MERCAPTOPURINE

In this column, Sharon Rees aims to refresh knowledge and interest in some of the commonly used drugs in a series of tweets. This month she is talking about #haloperidol

Dr Sharon Rees @reesprescribe
Day 1: Haloperidol was discovered mid-50s, as derived from chemical modification to opioids ie pethidine; found to have anti-psychotic effects, but no analgesia. Main uses include schizophrenia, manic episodes associated bipolar disorder, tic disorders such as Tourette's, anti-emetic post-op/palliative

Dr Sharon Rees @reesprescribe
Day 1 (cont): **#haloperidol** can be used in children for adolescent schizophrenia, rapid treatment of aggression and tic syndrome. UK unlicensed use in palliative care

Dr Sharon Rees @reesprescribe
Day 2: Anti-psychotic adult dose range #haloperidol 2-10 mg/day in divided doses; some conditions such as aggression, tic disorder 0.5-5 mg. NOTE: lower doses elderly e.g start half adult dose and typically max 5 mg/day. Children dose range lower/variable depends on age and (sometimes) weight

Dr Sharon Rees @reesprescribe
Day 2 (cont): **#haloperidol:** i.m & s.c infusion for nausea and vomiting and delirium. Deep i.m depot inj (gluteal) in form of haloperidol decanoate (oily) for long-term maintenance schizophrenia (where needed) dose 50-300 mg typically every 4 weeks

Dr Sharon Rees @reesprescribe
Day 3: MOA **#haloperidol**: Antagonism of dopamine receptors (mainly D2) in brain reward and motivation pathways believed responsible for main effects; considered better for the positive symptoms of schizophrenia such as hallucinations/aggression; less effective for negative symptoms such as apathy. **#haloperidol** also has role in palliative care as a potent anti-emetic (antagonises the D2 receptors in the CTZ) & management of restlessness/confusion (unlicenced). Some antagonism of α1-receptors (possible effects re judgement, cognition) and 5HT2 (possible anti-hallucinogenic effect)

Dr Sharon Rees @reesprescribe
Day 3 (cont): **#haloperidol** has higher affinity for D2 receptor than dopamine hence problematic ADR profile. As dopamine inhibits prolactin release, lower dopamine activity re **#haloperidol** use causes higher prolactin levels > breast enlargement, galactorrhoea,sexual dysfunction, menstrual irregularites

Dr Sharon Rees @reesprescribe
Day 4: Kinetics **#haloperidol**; good oral bioavailability & high volume of distribution (crosses placenta/found breast milk). Liver metabolism mainly via CYP3A4/2D6 (polymorphisms relevant re response variation) & glucuronidation. Oral t½ 14-36hr. Slow release depot forms peak concentration at 6 days, t½ 21 days

Dr Sharon Rees @reesprescribe
Day 5: ADRs, common; agitation, somnolence, hyperkinesia, insomnia, weight change, tremor, tardive dyskinesia, dystonia, constipation, dry mouth. Rare/serious hyperprolactinaemia, neuroleptic malignant syndrome, agranulocytosis (not exhaustive). Planned and supported withdrawal important

Dr Sharon Rees @reesprescribe
Day 5 (cont); Sudden death, QT-prolongation & Torsades de Pointes reported with **#haloperidol** especially with high doses. Potassium check at least once per year – monitoring also includes urea/electrolytes, FBG/HbA1c, prolactin levels, ECG before treatment and as appropriate during, LFTs, BMI, lipids

Dr Sharon Rees @reesprescribe
Day 6: DDIs; **#haloperidol** has severe interactions with all drugs associated with QT prolongation such as amitriptyline. All drugs which lower K+ increase risk of torsades de pointes such as diuretics, prednisolone, salbutamol. Ritonavir increases exposure (not exhaustive). Avoid alcohol as hypotension and CNS depressant effects

Dr Sharon Rees @reesprescribe
Day 7: Although **#haloperidol** is in the 'low risk' category for type 2 diabetes, all the anti-psychotics are obeseogenic drugs and are believed to have a direct effect on insulin resistance; screening and regular monitoring (at least annually) and lifestyle advice/support are important

Dr Sharon Rees
Associate Professor Therapeutics and Prescribing,
London South Bank University

sharon.rees@lsbu.ac.uk

EARN YOUR CPD CERTIFICATE

With the help of *Prescribing and Therapeutics Training Ltd* and the *Journal of Prescribing Practice*, you can earn your 1-hour CPD certificate.

In addition to the tweets, read the BNF section on 'psychoses and schizophrenia' and the monograph on haloperidol. Another useful source is the summary of product characteristics for haloperidol, and then answer the nine questions. Please submit the answers to reesprescribe@gmail.com as a numbered list with TRUE/FALSE or the correct A,B,C,D option. If you achieve seven or more out of nine eight or more out of ten on the questions, a CPD certificate will be emailed to you.

Further reading on #haloperidol

- *Haloperidol Injection BP 5mg/ml:* https://www.medicines.org.uk/emc/product/514/smpc#PRODUCTINFO
- **BNF Psychoses and schizophrenia**: https://bnf.nice.org.uk/treatment-summary/psychoses-and-related-disorders.html
- **Monograph on Haloperidol**: https://bnf.nice.org.uk/drug/haloperidol.html

Electronic Medicines Compendium (emc). Haloperidol Injection BP 5mg/ml. 2017. https://www.medicines.org.uk/emc/product/514/smpc#PRODUCTINFO (accessed 20 August 2020)

National Institute for Health and Care Excellence. Psychoses and related disorders. 2020. https://bnf.nice.org.uk/treatment-summary/psychoses-and-related-disorders.html (accessed 20 August 2020)

National Institute for Health and Care Excellence. Haloperidol. 2020. https://bnf.nice.org.uk/drug/haloperidol.html (accessed 20 August 2020)

1. Haloperidol is a second-generation anti-psychotic
TRUE or **FALSE**?

2. Haloperidol is licensed for use in children
TRUE or **FALSE**?

3. Which of the following is **TRUE**?
A. Haloperidol is used first-line to treat opioid dependence
B. Used as an i.v infusion for post-operative emesis
C. Doses are usually lowered in the elderly
D. Haloperidol was discovered in the 1970s

4. The major mechanism of action for haloperidol is antagonism of dopamine receptors in the brain
TRUE or **FALSE**?

5. Which of the following is **TRUE**?
A. Haloperidol affects all pituitary hormones including prolactin
B. Dopamine receptors in the pituitary gland modulate prolactin release, so dopamine antagonists such as haloperidol mean less restraint, more release
C. Dopaminergic pathways are enhanced by haloperidol and this encourages more prolactin release
D. Dopamine stimulates oestrogen and this switches on prolactin release

6. Tardive dyskinesia causes which of the following problems
A. Involuntary movements of the jaw, lips and tongue and sometimes limbs
B. Voluntary wave-like movements of the limbs
C. High velocity nystagmus
D. Muscle wasting

7. Which of the following is NOT a routine monitoring requirement for haloperidol?
A. HbA1c
B. Electrolytes
C. Prolactin concentration
D. EEG

8. An ECG is performed prior to haloperidol treatment because the anti-psychotics are obesogenic, so this is a baseline test to track cardiac stress while on the drug
TRUE or FALSE?

9. Haloperidol is a sedating anti-psychotic
TRUE or FALSE?

10. Drugs which lower potassium and cause QT prolongation increase arrhythmia risks when taking haloperidol
TRUE or **FALSE**?