Understanding Myositis Medications

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General Concepts: Myositis Therapies

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  - Methotrexate, imuran, cytoxan and rituximab
- Borrowed from transplant surgeons
  - Cyclosporine, tacrolimus, MMF (CellCept)

Myositis Medications

- Glucocorticoids (steroids)
- Immunosuppressive Agents
- Combinations of drugs
- IVIg (gamma globulin)
- Biologic agents

Myositis Medications

- Glucocorticoids (steroids)

Drug	Dose	Level of evidence for use in myositis
Glucocorticoids	Begin at 1 mg/kg/day, often in divided doses and generally not exceeding 80 mg daily. Taper by 20-25% of existing dose monthly until 5-10 mg/day reached. Hold tapering for total duration of therapy of 6 to 12 months.	Retrospective studies

Moghadam-Kia, Exp Rvw Clin Immun, in press

Drug	Dose	Common side effects	Level of evidence for use in myositis	Special comments
Corticosteroids	Starting at 1 mg/kg or 60–80 mg/d in 2 or 3 divided doses	Osteoporosis, steroid myopathy, glaucoma, cataract, risk of infection	Case series	Usual initial therapy with or without additional immunosuppression
Methotrexate	Starting at 10–15 mg/wk (orally or subcutaneously) with an increase to 25 mg/wk	Hepatic toxicity, bone marrow suppression, risk of infection	Uncontrolled cohort studies	First-line immunosuppression unless contraindicated
Azathioprine	Starting at 50 mg/d and increased by 50 mg every 2 wk up to 2–3 mg/kg/d	Gastrointestinal symptoms, bone marrow suppression, hepatic toxicity, pancreatitis, risk of infection	Uncontrolled cohort studies	First-line immunosuppression unless contraindicated
Cyclosporine	Starting at 50 mg twice daily and increasing to final dose of 100–150 mg twice daily	Nephrotoxicity, neurotoxicity, abnormal glucose metabolism, hyperkalemia, headache, tremor, hypertension, risk of infection	Case series	Second-line immunosuppression; some evidence of efficacy in myositis-associated lung disease
Tacrolimus	Starting at 1 mg twice daily and slowly increasing for trough level of 8–12	Similar to cyclosporine	Case series	Second-line immunosuppression; some evidence of efficacy in myositis-associated lung disease
Immunoglobulins	Starting at 2 g/kg/mo given over 2–5 d	Hypertension, volume overload, renal toxicity, headaches	One double-blind, placebo-controlled trial	Second-line immunosuppression for refractory myositis patients; some evidence of efficacy in dysphagia and refractory skin disease; can be used in patients with infection
Mycophenolate	Starting at 500 mg twice daily, slowly increasing to 2–3 g/d	Bone marrow suppression, gastrointestinal intolerance, risk of infection	Case series	For refractory cases; some efficacy in refractory skin disease and possibly in interstitial lung disease
Cyclophosphamide	Oral: 2-mg/kg/d dose	Malignancy, bone marrow suppression, hepatotoxicity	Case reports	Limited to very refractory cases with interstitial lung disease
Rituximab	2 doses of 1,000-mg intravenous infusion 2 wk apart	Risk of infection	Case series	For refractory cases; possible use in interstitial lung disease

Aggarwal/Oddis, Curr Rheum Rep, 2011

Myositis Medications

- Glucocorticoids (steroids)
- Immunosuppressive Agents
- Combinations of drugs

Medications After Prednisone

- Most physicians choose glucocorticoids as their initial treatment
- Methotrexate is often given next or even concomitantly with steroids
- Azathioprine may be given using same rationale

Rationale Behind Medications

- Published studies
- Experience of the treating physician
  - Art > Science
- Rheumatology vs. Neurology
  - Methotrexate: rheumatologist
  - Azathioprine: neurologist

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- Look at published studies
  - Case series with very few ‘controlled’ trials

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Mycophenolate mofetil	Begin at 250-500 mg twice daily (oral) with increase by 250 to 500 mg increments every 1-2 weeks to target dose of 1500-3000 mg/day.	Retrospective uncontrolled studies
Cyclosporine	Begin at 50 mg twice daily; increase up to 100-150 mg twice daily	Retrospective controlled studies
Tacrolimus	Begin at 1 mg twice daily; increase to reach trough level of 5-10 ng/ml	Retrospective controlled studies
Cyclophosphamide	Begin at 50-75 mg/day (oral) working up to 1.5-2 mg/kg/day.	Prospective uncontrolled studies on myositis-ILD; case reports on myositis

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Choosing the Right Drug

- How does your doctor decide how to treat you
- Simple decisions
- More complex decisions

Targets of Myositis

- Muscle (myositis)
- Skin
- GI tract: difficulty swallowing

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Intravenous immune globulin (IVIg)	Begin at 1-2 grams/kg/month over 1-2 days continuing for 3-6 months depending on response	Double-blind, placebo controlled trial

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- Skin
- GI tract: difficulty swallowing
- Joint pain (arthritis)
  - May get treated like you have rheumatoid arthritis

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- Joint pain (arthritis)
- Lung (ILD)
  - Shortness of breath
  - Inflammation in lung tissue
  - Fibrosis (scar tissue)

Treatment of ILD in Myositis Patients

- Steroids (prednisone) still the initial treatment
- Cyclophosphamide and azathioprine used early or in steroid-resistant cases with variable results
- CellCept is being increasingly used
- Cyclosporin A and tacrolimus (medications used to prevent rejection of transplanted organs)
- Maybe even some biologic agents like rituximab

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Drug	Level of evidence for use in inflammatory myopathy
Rituximab	Double-blind (improvement in IMACS definition of improvement)
Etanercept	One placebo-controlled trial of etanercept with significantly longer median time to treatment failure. Retrospective uncontrolled studies for infliximab Utility in myositis limited by negative studies as well as potential for *inducing* PM and DM
Infliximab	
Tocilizumab	Case reports
Abatacept	Ongoing clinical trial (ARTEMIS)
Sifalimumab (anti-Interferon) * Interferon is an inflammatory cytokine	Early study showed some clinical improvement