FOUR COMPONENT MEDICAL TREATMENT PROTOCOL FOR ADHESIVE ARACHNOIDITIS

GOALS OF THIS PROTOCOL

#1 Stop or slow progression of neurologic impairments and autoimmune manifestations.
#2 Allow patient to participate in activities of daily living and improve a quality of life.

METHOD OF
Forest Tennant M.D., Dr. P.H.

Arachnoiditis Medical Clinic
338 S. Glendora Ave.
West Covina, CA 91790
626-919-0064
Fax: 626-919-0065
E-mail: veractinc@msn.com
Websites: www.arachnoiditishope.com
www.foresttennant.com
www.hormonesandpaincare.com

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SPECIAL NOTES

This protocol is used only to treat patients who have MRI-documented adhesive arachnoiditis. The presence of neuroinflammation is validated by an elevated erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), MRI, and/or a clinical history of inflammatory symptoms such as episodes of sweating, increased temperature, and recurrent pain flares. This protocol is recurrently updated. It can be copied for use by health professionals. Some references are at the end of this protocol to provide some sources for this protocol.
THIS PROTOCOL IS BASED ON 4 PRIMARY COMPONENTS

THE FOUR LEGS OF CENTRALIZED PAIN AND NEUROINFLAMMATION TREATMENT

- Neuroinflammation Control
- Pain Relief
- Spinal Fluid Flow Exercises
- Neuroregeneration
PRE-PROTOCOL PREPARATION

We recommend a blood test be done prior to initiating medications in an MRI-documented case of adhesive arachnoiditis.

Here is our recommended blood panel:

1. Inflammation Markers
   a. ESR
   b. CRP-HS
   c. Option: cytokine panel with interleukins and tumor necrosis factor

2. Hormone Levels
   a. Cortisol
   b. Pregnenolone
   c. Progesterone
   d. Estradiol
   e. Testosterone
   f. DHEA
   g. Option: Adrenocorticotropin (ACTH)

3. Options: CBC, Liver function, renal function

Interpretation and Guidance

✓ If inflammatory markers are up, ketorolac by injection will likely be required.
✓ If inflammatory markers are normal, 1 or 2 oral anti-inflammatory or microglial suppressors will likely be adequate.
✓ Deficient serum hormone levels should be replenished for best results.
✓ Treatment can be initiated without laboratory testing if the patient cannot financially obtain them due to financial or logistical reasons.
COMPONENT NO. 1

NEUROINFLAMMATION CONTROL

<table>
<thead>
<tr>
<th></th>
<th>STARTING BASIC REGIMEN</th>
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<tbody>
<tr>
<td>1</td>
<td>Indomethacin 25 to 50 mg + With a meal on 3 to 5 days a week</td>
</tr>
<tr>
<td>2</td>
<td>Metformin 500 mg * At bedtime on 3 to 5 days a week</td>
</tr>
<tr>
<td>3</td>
<td>Dexamethasone .5 mg or methylprednisolone 4 mg At 3:00 PM on 3 to 5 days a week</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>OPTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ketorolac 30 mg By injection or by nasal spray, 1 to 3 times a week. Use for patients</td>
</tr>
<tr>
<td></td>
<td>with elevated serum inflammatory markers.</td>
</tr>
<tr>
<td>2</td>
<td>Pregnenolone 25 to 50 mg Daily</td>
</tr>
</tbody>
</table>

IMPLEMENTATION NOTES

1. Dosages of all medication can be raised over time to achieve more effectiveness, if needed.

2. *Alternates: acetazolamide 75 mg, minocycline 100 mg, pentoxifylline 400 mg. These are starting dosages.

3. Indomethacin and ketorolac are anti-inflammatory agents known to enter the central nervous system.

4. Only dexamethasone and methylprednisolone have been found by us to be effective corticosteroids in arachnoiditis. If one appears ineffective, switch to the other. They are started at a low intermittent dosage.

5. Not every measure in this protocol need be administered or prescribed to get a good therapeutic effect.

6. +Alternate: ibuprofen 800, 2 times a day on 3 to 5 days a week.
COMPONENT NO. 2

PAIN RELIEF

Listed here are most of the prescription pain relievers from which a physician or nurse practitioner may choose. Best results are obtained by using agents from more than one category. Starting dosages are listed, and effective dosage may need to be higher.

Pain relief is standard. The World Health Organization 3-Step Analgesic Ladder is recommended. (Attached)

A. Neuropathic Agents (Act to control electrical impulses by various mechanisms.)

<table>
<thead>
<tr>
<th>Component</th>
<th>Starting Dose</th>
<th>Component</th>
<th>Starting Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregabalin (Lyrica®)</td>
<td>50 mg TID</td>
<td>Gabapentin (Neurontin®)</td>
<td>100 mg TID</td>
</tr>
<tr>
<td>Topirimate (Topamax®)</td>
<td>25 mg BID</td>
<td>Baclofen (Lioresal®)</td>
<td>5 mg TID</td>
</tr>
<tr>
<td>Diazepam (Valium®)</td>
<td>2 mg BID</td>
<td>Carisoprodol (Soma®)</td>
<td>350 mg BID</td>
</tr>
<tr>
<td>Duloxetine (Cymbalta®)</td>
<td>20 mg BID</td>
<td>Tizanidine (Zanaflex®)</td>
<td>2-4 mg TID</td>
</tr>
</tbody>
</table>

B. N-Methyl-D-Asparate Receptor Antagonist

1. Ketamine 15 to 25 mg sublingual or oral BID. Increase up to 100-150 mg/day.
2. Pregnenolone 25-100 mg daily

C. Topical Agents (One or more. Apply as needed)

1. Lidocaine/Prilocaine gel
2. Lidocaine patch
3. Morphine 30-60 mg in 1 ounce of base cream or gel
4. Any other single or multi-agent topical that has been found to provide relief

D. Adrenergic Agent for Descending Pain

<table>
<thead>
<tr>
<th>Component</th>
<th>Dose</th>
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</thead>
<tbody>
<tr>
<td>Methylphenidate (Ritalin®)</td>
<td>5-10 mg BID</td>
</tr>
<tr>
<td>Amphetamine/dextroamphetamine Salts (Adderal®)</td>
<td>5-10 mg BID</td>
</tr>
<tr>
<td>Dextroamphetamine</td>
<td>5-10 mg BID</td>
</tr>
<tr>
<td>Other adrenergic agent– practitioner choice</td>
<td></td>
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</table>

E. Weak Opioids

1. Tramadol-50 to 100 mg-1 to 4 a day or prn pain
2. Codeine/Acetaminophen 30-60 mg 1 to 4 times a day or prn pain

F. Intermediate Opioids

1. Hydrocodone/Acetamophen-5 to 10 mg with 325 mg of acetaminophen; 1 to 4 times a day prn pain
2. Oxycodone/Acetaminophen 5 to 10 mg with 325 mg of acetaminophen 1 to 4 times a day or prn pain
G. Potent Opioids

1. Morphine-15 to 30 mg; 1 to 4 times a day
2. Hydromorphone 2 to 8 mg 1 to 4 times a day
3. Tapentadol-10 to 50 mg; 1 to 4 times a day
4. Oxycodone 10 to 30 mg 1 to 4 times a day

J. Long-Acting Opioids: Reserved for arachnoiditis patients with documented adhesions, active inflammation, and progressive neurologic impairments (paraparesis, bladder-bowel dysfunction, blurred vision, autoimmune symptoms). Add to a regimen of non-opioid agents and weak-intermediate opioids.

1. Methadone-5 BID, raise dosage as needed
2. Fentanyl Transdermal 50 mcg patch every 3rd day, raise dosage as needed.

SPECIAL NOTES:

1. Injectable opioids are reserved for very active adhesive arachnoiditis patients who have uncontrolled constant flares and/or poor gastrointestinal absorption of oral opioids
2. Ketorolac (Toradol®, Sprix®) by injection or nasal spray (15 to 60 mg) can be used for pain flare treatments
3. Intrathecal opioids and/or electric stimulators may be necessary to control pain if oral opioids are unsuccessful.
4. The pain of adhesive arachnoiditis has neuroinflammatory, centralization, and neuropathic components. All 3 components may have to be treated.
5. Except for “around-the-clock” long-acting opioids there is no clinical reason to give an analgesic on other than a prn basis and only on the days of pain.
6. Use agents from multiple categories for best response. Starting doses are given. They are low as arachnoiditis patients may be very sensitive to medications. An agent from every category may not be needed.

FLARE TREATMENT

OPTIONS

1. Methylprednisolone (Medrol®) – 6 Day Dose Pak with injectable or nasal ketorolac 30 to 60 mg for 3 consecutive days.
2. Injection or suppository (Choose One) Practitioners Choice
   a. Opium/Belladonna-Suppository
   b. Hydromorphone – 4 to 8 mg
   c. Morphine – 10 to 20 mg
   d. Meperidine – 50 to 100 mg
COMPONENT NO. 3

SPINAL FLUID FLOW EXERCISES

1. RELIEF OF PRESSURE

*Acetazolamide – 75 mg twice a day and increase up to 500 mg a day, if helpful

2. SPECIFIC DAILY EXERCISES/ThERAPIES – PATIENT SHOULD PICK

Walking  Maximal Stretch of Extremities
Arm/Upper Body Swings ("Power Walking")  Trampoline Walking
Walking”)  Rocking Chair
Straight Leg Raising  Massage

SPECIAL CONSIDERATIONS

1. *Acetazolamide should be attempted if symptoms of blurred vision, tinnitus, headaches, poor balance, or spinal fluid flow blockage are apparent on MRI. Start at ¼ (75 mg) tablet twice a day and increase as needed.

2. Spinal fluid may seep through the dura into the soft tissues over and around the lumbar/sacral spine if inflammation and adhesions damage the spinal canal lining.

COMPONENT NO. 4

NEUROREGENERATION

1. REPLENISH DEFICIENT HORMONES AS DETERMINED BY SERUM TESTING

<table>
<thead>
<tr>
<th>HORMONE</th>
<th>STARTING DOSE</th>
</tr>
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<tbody>
<tr>
<td>1 Pregnenolone</td>
<td>50-100 mg on 3 to 5 days a week</td>
</tr>
<tr>
<td>2 DHEA</td>
<td>50-100 mg on 3 to 5 days a week</td>
</tr>
<tr>
<td>3 Testosterone</td>
<td>Males: Follow commercial labeling- on 3 to 5 days a week Females: 20-25% of male dosage</td>
</tr>
<tr>
<td>4 Estradiol</td>
<td>.5 mg on 3 to 5 days a week</td>
</tr>
<tr>
<td>5 Progesterone</td>
<td>50-100 mg on 3 to 5 days a week</td>
</tr>
</tbody>
</table>

2. NUTRITIONAL SUPPLEMENTS: B-12 – Practitioner’s Choice

3. NEUROHORMONES:

1. Human Chorionic Gonadotropin, 250 to 500 units 3 times a week (starting by sublingual or injection routes)

2. Oxytocin, 20 units BID by sublingual route

3. Pregnenolone, high dose, 200 to 400 mg a day by oral route

SPECIAL NOTES

1. A neurohormone trial of 60 days is sufficient to see if there is clinical improvement.

2. If side-effects occur stop the agent.

3. It is recommended that reasonable pain relief and neuroinflammation control be in place before use of hormones.

These 3 hormones can be given individually or combined. Recommend starting one at a time. Side-effects can occur with any of the three. Starting dosages are given, and they can be raised.
SOME MEASURES OF TREATMENT SUCCESS

PHYSIOLOGIC
1. Normalized BP, pulse, O₂
2. Pupil size between 3 and 5.0mm in diameter
3. Increased range of motion and stride
4. Strength of hands

SOCIAL AND FAMILY ACTIVITIES
1. Leave home more often
2. More activities of daily living: dressing, hygiene/sanitation, diet/nutrition, sleep
3. More social/family interaction

PAIN RELIEF
1. Achieve some pain free hours
2. Fewer flares
3. Longer time between flares
4. Less flare medication
5. Increased physical activities

WORLD HEALTH ORGANIZATION
THREE STEP ANALGESIC LADDER
1982-1986
References


