Clinical decision making for ASFA Category I, II, III, IV, and uncategorized indications

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## Journal of Clinical Apheresis Special Issue: Clinical Applications of Therapeutic Apheresis

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.</td>
</tr>
<tr>
<td>II</td>
<td>Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.</td>
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<tr>
<td>III</td>
<td>Optimum role of apheresis therapy is not established. Decision making should be individualized.</td>
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<td>IV</td>
<td>Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken in these circumstances.</td>
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# Journal of Clinical Apheresis Special Issue: Clinical Applications of Therapeutic Apheresis

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Description</th>
<th>Methodological Quality of Supporting Evidence</th>
<th>Implications</th>
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<tbody>
<tr>
<td>Grade 1A</td>
<td>strong recommendation, high-quality evidence</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
<td>Strong recommendation, can apply to most patients in most circumstances without reservation</td>
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<tr>
<td>Grade 1B</td>
<td>strong recommendation, moderate quality evidence</td>
<td>RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies</td>
<td>Strong recommendation, can apply to most patients in most circumstances without reservation</td>
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<tr>
<td>Grade 1C</td>
<td>strong recommendation, low-quality or very low-quality evidence</td>
<td>Observational studies or case series</td>
<td>Strong recommendation but may change when higher quality evidence becomes available</td>
</tr>
<tr>
<td>Grade 2A</td>
<td>weak recommendation, high quality evidence</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
<td>Weak recommendation, best action may differ depending on circumstances or patients’ or societal values</td>
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<td>Grade 2B</td>
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<tr>
<td>Grade 2C</td>
<td>weak recommendation, low-quality or very low-quality evidence</td>
<td>Observational studies or case series</td>
<td>Very weak recommendations; other alternatives may be equally reasonable</td>
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General Approach to Requests for Apheresis

Request for therapeutic apheresis procedure

Evaluate patient (history, physical exam, assessment, and plan)

Is there an IRB approved protocol for TA in your facility?

1) Is the patient presentation similar to those reported in the literature? Is the considered diagnosis the most likely diagnosis?
2) Have the usual, standard treatment options either failed or are contraindicated in this patient?
3) Are there alternative treatments reported in the literature of equal efficacy as apheresis which may be less invasive, less expensive, or have more supporting evidence?
4) Will treatment harm the patient? What is the risk/benefit ration in the specific patient setting with consideration of comorbidities and ongoing therapy?

Therapeutic apheresis procedure according to the facility study protocol. Follow inclusion and exclusion criteria.

ASFA Guidelines 2013

Approach to Category I Indications

• Category I – Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes.

• Examples
  • Thrombotic thrombocytopenic purpura – Recommendation Grade 1A
    • Strong recommendation that can apply to most patients in most circumstances
  • Acute inflammatory demyelination polyneuropathy – Recommendation Grade 1A
    • Strong recommendation that can apply to most patients in most circumstances
  • Anti-glomerular basement membrane antibody disease, dialysis independent – Recommendation Grade 1B
    • Strong recommendation, can apply to most patients in most circumstances without reservation
Approach to Category I Indications

Consider the following:
1) volume status of the patient,
2) cardiovascular stability,
3) vascular access,
4) risk of indwelling central venous access,
5) impact of apheresis on other treatment modalities,
6) removal or interactions with concurrent medications,
and 7) effect on accuracy of diagnostic tests.

Risk/Benefit Analysis

- UNFAVORABLE
  - Deny the request for therapeutic apheresis

- FAVORABLE
  - Decide on the most appropriate number of procedures with the follow-up plan

Approach to Category II Indications

• Category II – Disorders for which apheresis is accepted as second-line therapy, either as standalone treatment or in conjunction with other modes.

• Examples
  • Graft-versus-host disease, skin, chronic – Recommendation Grade 1B
    • Strong recommendation that can apply to most patients in most circumstances
  • Lipoprotein (a) hyperlipoproteinemia – Recommendation Grade 1B
    • Strong recommendation, can apply to most patients in most circumstances without reservation
  • Babesiosis, High-risk population – Recommendation Grade 2C
    • Very weak recommendation; other alternatives may be equally reasonable
Approach to Category II Indications


Category II

- Has first-line therapy been tried?
  - NO: Initiate first-line therapy
  - YES: Consider the following: 1) volume status of the patient, 2) cardiovascular stability, 3) vascular access, 4) risk of indwelling central venous access, 5) impact of apheresis on other treatment modalities, 6) removal or interactions with concurrent medications, and 7) effect on accuracy of diagnostic tests

Risk/Benefit Analysis

- UNFAVORABLE: Deny the request for therapeutic apheresis
- FAVORABLE: Decide on the most appropriate number of procedures with the follow-up plan

Has first-line therapy failed or is adjunct therapy indicated?

- NO: Treat with first-line therapy
- YES: Has first-line therapy been tried?

Initiate first-line therapy

UNFAVORABLE

FAVORABLE
Approach to Category IV Indications

- Category IV – Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken in these circumstances.

- Recommendation grades are the OPPOSITE for other categories!
  - 1 recommendation is a strong recommendation NOT to perform the procedure.
  - 2 recommendation is a weak recommendation NOT to perform the procedure.

- Examples
  - Schizophrenia – Recommendation Grade 1A
    - Strong recommendation that can apply to most patients in most circumstances
  - Immune thrombocytopenic purpura – Recommendation Grade 2C
    - Very weak recommendation, other alternatives may be equally reasonable
Approach to Category IV Indications

Consider the following:
1) volume status of the patient,
2) cardiovascular stability,
3) vascular access,
4) risk of indwelling central venous access,
5) impact of apheresis on other treatment modalities,
6) removal or interactions with concurrent medications, and
7) effect on accuracy of diagnostic tests.

Risk/Benefit Analysis

Decide on the most appropriate number of procedures with the follow-up plan.

Deny the request for therapeutic apheresis.

Approach to Category III Indications

• Category III – Optimum role of apheresis therapy is not established. Decision making should be individualized.

• Examples
  • Post transfusion purpura – Recommendation grade 2C
    • Very weak recommendation; other alternatives may be equally reasonable
  • Anti-glomerular basement membrane antibody disease in a patient who is dialysis dependent – 2B
    • Weak recommendation, best action may differ depending on circumstances or patients’ or societal values
Approach to Category III Indications

Consider the following:
1) volume status of the patient,
2) cardiovascular stability,
3) vascular access,
4) risk of indwelling central venous access,
5) impact of apheresis on other treatment modalities,
6) removal or interactions with concurrent medications, and
7) effect on accuracy of diagnostic tests.

Risk/Benefit Analysis

- UNFAVORABLE
  - Deny the request for therapeutic apheresis
- FAVORABLE
  - Decide on the most appropriate number of procedures with the follow-up plan

Approach to Uncategorized Indications

1. Evaluate available literature
2. Apply modified McLeod’s criteria
3. Consider the following:
   1) volume status of the patient,
   2) cardiovascular stability,
   3) vascular access,
   4) risk of indwelling central venous access,
   5) impact of apheresis on other treatment modalities,
   6) removal or interactions with concurrent medications,
   and 7) effect on accuracy of diagnostic tests
4. Risk/Benefit Analysis
5. Deny the request for therapeutic apheresis
6. Decide on the most appropriate number of procedures with the follow-up plan

Approach to Uncategorized Indications

• Review the medical record and speak with requesting physician.
  • Confirm diagnosis.
  • What other treatments have been attempted/are available?
  • Why will apheresis work?
Approach to Uncategorized Indications

- Review medical literature
  - What is the pathophysiology of the disease?
- Will the requested apheresis procedure modify the disease process?
- Has apheresis been attempted before? What was tried and what was the outcome?
- Is the disorder similar to other disorders successfully treated with apheresis?

**TABLE 3. Modified McLeod’s criteria for evaluation of efficacy of TA**

<table>
<thead>
<tr>
<th>Evidence</th>
<th>Explanation</th>
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<tbody>
<tr>
<td>Mechanism</td>
<td>The current understanding of the disease process supports a clear rationale for the use of TA modality.</td>
</tr>
<tr>
<td>Correction</td>
<td>The abnormality, which makes TA plausible, can be meaningfully corrected by its use.</td>
</tr>
<tr>
<td>Clinical effect</td>
<td>There is a strong evidence that TA confers benefit that is clinically worthwhile and not just statistically significant.</td>
</tr>
</tbody>
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Approach to Uncategorized Indications

• Discuss treatment with requesting physician
  • Define treatment plan (replacement fluid, number of procedures, course of therapy, etc.).
  • Define OBJECTIVE measures of response.
    • If not available, define subjective measures.
  • Define stopping rules.
Approach to Uncategorized Indications

- Patient with a history of ovarian carcinoma presented with rapid onset bilateral vision loss.

- Ophthalmologist noted proliferation of melanocytes in the retina of both eyes.

- Diagnosis of bilateral diffuse uveal melanocytic proliferation (BDUMP) was made.

- Ophthalmologist requested plasma exchange.

Approach to Uncategorized Indications

- Review of the medical record revealed:
  - Diagnosis on the request was correct.
  - No other treatments had been attempted.
- Discussion with the requesting physician revealed:
  - Ophthalmology literature hypothesizes that a soluble substance secreted by the tumor or in response to the tumor causes BDUMP.
  - No effective treatment with complete blindness within weeks to months after onset.
Approach to Uncategorized Indications

• Application of Modified McLeod’s Criteria
  • Mechanism – There appears to be a soluble substance present in BDUMP that drives melanocyte proliferations.
  • Correction – The type of substance is unknown but response in some patients to steroids suggests that it could be an immunoglobulin which could be removed by plasma exchange.
  • Clinical Effect – No reports of the treatment of BDUMP with plasma exchange but plasma exchange has been used to treat paraneoplastic neurologic syndromes.
Approach to Uncategorized Indications

• Discussion with the requesting physician
  • Follow treatment plan for paraneoplastic neurologic syndromes.
    • Six treatments every-other-day with albumin as the replacement.
  • Repeat ophthalmologic exam including visual acuity two weeks after completion of plasma exchange (objective measure of outcome).
• Consider additional procedures beyond six if objective improvement.
Approach to Uncategorized Indications

• Two patients with objective improvement in visual acuity and ophthalmologic exam.

• Sustained response of 13 months in one patient.
  • Worsening with response of 12 months to a second course.
  • Worsening with response of 10 months to a third course.

• IgG found in both patients’ plasma that induces proliferation in melanocyte culture assays.


Approach to Uncategorized Indications

• Subsequent independent report of use of plasma exchange in the treatment of BDUMP published.

References


