From Compression To Injections: Are Prostaglandins Paving A New Direction For Venous Ulcer Treatment

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Introduction

• Venous ulcers - *highly morbidity*
• Incidence: 0.25 – 1.25 %
• Poor tendency to heal
• Long treatment
• Longer follow up
• Origin – *Multifactorial*

• **VENOUS HYPERTENSION - STASIS**
Review of Literature

• Milio G, Mina C, Cospite V et al - 100% healed <100 days, 84.2% in placebo

• G Rudofsky et al - PGE1 (40%) : Placebo (9%) healing

• Beitner H, Hammar H, Olsson A et al : PGE1 (90%)


PG- E1

- Metabolite of polyunsaturated di homo-gamma-linoleic acid
- Acts on membrane receptors of intercellular adenyl-cyclase - $\uparrow$ cAMP

- Reduction of endothelial permeability and inhibition of vasoconstrictive activity of thromboxane A2, serotonin, leukotrienes, and endothelin
Other Actions PG E1

- Reduction of the adhesiveness and platelet aggregation
- Inhibition of the proliferation of the smooth muscle cells of the media
- Reduction of the hematic viscosity
- Pro-fibrinolytic effect
- Inhibition of chemotaxis and activation of white cells, stimulation of formation and growth of collateral circulation
<table>
<thead>
<tr>
<th>Cardiac</th>
<th>Others</th>
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</thead>
<tbody>
<tr>
<td>Bradycardia</td>
<td>Injection-site haematoma</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>Pain: Back, Pelvic, Penile, Urethral</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Prolonged erection</td>
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<tr>
<td>Tachycardia</td>
<td>Seizures</td>
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<tr>
<td>Ventricular fibrillation</td>
<td>Apnea</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Bleeding: Cerebral, Urethral</td>
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<tr>
<td>Shock</td>
<td>Diarrhea, Fever</td>
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<td></td>
<td>DIC, Edema</td>
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</table>
Aim

• Evaluate efficacy:
  
  *PGE-1 on healing of refractory venous ulcers*
Method of Study

- **44 patients** - venous leg ulcers homogeneous for dimensions and characteristics

- **PGE1 + 4 layer compression VS plain 4 layer compression**

- Dimension and number of ulcers

- **Monitoring done every 21 days up to 3 months** (until complete recovery)
INCLUSION CRITERIA

- **Venous ulcers of lower limbs**, defined as non-healing wound of the skin of the lower extremities caused by impaired venous return
- Proved clinically & by Doppler examination.
- No contraindication to PGE-1

EXCLUSION CRITERIA

- Not willing
- Congenital Venous insufficiency
- Arterial insufficiency (ABI < 0.7),
- Diabetic non healing ulcer, neurotrophic ulcer
- Vasculitis.
Study

• **Dose**: 500mcg/ml diluted in 4ml NS (1 ml each into 100ml NS)

• @ 10ml/hr/day

• @100mcg/day

• Follow up was 3 weekly

• Size of ulcer was measured during follow up

• First day – Observed in ICU

• Percentage of Recovery was observed from initiation of therapy up to 3 months, or till the ulcer healed
## Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>PGE-1 + Compression</th>
<th>Compression</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of Patients</strong></td>
<td>18</td>
<td>26</td>
</tr>
<tr>
<td><strong>Mean Age</strong></td>
<td>46 ± 9.7</td>
<td>56 ± 9.5</td>
</tr>
<tr>
<td><strong>Sex (Males %)</strong></td>
<td>90.5%</td>
<td>84.6%</td>
</tr>
<tr>
<td><strong>Doppler Findings</strong></td>
<td></td>
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<tr>
<td>Total / Partial Obstruction</td>
<td>14 (31.81%)</td>
<td>10 (22.72%)</td>
</tr>
<tr>
<td>Superficial Venous Incompetence</td>
<td>12 (27.27%)</td>
<td>8 (18.18%)</td>
</tr>
<tr>
<td>Deep Venous Reflux</td>
<td>9 (20.45%)</td>
<td>7 (15.90%)</td>
</tr>
<tr>
<td>Junctional / Perforator Incompetence</td>
<td>4 (0.9%)</td>
<td>6 (13.63%)</td>
</tr>
<tr>
<td><strong>Ulcer Features</strong></td>
<td></td>
<td></td>
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<tr>
<td>Area (cm²)</td>
<td>20.5 (6 – 48)</td>
<td>19.4 (8 – 40)</td>
</tr>
</tbody>
</table>
Patient Distribution

- 26 Post Surgery
- 8 Junctional Incompetence not willing for SX
- 2 Perforator Incompetence
- 2 Iliac Stenting
Results

Ulcer healing

- 97% healing within < 120 days
- 74% healing within < 90 days

Graph showing percentage healing over time for P + C and C treatments.
Complication

- Hypotension (3)
- Bradycardia (1)
- Diarrhoea (1)
Cases
Cases
Cases
Cases
Conclusion

- Pharmacologic treatment with PGE-1 + 4 layer bandage and local therapy, has a favorable effect on the healing of venous ulcers

- Side effects of treatment – acceptable

- Drug well tolerated by patients

- High Quality RCT: Confirm Efficacy and Safety
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