Haloperidol and QTc Interval Prolongation

Following a review by the European Medicines Agency (EMA) the Summaries of Product Characteristics (SmPC) for all haloperidol formulations (oral, intramuscular/intravenous immediate release injections & intramuscular long acting injections) have been harmonised.

A significant change has been made to the contra-indications for haloperidol.

The use of haloperidol is now contra-indicated in combination with other drugs known to prolong the QTc interval.

That haloperidol can prolong the QTc interval has been known for many years and this was a clear caution within previous SmPCs. The EMA review has concluded that the risks are such that the combination of haloperidol with other drugs known to prolong QTc is high enough to warrant contra-indication and a recommendation that such combinations are avoided.

(Details of drugs that are known to be associated with QT prolongation can be found in Table 9, page 1266 BNF 74 and https://www.crediblemeds.org/ [The 'Quick Scan' scan function can be used to search for drugs on the QT Drugs lists. Access to download the combined QTdrugs lists requires registration (free)] Alternatively, users with an Athens password can access a table from Stockley's Drug Interactions at https://www.medicinescomplete.com/mc/stockley/current/Table9.2.htm[6] Ensure that you have logged in to your Athens account before following this link.)

Haloperidol has a wide range of indications within mental health and acute care e.g. acute and maintenance treatment of psychosis, short term treatment of disturbed behaviour and delirium, and nausea in palliative care. Therefore the implications of this contra-indication affect treatment across all healthcare settings. It is recognised that in some circumstances the use of such combinations may be clinically appropriate and unavoidable.

Clinicians are advised to take the following actions

1. Review the medication of all patients prescribed haloperidol on a regular basis. If treatment with haloperidol is essential, where possible discontinue any other medicines known to prolong QTc.
2. Review the medication of all patients prescribed haloperidol on an 'as required' basis for the management of disturbed behaviour. If intermittent use of an antipsychotic for this purpose is still required discontinue haloperidol and prescribe an alternative antipsychotic.
3. If on review, the use of haloperidol in combination with other drugs is clinically appropriate and therefore unavoidable ensure that the rationale for treatment and relevant patient consents are obtained and documented.
4. Do not prescribe haloperidol to patients whose cardiac status is unknown or unstable.

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Monitoring

- The SmPCs all recommend pre-treatment ECG for all patients prior to use of haloperidol. If circumstances make this impractical either do not use haloperidol or if use is unavoidable, a clear justification must be recorded in the chronological account of care.
- SmPCs further recommend that during therapy, the need for ECG monitoring for QTc interval prolongation and for ventricular arrhythmias must be assessed in all patients. For patients on long term treatment an annual ECG as part of routine physical health monitoring is recommended. More frequent ECG monitoring may be necessary on a case by case basis.
- Electrolyte disturbances (e.g. hypokalaemia, hypocalcaemia and hypomagnesaemia) should be corrected before treatment with haloperidol. If circumstances make this impractical either do not use haloperidol or if use is unavoidable a clear justification must be recorded in the chronological account of care.
- If cardiovascular symptoms suggestive of arrhythmias develop, such as palpitations, dizziness, syncope or seizures during treatment, cardiac evaluation including an ECG should be undertaken to exclude a possible malignant cardiac arrhythmia. If the QTc interval is >500 milliseconds treatment should be stopped.

The following section describes actions to be taken in scenarios where use of haloperidol is common.

Managing a patient on regular oral haloperidol or on haloperidol decanoate (depot) and a contraindicated medication known to prolong QTc interval

- Review ongoing need for haloperidol or concurrent contraindicated medication. Consider changing one or other medications to a medication with no effect on QTc interval.
- If combination cannot be avoided;
    - Assess risk factors for QTc prolongation
    - Consider increased monitoring and do an ECG and biochemical monitoring if not recently performed
    - Obtain and document consent. Or ensure a DMP second opinion is obtained.
    - Ensure the rationale for continuing the combination is clearly documented within the individual's chronological account of care.
    - Ensure ongoing review of combination, including review of physical risk factors and close monitoring of ECG and biochemical parameters.

Managing a patient who requires 'as required' psychotropic medication and is already on a medication that would be contraindicated with haloperidol e.g. a regular antipsychotic

- Consider all options available for managing for acute psychiatric disturbance including non-medication options.
- Avoid the use of 'as required' haloperidol in individuals who are already receiving medications known to prolong QTc interval.
- Where 'as required' medication is deemed to be appropriate, develop a clear individualised treatment plan which incorporates the use of oral and if appropriate, IM 'as required' medication.
- Oral 'as required' medication- consider the use of;
    - Benzodiazepines

    - Using a small dose of the individual's regular antipsychotic as an as required treatment being mindful of the potential for this to breach high dose antipsychotic therapy e.g. the use of 2.5mg olanzapine or 25mg quetiapine.
    - promethazine
- IM 'as required' medication- consider the use of;
    - Benzodiazepines- lorazepam or midazolam
    - Alternative IM antipsychotics e.g. aripiprazole or olanzapine (NB olanzapine IM is an unlicensed preparation in the UK) GG&C MHS protocol for the use of unlicensed olanzapine injection
    - IM promethazine
      IM guidelines

- If it is felt to be clinically appropriate to consider the use of 'as required' haloperidol in an individual who is prescribed a contraindicated combination, e.g. due to previous good response, or because alternatives are not appropriate, the following advice should be adhered to;
    - Assess risk factors for QTc prolongation
    - Consider increased monitoring and do an ECG and biochemical monitoring if not recently performed
    - Obtain and document consent. Or ensure a DMP second opinion is obtained.
    - Ensure the rationale for continuing the combination is clearly documented within the individual's care plan.
    - Ensure ongoing review of combination, including review of physical risk factors and close monitoring of ECG and biochemical parameters.

Please note, current NHS GG&C guidance involving the use of haloperidol, including High Dose Antipsychotic Guidelines, Intramuscular Sedation and Management of Delirium are currently undergoing updates to reflect the changes in haloperidol SmPCs.

Prescribing Management Group – Mental Health

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