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The use of oral glycopyrronium in palliative care

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Summary

There is limited information on the use of oral glycopyrronium in palliative care. It has, however, been proposed for use in the management of drooling and paraneoplastic sweating in patients with palliative care needs[1]. Of note, information available to support the use of oral glycopyrronium to treat excessive respiratory secretions at the end of life is not available – the literature only refers to its use when administered subcutaneously. Glycopyrronium bromide is poorly absorbed from the gastrointestinal tract following oral use which has implications for its dosing. If glycopyrronium is to be used orally the lowest effective dose should be initiated and titrated according to response. The patient should also be monitored for any adverse effects.

Mechanism of action

Glycopyrronium is an anticholinergic agent which inhibits the acetylcholine activity on smooth muscles and structures innervated by parasympathetic nerves.[2,3] Salivation is primarily mediated by parasympathetic innervation of the salivary glands and glycopyrronium competitively inhibits cholinergic receptors in salivary glands and other peripheral tissues, thus indirectly reducing the rate of salivation[3]. Other effects of glycopyrronium include bronchodilation, decreased volume and acidity of gastric secretions, as well as control of excessive pharyngeal, tracheal and bronchial secretions.[2]

Pharmacokinetics

Oral glycopyrronium is poorly absorbed from the gastrointestinal tract.[4,5] It is estimated that approximately 10-25% is absorbed following oral administration[4] however other sources have reported the bioavailability to be as low as 3[2,3]-5[1]%.Despite this, oral glycopyrronium is reported to produce anticholinergic effects which may persist for 8-12 hours.[5] The onset of action of oral glycopyrronium is 30-40 minutes.[1]

Dosing and administration

For the treatment of drooling the following is advised:

- Start with 200 micrograms orally every 8 hours.[1]
- If necessary the dose can be increased progressively every 2–3 days to 1mg every 8 hours.[1]
- Occasionally doses of ≤2mg every 8 hours are needed.[1]
- The maximum adult oral dose is 7.2[3] - 8[5]mg daily.

A subsequent reduction in dose may be possible, particularly when initial dose escalation has been rapid.[1] Glycopyrronium should be given 1 hour before or 2 hours after meals.[3,4]

Availability

Glycopyrronium oral solution “Sialanar®” contains 400micrograms***** of glycopyrronium bromide per mL[3]. This product is licensed in Ireland, but is only authorized for drooling in children and adolescents aged 3 years and older with chronic neurological disorders[1,3].

*****Importantly, the concentration of glycopyrronium in Sialanar® is expressed as 320 microgram/mL – equivalent to 400 micrograms of glycopyrronium bromide per mL. In practice and in the literature, the term “glycopyrronium” is used colloquially in reference to glycopyrronium *bromide*. Thus a recommended dose of glycopyrronium 400micrograms is equivalent to 400 micrograms of glycopyrronium *bromide*, or 1mL of Sialanar®.

Glycopyrronium 1mg and 2mg tablets are unlicensed in Ireland but are available from specialist wholesalers. The 1mg tablets can be halved for use[7,8] but, the resultant dose (500 micrograms) is far in excess of recommended starting doses in the treatment of drooling. In the US, glycopyrronium tablets are licensed as add on therapy for the treatment of peptic ulcers at a dose of 1-2mg two to three times daily[8].

Glycopyrronium injection is not licensed for oral administration.[9] However, limited information suggests that it can be administered orally.[7] The oral administration of glycopyrronium 200microgram/mL solution for injection should be restricted to occasions when Sialanar® oral solution and glycopyrronium tablets are unavailable or intolerable.

Reimbursement

Sialanar® Oral Solution and glycopyrronium injection 200micrograms/mL are reimbursed under the General Medical Scheme (GMS) and the Drugs Payment Scheme (DPS). Glycopyrronium 1mg and 2mg tablets are not reimbursed on the GMS or DPS.[10]

Enteral tube administration

Glycopyrronium is not licensed for administration via enteral feeding tubes. However information is available to support the following methods of administration[6,7,11]

- The tablets can be dispersed in water[6,7]
- The oral solution may be used[7,11]
- The injection may be used[7,11]

Common Adverse Effects

Side-effects of antimuscarinics include difficulty swallowing, thirst, constipation, urinary urgency and retention.[3,9] Confusion (particularly in the elderly), nausea, vomiting, drowsiness, dizziness and angle-closure glaucoma are also associated with its use.[3,9] The concomitant use of glycopyrronium with other medicines with anticholinergic properties has the potential to further potentiate adverse effects.

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