Therapeutic Efficacy of Plasma Exchange for Idiopathic Pulmonary Fibrosis (IPF)

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Background

- Spontaneous, chronic parenchymal disease.
- Dyspnea and cough.
- Usual interstitial pneumonia (UIP) – peripheral, bibasilar, reticular opacities, honeycombing and bronchiectasis.
- Rheumatologic, environmental or drug, irradiation, other.

Background

- Cigarette smoking, viral infections, dusts, possibly GERD, and drugs.
- Inheritance - < 5% inherited a familial type.
- Trends - Incidence is ↑ (more men, 6\textsuperscript{th} and 7\textsuperscript{th} decades).

King TE, Jr. Image: Idiopathic pulmonary fibrosis. In: UpToDate, Flaherty KR et al. (Eds), UpToDate, Waltham, MA. (Accessed on April 30, 2016.)

Background

- Frequency / 100,000 in the U.S.:
  - Estimated: 14-43 (prevalence [persons]) and 7-16 (incidence [person-years]).\(^1\)
  - 494 (prevalence [persons]) and 94 (incidence [person-years]), respectively, amongst a sample of primarily 65+ year-olds.\(^2\)
  - Median survival is ≤ 3 years; 10-50% develop acute exacerbations (AE).\(^3\)
  - Median survival after AE is 3-4 months; it can lead to death within days.\(^4\)

Pathogenesis

- Epithelial injury → dysregulated repair.
- Basement membrane damage.
- Cytokines, growth factors (TGF-β), macrophages, collagen deposition.
- Mild inflammation, fibroblast foci → honeycombing.

Integration and Hypothesis

• CXCL13 promotes B cell migration to sites of inflammation.\textsuperscript{1,2}
• Immune complexes and complement deposits are present.\textsuperscript{3}
• B lymphocyte stimulator factor is increased.\textsuperscript{4}
• IPF may be antibody-mediated, so therapeutic plasma exchange (TPE) was performed along with administration of an immunosuppressive regimen.

Methods

• Critically ill patients with acute exacerbations and no evidence of other interstitial pneumonias from 2013-2016 were enrolled.

• Historical controls from one institution with IPF or post-inflammatory pulmonary fibrosis during a 3-year period prior to the enrollment of the first patient in this study.

• Controls treated with antibiotics and steroids only.
Methods

• Patients fulfilled histopathologic and/or radiographic criteria.
• Acute exacerbation - worsening hypoxemia and dyspnea, new pulmonary infiltrates on chest computed tomography (CT); no other cause of respiratory dysfunction.
• Primary outcome - survival at 6-months.
• Secondary outcome - presence of at least a 50% reduction in oxygen requirement.
• Wilcoxon signed-rank tests, Fisher exact tests, and Cox-proportional hazard models were used for analysis.
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Treatments

• Large steroid doses are standard of practice.
• Rituximab is indicated for autoimmune disease.
• Intravenous immunoglobulin (IVIG) blocks Fc receptors and neutralizes complement.
• Not included in ASFA guidelines.

Potential Model for Anti-inflammatory Activity


Results

• 13 in experimental group (9 [69%] males/4 females; age 68 years, range 52-82).
• 20 controls (15 [75%] males/5 females; age 67 years, range 45-80).
• No statistically significant difference (p=0.42 and 1, respectively).
• Side effects of TPE: transient nausea and epistaxis one night after the procedure.
Results

• Primary outcome:
  • Survival rates were 4 times higher in the experimental group: 62% (n=8/13) versus 15% (n=3/20), respectively (p=.0092).
  • Hazard ratio was: 3.7 (95% CI=1.3-10.4, p=.01)

• Secondary outcome:
  • 69% in experimental and 5% in control group had at least a 50% reduction in oxygen requirements (p=.0002).
Kaplan-Meier cumulative survival plot

8 patients were still alive at almost 10 months.
<table>
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<th>Strengths and Weaknesses</th>
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<tr>
<td><strong>Strengths</strong></td>
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<tr>
<td>- Heterogeneity among control patients</td>
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<tr>
<td>- Supported by evidence of autoimmunity</td>
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<td>- Patients from several treatment centers</td>
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<tr>
<td>- Minimal side-effects of TPE thus far</td>
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<tr>
<td><strong>Weaknesses</strong></td>
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<td>- Heterogeneity among control patients</td>
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<td>- 6-month follow-up only</td>
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<td>- Improvement confounded by other interventions</td>
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Review and Conclusions

• The data showed a statistically significant survival benefit and reduction of oxygen requirements in the experimental group compared to historical controls at 6-months.
• Larger studies incorporating the use of TPE with other immunosuppressants are necessary to confirm these observations.
• Research for novel immunotherapy regimens should continue.
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References


