Effects of Additional Sarpogrelate HCL (ANPLAG) on Platelet Inhibition in Patients Underwent Percutaneous Coronary Intervention

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Fig. 1. A diagram of pharmacological actions of sarpogrelate (Anplag™) as a selective 5-hydroxytryptamine (HT) subtype 2A receptor antagonist.

INTRODUCTION

Previous studies and results

- Coronary stenting induces a greater release of 5-HT into the coronary circulation. It may contribute to subacute stent thrombosis and restenosis.

- High plasma 5-HT are associated with occurrence of cardiac events.

- Sarpogrelate in addition to aspirin and ticlopidine significantly decreased the restenosis rate.
OBJECTIVES

- To assess effects of sarpogrelate in addition to aspirin and clopidogrel on post-treatment platelet reactivity in patients underwent DES implantation.

- To find clinical evidences for large scale trial of sarpogrelate.
MATERIALS AND METHODS

Patients who underwent PCI with DES implantation and given traditional dual loading regimen at least 6 h prior to PCI

Randomization process and blood sampling within 12 to 24 h post-PCI and before drugs administration

Group 1 (n = 15 pts)
Dual therapy for 2 weeks

Group 2 (n = 15 pts)
Triple therapy for 2 weeks

Group 2 (n = 15 pts)
Dual therapy for 2 weeks

Group 1 (n = 15 pts)
Triple therapy for 2 weeks

Fig. 1. Flow diagram of the study
MATERIALS AND METHODS

Inclusion Criteria

① Age of ≥18 years;

② Acute coronary syndrome or stable angina with ≥ 3 risk factors;

③ Underwent PCI with DES implantation after receiving dual loading therapy at least 6 h prior to PCI (300 mg aspirin and 300~600 mg clopidogrel).
Exclusion Criteria

① Age of ≥80 years;
② Who implanted with bare metal stents (BMS);
③ Use of GP 2b/3a inhibitors during PCI procedure;
④ History of ISR or CABG or stroke within 6 months prior to screening;
⑤ Active internal bleeding;
⑥ Need for oral anticoagulation;
⑦ Intolerance to antiplatelet agents (aspirin, etc.)
⑧ AST and ALT levels more than 3 times upper normal limit;
⑨ Severe renal failure (serum creatinine >2.5 mg/dl);
⑩ Thrombocytopenia (PLT count <80,000/L) or anemia (Hb <8.0 g/dL);
⑪ Left ejection fraction less than 40%;
⑫ Who has received any investigational drug within 2 months prior to screening.
MATERIALS AND METHODS

Medication

- **Dual maintenance dose therapy**
  Aspirin 100 mg/d plus clopidogrel 75 mg/d

- **Triple maintenance dose therapy**
  Aspirin 100 mg/d plus clopidogrel 75 mg/d plus sarpogrelate 100 mg TID
MATERIALS AND METHODS

- Light transmittance aggregometry (LTA)
  - 0.5 mM arachidonic acid
  - 10 µM adenosine diphosphate
  - 2 µg/mL collagen

- Multiple electrode aggregometry (MEA)
  - ADPtest
  - ASPItest
  - COLtest

Maximum platelet aggregation

Area under the aggregation curve (U)
MATERIALS AND METHODS

Statistical Analysis

- Two-way Repeated-Measures ANOVA => To assess effects of treatment, period and treatments*period and calculate carryover effects.

- A p-value of <0.05 was considered as statistical significance.

- SPSS version 14.0 (SPSS Inc. Chicago, USA)
# RESULTS

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1 (n=14)</th>
<th>Group 2 (n =12)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(From dual to triple)</td>
<td>(From Triple to dual)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>67.2 ± 8.0</td>
<td>62.1 ± 10.4</td>
<td>0.168</td>
</tr>
<tr>
<td>Gender (Male/Female)</td>
<td>8/6</td>
<td>8/4</td>
<td>0.701</td>
</tr>
<tr>
<td>Diagnosis, n (%)</td>
<td></td>
<td></td>
<td>0.952</td>
</tr>
<tr>
<td>Stable angina (SA)</td>
<td>1/14 (7.1%)</td>
<td>1/12 (8.3%)</td>
<td></td>
</tr>
<tr>
<td>Unstable angina (UA)</td>
<td>10/14 (71.4%)</td>
<td>9/12 (75.0%)</td>
<td></td>
</tr>
<tr>
<td>NSTEMI</td>
<td>3/14 (21.4%)</td>
<td>2/12 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>STEMI</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Risk factor, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>4/14 (28.6%)</td>
<td>4/12 (33.3%)</td>
<td>0.793</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9/14 (64.3%)</td>
<td>5/12 (41.7%)</td>
<td>0.249</td>
</tr>
<tr>
<td>Active Smoker</td>
<td>0/14</td>
<td>1/12 (8.3%)</td>
<td>0.462</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1/14 (7.1%)</td>
<td>1/12 (8.3%)</td>
<td>0.910</td>
</tr>
<tr>
<td>Pre-PCI, n (%)</td>
<td>2/14 (14.3%)</td>
<td>5/12 (41.7%)</td>
<td>0.190</td>
</tr>
<tr>
<td>Pre-MI, n (%)</td>
<td>3/14 (21.4%)</td>
<td>3/12 (25.0%)</td>
<td>0.829</td>
</tr>
<tr>
<td>Pre-stroke, n (%)</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>13.0 ± 2.0</td>
<td>12.7 ± 1.6</td>
<td>0.742</td>
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<tr>
<td>WBC count (10³/µL)</td>
<td>7.20 ± 1.91</td>
<td>7.00 ± 2.13</td>
<td>0.806</td>
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<tr>
<td>Platelet count (10³/µL)</td>
<td>207.7 ± 47.6</td>
<td>227.7 ± 45.9</td>
<td>0.289</td>
</tr>
</tbody>
</table>
## RESULTS

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1 (n=14) (From dual to triple)</th>
<th>Group 2 (n =12) (From Triple to dual)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiographic diagnosis</td>
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<td></td>
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<tr>
<td>1-VD, n (%)</td>
<td>5/14 (35.7%)</td>
<td>6/12 (50.0%)</td>
<td>0.763</td>
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<tr>
<td>2-VD, n (%)</td>
<td>6/14 (42.9%)</td>
<td>4/12 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>3-VD, n (%)</td>
<td>3/14 (21.4%)</td>
<td>2/12 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>Target lesion</td>
<td></td>
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<tr>
<td>LAD, n (%)</td>
<td>6/14 (42.9%)</td>
<td>5/12 (41.7%)</td>
<td>0.420</td>
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<tr>
<td>LCx, n (%)</td>
<td>5/14 (35.7%)</td>
<td>2/12 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>RCA, n (%)</td>
<td>3/14 (21.4%)</td>
<td>5/12 (41.7%)</td>
<td></td>
</tr>
</tbody>
</table>
RESULTS

1. Two-way ANOVA
   - Multivariate Tests:
     Period: $p = 0.007$;
     Treatment*period: $p = 0.926$.
   - Mauchly’s Test of Sphericity: $P = 0.333$.
     Period: $p = 0.002$;
     Treatment*period: $p = 0.944$.
   - Tests of between subjects effects: $p = 0.902$.

2. One-way ANOVA
   - Dual-Triple group: $p = 0.034$;
   - Triple-Dual group: $p = 0.057$.

3. Paired Samples test
   Baseline & 2 weeks: $p = 0.050$, in the triple-dual group.
RESULTS

1. Two-way ANOVA
   - Multivariate Tests:
     Period: $p = 0.445$;
     Treatment*period: $p = 0.441$.
   - Mauchly’s Test of Sphericity: $P = 0.074$.
     Period: $p = 0.404$;
     Treatment*period: $p = 0.413$.
   - Tests of between subjects effects: $p = 0.362$.

2. One-way ANOVA
   Dual-Triple group: $p = 0.999$;
   Triple-Dual group: $p = 0.327$.

3. Paired Samples test
   There was no significant difference in both groups.
RESULTS

1. Two-way ANOVA
   - Multivariate Tests:
     Period: $p = 0.341$;
     Treatment*period: $p = 0.872$.
   - Mauchly’s Test of Sphericity: $P = 0.016$.
     Period: $p = 0.377$;  (Greenhouse-Geisser)
     Treatment*period: $p = 0.790$.
   - Tests of between subjects effects:
     $p = 0.301$.

2. One-way ANOVA
   - Dual-Triple group: $p = 0.464$;
   - Triple-Dual group: $p = 0.365$.

3. Paired Samples test
   There was no significant difference in both groups.
RESULTS

1. Two-way ANOVA
   - Multivariate Tests:
     Period: \( p = 0.106 \);
     Treatment*period: \( p = 0.062 \).
   - Mauchly’s Test of Sphericity: \( P = 0.163 \).
     Period: \( p = 0.123 \);
     Treatment*period: \( p = 0.114 \).
   - Tests of between subjects effects:
     \( p = 0.851 \).

2. One-way ANOVA
   Dual-Triple group: \( p = 0.866 \);
   Triple-Dual group: \( p = 0.051 \).

3. Paired Samples test
   Baseline & 2 weeks: \( p = 0.050 \),
in the triple-dual group.
RESULTS

1. Two-way ANOVA
   - Multivariate Tests:
     Period: $p = 0.556$;
     Treatment*period: $p = 0.561$.
   - Mauchly’s Test of Sphericity: $P = 0.000$.
     Period: $p = 0.358$; (Greenhouse-Geisser)
     Treatment*period: $p = 0.281$.
   - Tests of between subjects effects:
     $p = 0.341$.

2. One-way ANOVA
   - Dual-Triple group: $p = 0.866$;
   - Triple-Dual group: $p = 0.051$.

3. Paired Samples test
   There was no significant difference in both groups.
RESULTS

1. Two-way ANOVA
   - Multivariate Tests:
     - Period: $p = 0.518$;
     - Treatment*period: $p = 0.880$.
   - Mauchly’s Test of Sphericity: $P = 0.464$.
     - Period: $p = 0.594$;
     - Treatment*period: $p = 0.881$.
   - Tests of between subjects effects: $p = 0.612$.

2. One-way ANOVA
   - Dual-Tripple group: $p = 0.853$;
   - Triple-Dual group: $p = 0.618$.

3. Paired Samples test
   There was no significant difference in both groups.
LIMITATION

- Total number of eligible patients: small (26 patients).
-Insensitive of LTA and MEA to detect small platelet aggregates by 5-HT.
- Negative Lab results did not absolutely concern with clinical effects of sarpogrelate.
CONCLUSION

The adjunctive sarpogrelate to aspirin and clopidogrel did not benefit in reduction of post-treatment platelet reactivity in patients with DES implantation based on this study.