NHS

Gloucestershire Health Community

Midodrine (Unlicensed in UK) Shared Care Guideline

Therapeutic Use

Midodrine is an alpha adrenergic agonist. It therefore acts to increase blood pressure through peripheral vasoconstriction, and this mode of action provides particular increase in standing blood pressure, and hence a reduction in postural drop in blood pressure. It tends to increase systolic more than diastolic blood pressure. It is actually a pro-drug, and is metabolised to the active metabolite desglymidodrine. It is licensed in a number of countries in the EU and in the US, but is not currently licensed in the UK. Relevant details have been taken from the Eire SPC (http://www.medicines.ie/medicine/6209/SPC/Midon+Tablets+2.5mg/)

Cautions

Avoid in pregnancy unless patient benefits clearly outweigh patient hazards

Contra-indications

Contraindications: - hypertension, severe organic heart disease, thyrotoxicosis, phaeochromocytoma, acute nephritis, severe renal impairment (creatinine clearance <30ml/min), urinary retention, narrow angle glaucoma or known hypersensitivity to any component of the product.

Dosage and administration

The usual starting dose is 2.5 mg twice daily. The dose should be increased slowly until an optimal response is obtained. Most patients are controlled at 20-30 mg daily given in divided doses, three to four hours apart. Doses in excess of 30 mg daily are to be prescribed by the specialist only. The last dose should be taken at least four hours before bedtime to reduce the risk of supine hypertension.

Great caution should be exercised in patients with mild to moderate renal insufficiency (Creatinine clearance between 30 and 90 ml/min).

When the dose has been stabilised over 2 reviews, and the GP informed with a month's notice of handing over (to allow any discussion between GP and specialist), the patient can be handed over to Primary care prescribing.

Side-effects

- CVS: Palpitations, tachycardia, reflex bradycardia, arrhythmias and supine hypertension
- GI disorders: nausea/dyspepsia, vomiting
- Urinary: urinary retention and dysuria
- CNS: headache, restlessness, excitability, irritability, light-headedness or dizziness
- Skin: Piloerection, chills, parasthesia, rash, pruritus (mostly scalp) and flushing
- Other reported symptoms include increased tear production

The management of postural hypotension

A step-wise approach is generally recommended. Full assessment should enable a diagnosis of the likely cause of postural hypotension – whether drug-related, secondary to systemic disease such as anaemia or dehydration, or related to autonomic neuropathy. Treatment steps can then be summarised:

1. Review medication, and stop, or reduce dose of possible offending medications, with particular attention to diuretic use.
2. Prescribe graduated compression stockings (**NOT** TEDS) – and consider practical assistance to enable their usage. Some situations will preclude their use – peripheral vascular disease, or inability to apply the stockings daily.

3. Review progress after a reasonable period (several weeks), and consider further drug changes
4. Prescribe fludrocortisone if it is considered that this will not induce heart failure, starting with 50 micrograms at night.
5. Titrate fludrocortisone slowly over several weeks until either the desired effect has been achieved or maximum dose of 300mcg reached.
6. Where fludrocortisone cannot be prescribed, or has proved ineffective, then midodrine should be considered at an initial dose of 2.5mg two to three times daily.
7. Titrate midodrine to a usual maximum dose of 10mg three times per day. Midodrine should only be continued if symptoms of hypotension have been significantly reduced.

Drug interactions

The hypertensive effect may be enhanced by guanethidine, atropine, antihistamines, thyroid hormones, methyldopa or tricyclic antidepressants.
Effect may be antagonised by alpha blockers.
An exaggerated response to this drug may be expected in those patients who have received MAOIs within the previous 14 days and in patients receiving other sympathomimetic agents e.g. decongestants and some appetite suppressants.
May intensify bradycardia produced by beta-blockers, digoxin (or other glycosides) or psychopharmaceutical drugs.
Increased risk of glaucoma/increased intraocular pressure in combination with mineralcorticoids or glucocorticoids (e.g. fludrocortisone).

Monitoring

The major difficulty with midodrine is that it will increase supine blood pressure, as well as reducing postural drop, and hence it is difficult to use where supine blood pressure is already on the high side.
It is essential to monitor supine and sitting blood pressures during the use of the drug. Where supine blood pressure rises above 160mmHg, dose of midodrine should be reduced. If this results in a return of symptoms, then a review in secondary care is indicated.
Electrolyte monitoring on midodrine is not essential, although may be indicated for other reasons in these patients. It is essential to monitor blood pressure, and a minimum of every 3 months is suggested. Rising supine blood pressure is a reason to reduce or stop the midodrine.
Where a patient remains free of symptoms and free of an excessive drop in blood pressure on standing, attempts should be made to withdraw the drug stepwise.

Aspects of care for which the hospital is responsible

- To initiate midodrine therapy having followed an approach consistent with that described above. This means that midodrine is an unusual prescription where other approaches have failed to resolve the problem.
- To monitor in out-patients and adjust dosage accordingly, and review the balance of efficacy with any side-effects.
- To write to the GP requesting shared care at least 1 month before this will be required to commence and inform the GP of the existence of the shared care guideline on the Intranet and/or provide a copy directly. The letter must include the pre-treatment blood pressure reading.
- To perform ongoing reviews of the patients' treatment when requested by the GP and advise on treatment withdrawal when it is no longer considered appropriate.

Aspects of care for which the GP is responsible

- After agreeing to accept shared care, to prescribe midodrine on an ongoing basis.
- Monitor patient for adverse effects and control of symptoms and refer to the hospital specialist when appropriate.
- Monitoring blood pressure every 3 months, and referring to the hospital specialist where standing blood pressure rises consistently by more than 20 mm Hg, or where symptoms of orthostatic hypotension return. To perform the primary care monitoring test as described above and adjust doses as directed.

Aspects of care for which the patient is responsible

- To ensure they have a clear understanding of their treatment.
- To request future supplies when needed, store the medication appropriately and take as directed.
- To report adverse effects or worsening symptoms to their GP. Patients should report symptoms of supine hypertension immediately such as cardiac awareness (palpitations, chest pain and shortness of breath), headache, blurred vision etc, and the patient should be advised to discontinue the medication immediately

Cost

12 months treatment at 10mg twice daily is approximately £423, but this may vary depending on supplier because as it is currently unlicensed, it is classed as a "special item" which may incur various extra charges.

Availability of back-up advice and support

Hospital number: 08454 222222

Reviewed by Dr Arnold Deering June 2010

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