PMR Treatment Guidelines Handout

Target population: Patients with PMR based on clinician diagnosis which may be supported by currently available diagnostic or classification criteria.

Overarching principles for the management of PMR

1. Adoption of a safe and specific approach to ascertain the PMR case definition. The clinical evaluation should be directed toward exclusion of relevant mimicking (eg, non-inflammatory, inflammatory (such as giant cell arteritis or rheumatoid arthritis), drug-induced, endocrine, infective and neoplastic) conditions.
2. Every case of PMR should have the following assessments prior to the prescription of therapy (primary or secondary care):
    - Documentation of a basic laboratory dataset. This will help to exclude mimicking conditions and establish a baseline for monitoring of therapy. This should include rheumatoid factor and/or anti–cyclic citrullinated peptide antibodies (ACPA), C-reactive protein and/or erythrocyte sedimentation rate (ESR), blood count, glucose, creatinine, liver function tests, bone profile (including calcium, alkaline phosphatase) and dipstick urinalysis. Additional investigations to consider are protein electrophoresis, thyroid stimulating hormone (TSH), creatine kinase and vitamin D.
    - Depending on clinical signs and symptoms and the likelihood of the alternative diagnoses, additional more extensive serological tests such as anti-nuclear antibodies (ANA), anti–cytoplasmic neutrophil antibodies (ANCA) or tuberculosis tests may be performed to exclude mimicking conditions. Additional investigations such as chest radiographs may be considered at the discretion of the physician in order to exclude other diagnoses.
    - Determination of comorbidities (particularly hypertension, diabetes, glucose intolerance, cardiovascular disease, dyslipidemia, peptic ulcer, osteoporosis [and particularly recent fractures]), presence of cataract or (risk factors for) glaucoma, presence of chronic or recurrent infections, and co-medication with non-steroidal anti-inflammatory drugs (NSAIDs) as outlined in Smolen et al and Gossec et al, other relevant medications and risk factors for steroid-related side effects. Female sex was associated with a higher risk of glucocorticoid (GC) side effects in low to moderate quality studies.
    - The role of risk factors for relapse/prolonged therapy is not clear yet. Baseline factors that were associated in low to moderate quality studies with a higher relapse rate and/or prolonged therapy in PMR studies were: female sex (24,26), high ESR (.40 mm/hour) and peripheral inflammatory arthritis. A number of equally low to moderate quality studies, however, failed to demonstrate an association between these factors and relapse/prolonged therapy.
3. Consideration of specialist referral, particularly in case of atypical presentation (such as peripheral inflammatory arthritis, systemic symptoms, low inflammatory markers, age ,60 years), experience of or high risk of therapy-related side effects, PMR refractory to GC therapy, and/or relapses/prolonged therapy.
4. Treatment of PMR patients should aim at the best care and must be based on a shared decision between the patient and the treating physician.
5. Patients should have an individualized PMR management plan. Patient perspective and preferences should be considered in the individualized choice of initial GC dose and subsequent tapering of GCs in PMR.

6. Patients should have access to education focusing on the impact of PMR and treatment (including comorbidities and disease predictors) and advice on individually tailored exercise programs.
7. Every patient treated for PMR in primary or secondary care should be monitored with the following assessments: risk factors and evidence for steroid-related side effects, comorbidities, other relevant medications, evidence and risk factors for relapse/prolonged therapy. Continuous documentation of a minimal clinical and laboratory dataset should be conducted while prescribing GCs. Follow-up visits are suggested every 4–8 weeks in the first year, every 8–12 weeks in the second year, and as indicated in case of relapse or as prednisone is tapered and discontinued.
8. It is important for patients to have rapid and direct access to advice from doctors, nurses or trained allied healthcare staff to report any changes in their condition such as flares and adverse events.

Specific recommendations for the management of PMR patients

1. The panel strongly recommends using GC instead of NSAIDs in patients with PMR, with the exception of possible short-term use of NSAIDs and/ or analgesics in PMR patients with pain related to other conditions. No specific recommendation can be made for analgesics.
2. The panel strongly recommends using the minimum effective individualized duration of GC therapy in PMR patients.
3. The panel conditionally recommends using the minimum effective GC dose within a range of 12.5–25 mg prednisone equivalent daily as the initial treatment of PMR. A higher initial prednisone dose within this range may be considered in patients with a high risk of relapse and low risk of adverse events, whereas in patients with relevant comorbidities (eg, diabetes, osteoporosis, glaucoma, etc.) and other risk factors for GC-related side effects, a lower dose may be preferred. The panel discourages conditionally the use of initial doses #7.5 mg/day and strongly recommends against the use of initial doses .30 mg/day.
4. The panel strongly recommends individualizing dose tapering schedules, predicated to regular monitoring of patient disease activity, laboratory markers and adverse events.The following principles of GC dose tapering are suggested:

   A. Initial tapering: Taper dose to an oral dose of 10 mg/day prednisone equivalent within 4–8 weeks.

   B. Relapse therapy: Increase oral prednisone to the pre-relapse dose and decrease it gradually (within 4–8 weeks) to the dose at which the relapse occurred.

   C. Tapering once remission is achieved (following initial and relapse therapies): Taper daily oral prednisone by 1 mg every 4 weeks (or by 1.25 mg decrements using schedules such as 10/7.5 mg alternate days, etc.) until discontinuation given that remission is maintained.
5. The panel conditionally recommends considering intramuscular (i.m.) methylprednisolone as an alternative to oral GCs. The choice between oral GCs and i.m. methylprednisolone remains at the discretion of the treating physician. In one clinical trial, a starting dose of 120 mg methylprednisolone i.m. injection every 3 weeks was applied (23).
6. The panel conditionally recommends using a single rather than divided daily doses of oral GCs for the treatment of PMR, except for special situations such as prominent night pain while tapering GCs below the low-dose range (prednisone or equivalent ,5 mg daily).
7. The panel conditionally recommends considering early introduction of methotrexate (MTX) in addition to GCs, particularly in patients at a high risk for relapse and/or prolonged therapy as well as in cases with risk factors, comorbidities and/or concomitant medications where GC-related adverse events are more likely to occur. MTX may also be considered during follow-up of patients with a relapse, without significant response to GC or experiencing GC-related adverse events. MTX has been used at oral doses of 7.5–10 mg/week in clinical trials (24–27).

8. The panel strongly recommends against the use of TNFa blocking agents for treatment of PMR.
9. The panel conditionally recommends considering an individualized exercise program for PMR patients aimed at the maintenance of muscle mass and function, and reducing risk of falls especially in older persons on long-term GCs as well as in frail patients.
10. The panel strongly recommends against the use of the Chinese herbal preparations Yanghe and Biqi capsules in PMR patients.

Reference

Dejaco, C., Singh, Y. P., Perel, P., Hutchings, A., Camellino, D., Mackie, S., Abril, A., Bachta, A., Balint, P., Barraclough, K., Bianconi, L., Buttgereit, F., Carsons, S., Ching, D., Cid, M., Cimmino, M., Diamantopoulos, A., Docken, W., Duftner, C., & Fashanu, B. (2015). 2015 recommendations for the management of polymyalgia rheumatica: A European League Against Rheumatism/American College of Rheumatology collaborative initiative. *Arthritis & Rheumatology*, *67*(10), 2569–2580. https://doi.org/10.1002/art.39333