Condition: Meibomian gland dysfunction

Description:
Meibomian gland dysfunction (MGD) is a common condition characterised by a chronic, diffuse abnormality of the meibomian glands resulting in duct obstruction and changes in glandular secretion (1). Patients with early MGD may be asymptomatic, in which case the condition is considered subclinical. As the condition progresses patients are likely to become more symptomatic and changes to the posterior lid margin occur.

Significance:
Meibomian gland dysfunction is one of the most frequent presentations to the eye care professional and is recognised to have a significant, adverse impact on quality of life in affected individuals.

Prevalence:
It is believed that MGD is the leading cause of dry eye disease (1) and up to 50% of patients seen in optometric practice show signs and/or symptoms of MGD (2).

Signs:
The following sequence of tests has been recommended for the evaluation of patients with ocular surface disease (1):

1. Administration of a validated dry eye questionnaire, e.g. the Ocular Surface Disease Index (3) (http://dryeyezone.com/documents/osdi.pdf) or McMonnies dry eye questionnaire (4)
2. Calculation of blink rate and blink interval
3. Measurement of tear meniscus height
4. Measurement of tear osmolarity if possible (5)
5. Non-invasive break-up time, or tear break-up time with minimal fluorescein
6. Grading of conjunctival and corneal staining
7. Schirmer or phenol red thread test
8. MGD assessment – quantification of morphological lid features, expressibility and quality of meibum, and meibography to determine drop out (6).

**Differential Diagnosis:**

1. Aqueous deficient dry eye
2. Anterior blepharitis
3. Posterior blepharitis – (of which MGD is one sub-category) describes inflammatory changes of the posterior lid margin, which could have underlying causes such as infection, allergy or systemic conditions such as acne rosacea (7)
4. Conjunctivitis – bacterial, viral or allergic
5. Floppy eyelid syndrome
6. Demodex infestation of the eyelids.

**Management:**

**Non-pharmacological treatment**

1. **Warm compresses and lid massage**: for 15 minutes up to four times daily. However, compliance with lid hygiene practices is generally poor and often abandoned prematurely.
2. **Diet**: increase in intake of omega-3 fatty acids has been shown to have anti-inflammatory properties and may help to improve the signs and symptoms of dry eye disease. (8) However, practitioners should caution patients against excessive doses of omega-3 fatty acids due to their anticoagulation effects.
3. **Environment management**: improving ambient humidity and optimizing work stations.
4. **Tear supplementation**: often MGD and aqueous-deficient dry eye co-exist, and supplementation with artificial tears may reduce tear film hyper-osmolarity and
lid wiper epitheliopathy. The frequent use of artificial tears may also dilute toxins and pro-inflammatory mediators found in tears, and address any evaporative component of dry eye disease associated with MGD.

Tear supplementation that increases the lipid layer, e.g. lipid-containing drops or liposomal sprays, may be particularly beneficial for relieving the symptoms of MGD and evaporative dry eye.

5. **Intense pulsed light (IPL) therapy**: Application of IPL has proven benefits in MGD by improving meibomian gland function. Improvements in lipid layer thickness, tear film stability and symptoms have been demonstrated in a randomised, double-masked clinical trial. (9) Melanin preferentially absorbs the emitted energy placing darker skins at higher risk of burning, therefore modifying the fluence (power) level according to skin pigmentation is essential. Tightly fitting metal goggles are necessary to protect the globe from the emitted light.

**Topical Treatment**

1. **Topical antibiotics**: may be useful in decreasing the bacterial load on the eyelids. Topical azithromycin 1% eye drops (twice daily) have been shown to be particularly effective and significantly improve meibomian gland plugging, meibomian gland secretions and eyelid hyperaemia, as well as patients symptoms (10), however, topical azithromycin is not currently available in NZ.

2. **Topical corticosteroids**: inflammation may be present or absent in MGD and therefore, the use of steroid eye drops is not necessarily beneficial. Furthermore, use of steroids is questionable when there is the potential of sight-threatening complications in a disease entity that is non-sight threatening (11). Where deemed necessary in a flare-up, topical steroid use should be prescribed for a restricted period (e.g. 2 weeks), and should be limited as much as possible to low potency steroids (e.g. FML).

3. **Topical cyclosporine (Restasis)**: indicated primarily for aqueous deficiency, this may play some role in treating MGD, although evidence is equivocal. In one small study of 33 patients, topical cyclosporine did not improve symptoms, but did decrease the number of blocked meibomian glands (12).
Oral Treatment

1. **Tetracyclines:** e.g. doxycycline, minocycline and tetracycline, can be used to treat a number of ocular surface diseases including ocular rosacea, blepharitis, recurrent corneal erosion and dry eye disease. Tetracyclines decrease the secretion of bacterial lipases that break down the normal meibum lipids into free fatty acid fragments. They also have anti-collagenase and anti-matrix metalloproteinase (MMP) properties, which reduce the inflammatory effects of MGD. Although the mechanisms of action of tetracyclines are not fully understood, tetracyclines appear to improve the lipid profile of the tear film in patients with MGD.

The recommended dosage of doxycycline and minocycline for anti-inflammatory treatment of MGD is 50mg – 100mg once daily, for 3 months (this is much less than the therapeutic antibiotic dose) (11). Tetracyclines should always be administered with food or adequate amounts of fluid and the patient should remain sitting or standing for up to 2 hours after administration to minimise oesophageal irritation.

Tetracyclines should not be administered to patients taking Warfarin (brand name, COUMADIN®), as the interaction may enhance warfarin’s blood-thinning properties. Tetracyclines are also contraindicated during pregnancy and childhood (up to 12 years of age) as they affect tooth development and can lead to permanent discolouration of the teeth. They can also interfere with bone development, although in neonates this appears to be reversible when tetracyclines are discontinued. Tetracyclines can cross the placenta and have been found in the breast milk of lactating women, and therefore should not be used during pregnancy or while breast feeding.

Gastrointestinal side effects are common, particularly with higher doses of tetracyclines, and these include nausea, dyspepsia, diarrhoea and anorexia. Photosensitivity can occur in some individuals and treatment should be discontinued at the first sign of skin erythema. Patients should be warned to apply adequate sunscreen and cover up to ensure protection. Less common adverse reactions include rashes, dermatitis, benign intracranial hypertension and haematological abnormalities.

Minocycline is generally used less frequently due to its comparatively higher rate of side effects, including drug-induced lupus. (13)
2. **Macrolides**: also have anti-inflammatory and anti-MMP properties and azithromycin has been shown to have some success in treating patients with MGD by altering the lipid properties of meibomian gland secretions (14).

Current prescribing protocols for posterior blepharitis vary, but a typical dosage prescribed in NZ is a 500mg tablet daily on two consecutive days, with a view to providing anti-inflammatory benefits for 3 months. Alternatively, a pulsed dosage has been suggested, with oral azithromycin prescribed at 500 mg per day for 3 days in 3 cycles, with an interval of 7 days between each cycle (15).

Oral erythromycin has also demonstrated efficacy in children with ocular rosacea (16) and blepharokeratitis (17), and may be considered an alternative therapy option for patients where other oral medications are contraindicated or poorly tolerated. In children, the recommended dose is 250 mg four times daily, although adult doses have not been established (17).

Macrolides are contraindicated in patients with known hypersensitivity, and patients with severely impaired hepatic function. Erythromycin has been reported to aggravate muscle weakness associated with myasthenia gravis. It should not be used in patients who are taking theophylline due to the potential of theophylline toxicity and reduced efficacy of erythromycin. Erythromycin should also not be combined with anti-coagulant agents or benzodiazepines.

The most common side effects of macrolides are gastrointestinal upset including nausea, diarrhoea, vomiting and abdominal pain. There have also been isolated reports of central nervous system disturbance including confusion, hallucinations, tinnitus, seizures and vertigo.

**Review:**

There are no specific guidelines for follow-up of patients with MGD, and review will depend on the severity of signs and symptoms. Regular follow-up visits are required for all patients to monitor treatment efficacy and compliance.

**Referral criteria:**

MGD would not generally be referred for ophthalmological opinion, however, in severe cases, where there is significant central corneal staining and long-term anti-
inflammatory management may be needed, co-management with an ophthalmologist should be considered.

References:


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