Results normal or abnormal?

Normal

Continue treatment

Health IT used within intervention*
Mandatory Monitoring Protocol

Pre-initiation

- Baseline ECG, CRP, and Troponin
- Identification of pre-existing cardiac disease

Troponin lab test

CRP lab test
Mandatory Monitoring Protocol

Post-initiation

- Weekly clinical assessments
- CRP and Troponin monitoring x 4 weeks
- Regular Agranulocytosis monitoring
Effect of Interventions on Data

**Policy**
- Included Myocarditis monitoring protocol into Clozapine policy (Oct. 2014)
- Increased clinical awareness and regulations to educate staff about clozapine-induced myocarditis and the effective monitoring protocol

**Order Sets**
- Integrated Myocarditis monitoring protocol into I-CARE order sets (Nov. 2014)
- Integration of monitoring protocol increased speed of ordering and provided a visual reminder about the monitoring protocol for clinicians

**Mandatory Fields (Locking)**
- Reinforced education with cardiology expert (Apr. 2015); monitoring protocol elements made mandatory within I-CARE order sets (Jun. 2015)
- Increased clinical awareness and enforced regulations to standardize practice for Clozapine-naïve patients
Post-Implementation Adherence Data

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Percentage of Patients</td>
<td>4.2%</td>
<td>97.0%</td>
</tr>
</tbody>
</table>

Clozapine-naive Patients with Myocarditis Monitoring Protocol

Pre-implementation: 0% in Q1 2013, 7% in Q4 2014

Post-implementation: 88% in Q1 2015, 94% in Q2 2017, 89% in Q1 2018, 100% in Q2 2018
Number of patients discontinued from Clozapine due to suspected Myocarditis

Nov 2013 - Oct 2014: 0
Nov 2014 - May 2018: 27
### Discontinued Patient Demographics

#### Number of Clozapine Patients with Myocarditis Risk by Age and Sex

<table>
<thead>
<tr>
<th>Age</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 21</td>
<td>1</td>
</tr>
<tr>
<td>21 to 32</td>
<td>13 *13.5%</td>
</tr>
<tr>
<td>33 to 42</td>
<td>2</td>
</tr>
<tr>
<td>43 to 53</td>
<td>2</td>
</tr>
<tr>
<td>53 to 64</td>
<td>4</td>
</tr>
</tbody>
</table>

*13 / 96 (13.5%) of males aged 21 to 32 discontinued
Twenty-seven Clozapine-naïve patients had suspected myocarditis detected in early stages.

Savings = (Cost of adverse event * # of patients detected)

Cost averted = $108,756
Return on Investment

27 patients removed from Clozapine due to myocarditis warning signs (3 lives saved)

- Able to measure the true incidence (8.6%) of Clozapine-induced myocarditis; 27 patients removed from Clozapine due to warning signs
- Clinicians are able to more easily screen for Clozapine associated Myocarditis
- Developed guidelines for Clozapine cessation and reintroduction
- CAMH is locally leading the way for Clozapine-induced myocarditis monitoring and we expect uptake on a regional and national level after publishing
Lessons Learned

Policy change can be supported by health IT to support adoption and enforcement

Order sets are effective at driving adoption of mandatory protocols

Data sharing with clinicians is an effective method for practice awareness
Thank You

camh