INTRODUCTION

Heparin-induced thrombocytopenia (HIT) is an immune-mediated adverse reaction to heparin resulting in significant patient morbidity.

Although guidelines for the management of HIT provide guidance on initiation of therapy, they fall short of directing decisions regarding continuation of therapy.

A multidisciplinary, comprehensive HIT Recognition and Management Protocol was developed and implemented in the fall of 2010 within our health system.

The protocol involved:
- An IgG-specific platelet factor 4/ELISA immunoassay (HPF4 EIA) with improved specificity
- Automatic serotonin release assay (SRA)
- A requirement to calculate a 4T score (Thrombocytopenia, Timing, Thrombosis, Other)
- A low score (≤3) has a high negative predictive value for HIT

An initial evaluation showed an improvement in HIT management.

OBJECTIVE

To assess the continuing impact of the HIT protocol two years post-implementation.

METHODS

Retrospective observational cohort study approved by our Institutional Review Board

Data collection period from October 2012 to May 2013 (Post-Protocol 2)

Inclusion criteria
- Patient 18 years of age and older
- Received a direct thrombin inhibitor (DTI)

Exclusion criteria
- Patients with a history of HIT
- Received a DTI for an indication other than HIT

Data collected: patient demographics, type of patient, medication use, laboratory data, protocol adherence, clinical outcomes and cost of inappropriate DTI therapy

Endpoints analyzed
- DTI Initiation
  - 4Ts score ≥3 and DTI initiated within 12 hours of a HPF4 EIA order
  - Started on DTI with a low 4Ts score (≤3)
- DTI Cessation
  - Within 12 hours of a negative HPF4 4EIA
  - Within 12 hours of a negative SRA and a positive HPF4 EIA

Protocol adherence
- Appropriate medical record documentation of HIT documentation
- Confirmed HIT education
- Clinical outcomes
- Major bleeding up to 24 hours post DTI discontinuation
- Thrombosis post-DTI administration
- Cost of Inappropriate Therapy
- DTI dispensed beyond 12 hours after a negative HPF4 4EIA
- DTI dispensed beyond 12 hours after a negative SRA and a positive EIA

Data Analysis – Compared previous evaluation (Pre-Protocol and Post-Protocol 1) to current evaluation (Post-Protocol 2)
- Descriptive statistics, chi-square, t-test, Mann-Whitney
- Level of significance set at p < 0.05

RESULTS

Table 1. Patient Information

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Medical</th>
<th>Surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Protocol</td>
<td>36 ± 13</td>
<td>26 ± 12</td>
</tr>
<tr>
<td>Post-Protocol 1</td>
<td>36 ± 14</td>
<td>26 ± 14</td>
</tr>
<tr>
<td>Post-Protocol 2</td>
<td>61 ± 14</td>
<td>61 ± 14</td>
</tr>
</tbody>
</table>

Table 2. Impact of HIT Protocol on DTI Use

<table>
<thead>
<tr>
<th>DTI Initiation</th>
<th>Pre-Protocol (n=61)</th>
<th>Post-Protocol 1 (n=46)</th>
<th>Post-Protocol 2 (n=46)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>4Ts score ≥3 and HIT ruled in</td>
<td>28/59, 47.5%</td>
<td>25/46, 54.3%</td>
<td>23/46, 50%</td>
<td>N/A</td>
</tr>
<tr>
<td>HIT ruled in</td>
<td>25/46, 54.3%</td>
<td>22/46, 47.8%</td>
<td>20/46, 43.5%</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Table 3. Clinical Outcomes and Documentation

<table>
<thead>
<tr>
<th>HIT Documentation</th>
<th>Pre-Protocol</th>
<th>Post-Protocol 1</th>
<th>Post-Protocol 2</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre vs. Post 1</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Post 1 vs. Post 2</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

DISCUSSION

- Protocol implementation appeared to be sustainable over a several year period as evidenced by a similar number of patients in the post periods with:
  - A low 4 Ts score who were started on a DTI
  - An intermediate to high 4 Ts score who were started on DTI therapy in a timely manner
- Prompt discontinuation of DTI therapy after a negative HPF4 EIA or SRA
- There was a decrease in the median hours of inappropriate DTI therapy per patient after a negative laboratory assay
- Total cost of inappropriate therapy for protocol post-2 evaluation
  - Lower than pre-protocol costs (annualized cost decreased by $200,000)
  - Higher than post-protocol 1 costs (annualized costs increased by $100,000)
  - Due to an increase in inappropriate use after negative SRA (three patients accounted for over 80% of inappropriate use)

- Clinical outcomes were equivalent between post-evaluation periods
- Initial HIT documentation (i.e. suspected HIT) dropped slightly between post-protocol groups
- Updated HIT documentation (i.e. removed when HIT ruled out or changed to confirmed when HIT ruled in) also decreased slightly in the post-protocol 2 evaluation period
- Appropriate education was lacking in the post-protocol 2 evaluation period

CONCLUSIONS

- Pharmacists managed HIT protocol demonstrated a sustained beneficial impact over a multi-year period by:
  - Limiting inappropriate DTI initiation
  - Initiating DTI therapy in those with moderate-high suspicion for HIT in a timely manner
  - Reducing the duration of inappropriate DTI therapy
- A physician champion might be helpful in promoting appropriate DTI discontinuation after negative laboratory results
- Post HIT documentation and education will prompt further education of our clinical pharmacy staff

Disclosure

Authors of this presentation have the following disclosures concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:
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