SCOTTISH MUSCLE NETWORK

Scottish guideline for Management of Mitochondrial disorders

NOTE
This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined based on all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

Patients with mitochondrial disease typically have a heterogeneous multisystem disorder. This guideline suggests surveillance to be considered at review appointments. Given the heterogeneous nature of mitochondrial disorders, some aspects of this guidance may be of varying relevance. Specific genotype focused guidance can be sought from local neurology or specialist mitochondrial services.

Further advice can be found at Care Guidelines - Rare Mitochondrial Disorders Service (mitochondrialdisease.nhs.uk)

Neurology

At each review, enquiry should be made regarding the possible development of ataxia, hearing loss, seizures, muscle weakness/pain, migraine, neuropsychiatric features, cognitive decline, autonomic dysfunction, weight loss, and dysphagia. Patients with any suspicion of these or other neurological symptoms should be referred to a neurologist.

Episodes of encephalopathy, recurrent seizures, a rapidly evolving visual field defect, or prolonged headache should prompt consideration of a possible stroke-like episode, and urgent advice from local neurology department or specialist mitochondrial service should be sought.

Drugs

Care should be taken when prescribing new medications as they may interfere with mitochondrial function. The following should be avoided where possible: metformin, aminoglycosides, zidovudine. Sodium valproate should be avoided in patients with POLG-related mitochondrial disorders, and use should be discussed with local neurology department or specialist mitochondrial service. CK should be monitored before and after starting a statin. There is limited evidence supporting the use of Coenzyme Q10 and riboflavin, and these should only be prescribed by a neurologist.

Endocrine

HbA1c and random glucose should be tested annually. If >48mmol/mol OR, if > 42mmol/mol AND fasting random glucose >7mmol/l, the patient should be referred to diabetes team.

Cardiology

Abnormalities can include cardiomyopathy, conduction defects and cardiac autonomic dysfunction.

ECG should be done annually. If paroxysmal symptoms consider a 24-hour tape, particularly in those at high risk (single large-scale deletion, m.3242A>G or m.8344A>G mutations).

Echocardiogram should be done annually. This can be done three-yearly if normal after 3 consecutive years.

Patients with abnormal ECG, echocardiogram or concern over cardiac symptoms, should be referred to a cardiologist, preferably with an interest in inherited cardiac conditions.

Visual

At each review, enquiry should be made regarding visual acuity, development of ocular dysmotility, or ptosis. If vision is deteriorating, patients should be referred to ophthalmology for detailed fundoscopy examination in addition to conventional diabetic retinopathy screening. Note a rapidly evolving visual field defect may reflect a stroke-like episode and requires urgent input (see above).

Respiratory

At each review, enquiry should be made of aspiration, recurrent infection, sleep disordered breathing, or ventilatory failure. Any symptoms should prompt consideration of pulmonary function tests and referral to a respiratory physician, ideally with an interest in muscle disorders. Patients with limb weakness should be referred to a respiratory physician even in the absence of symptoms.

Nephropathy

Patients with mitochondrial disease are at risk of developing chronic kidney disease, in particular diabetic nephropathy and focal segmental glomerulosclerosis.

U&Es and eGFR should be tested annually. A sustained decrease in eGFR of 15mL/min/1.73m2 within 12 months, albumin: creatinine ratio >70mg/mmol or symptomatic renal disease should prompt referral to a nephrologist (NICE guidelines).

Gastrointestinal

At each review, BMI should be assessed. The importance of regular balanced meals, avoiding fasting and adequate hydration should be emphasised. There should be a low threshold for referral to dietetics. Enquiry should be made about bowel habits, aiming for at least one motion per day, and any features suggestion of intestinal pseudo-obstruction or malabsorption. Referral to gastroenterology may be required. Please note the management of intestinal pseudo-obstruction is conservative and surgery should be avoided where possible.

Pre-pregnancy / pregnancy

All women considering a pregnancy should be commenced on high dose folic acid (5mg) and referred for pre-conception counselling, ideally to an obstetric clinic for review of medication and discussion of medical co-morbidities, including diabetes. Women should be screened for gestational diabetes. Neurology advice should be sought for optimisation of anti-seizure medication. Patients can be referred to the specialist mitochondrial reproduction clinic at Newcastle for genetic counselling and discussion of reproductive options, including pre-implantation genetic diagnosis and mitochondrial donation.

Genetics

All patients should be referred to their local clinical genetics clinic at the point of diagnosis for genetic counselling and to allow cascade testing of relatives. Clinicians managing diagnosed patients should ensure that a clinical genetics referral has been offered.