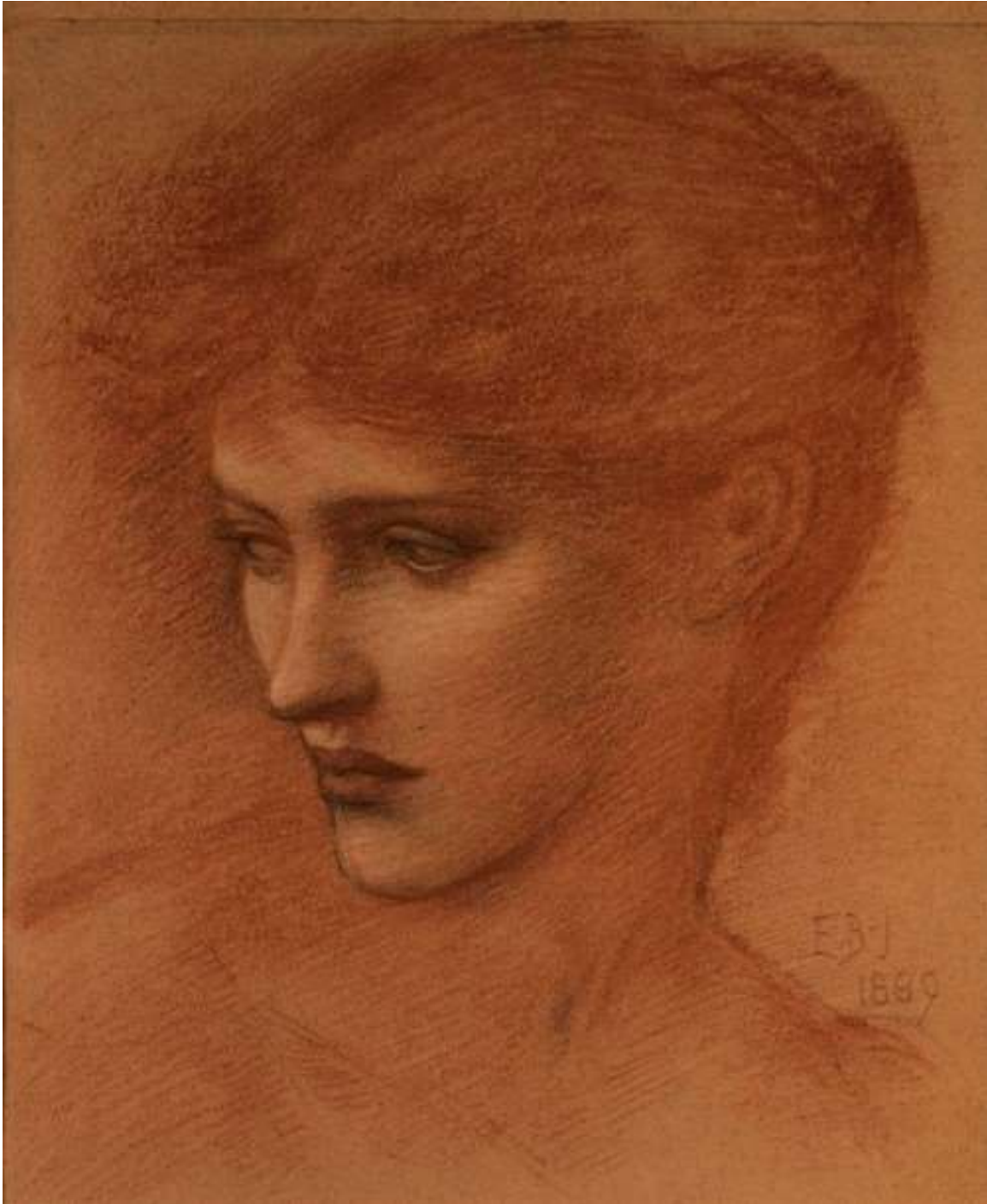


DROPERIDOL



“Study for a female face”, red chalk on paper, 1889, Edward Burne-Jones.

The magisterial Pre-Raphaelite painter, Edward Burne-Jones Jones was well known for his masterful and beautiful studies. So meticulous was he in these, that those of them that survive today, are keenly sought after and highly valued. The brilliance of Burne-Jones' works were the result of tireless, and meticulous planning, with almost as much effort being put into his studies as that of the actual finished work! Among the most beautiful sketches that have survived are those portraits of what the Pre-Raphaelites referred to as their "stunners". These were very beautiful women that were spotted at random on the streets of London or at the Opera houses or theatres, or simply in shops. The Pre-Raphaelites would simply approach them and ask if they would like to be immortalized! In the early days this proposal more often than not met with an indignant refusal, "Certainly not Sir, you are much too forward I think, I do not know you at all, good day! ".

But as time went by the Pre-Raphaelites became very well known indeed, and extremely famous for their beautiful and haunting depictions of medieval idylls. Soon many young women were clamouring to be "discovered", as the next Pre-Raphaelite stunner. Many did indeed become the immortalized muses, of the Pre-Raphaelites. Today we see the legacy of the "outrageous" forwardness of the Pre-Raphaelites, in the contingent discoveries of the likes of Marilyn Monroe or Claudia Schiffer.



Like a great Pre-Raphaelite masterpiece, we strive to medical wisdom that is firmly based on masterful and meticulous studies. One such study that has guided us in the form of the sedation of the acutely disturbed is the DORM study. Though sadly very few of our studies in the world of the Medical Sciences will ever achieve the true immortality of a Pre-Raphaelite stunner, for the present time, at least, the DORM study does serve us well.

Desiderium, Study for the Masque of Cupid, pencil on paper, Edward Burne-Jones, 1873.

DROPERIDOL

Introduction

Droperidol is a first-generation antipsychotic agent.

Despite some previous unwarranted adverse press, it remains a widely used, safe and effective antipsychotic agent. ^{5,6}

It is commonly used in combination with **midazolam** in the ED setting for **urgent chemical sedation** in acute behavioral and/ or psychotic emergencies.

It has advantages over the more traditional anti-psychotic agent haloperidol, in that it is more quickly acting, is more sedating and has *less* CVS adverse effects.

All patients who have had emergency sedation with this agent should be closely monitored following its administration.

Classification

There is no formal classification of the antipsychotic agents, however by tradition they are loosely divided into two principal groups.

1. The older “**first generation**” or “**typical**” group.
2. The newer “**second generation**” or “**atypical**” group.

In general the second generation agents have significantly less adverse effects profiles such as sedation, extrapyramidal side effects, anticholinergic effects or the development of neuroleptic malignant syndrome. The risk of these particular adverse effects although small is not completely eliminated with the second generation agents.

It has also been claimed that the second generation agents are more effective against the “negative” symptoms of schizophrenia, but this has *not* been convincingly proven as a *class* effect.

It should be noted that designating antipsychotics as first generation and second generation may be of limited value as it probably exaggerates the differences between groups and overstates similarities between members within each group. On this basis some prefer not to use this classification; nonetheless the terminology remains widely used.

First Generation Antipsychotic Agents :

These fall into two major groups:

1. **Phenothiazines:**

- *Lower potency:*
 - Chlorpromazine.
 - Pericyazine.
 - Thioridazine.
- *Higher potency:*
 - Fluphenazine.
 - Flupenthixol
 - Prochlorperazine
 - Trifluoperazine.
 - Zuclopenthixol

2. **Butyrophenones:**

- **Droperidol.**
- Haloperidol.

Second Generation Antipsychotic Agents :

These include:

1. Amisulpride
2. Aripiprazole
3. Asenapine
4. Clozapine
5. Olanzapine
6. Paliperidone
7. Quetiapine
8. Risperidone
9. Ziprasidone

Preparations

Ampoules:

- 2.5 mg / 1 mL

Chemistry

Droperidol is a neuroleptic drug of the **butyrophenone** group that also includes haloperidol

Mechanism of Action

Antipsychotic actions are thought to be mediated (at least in part) by blockade of dopaminergic transmission in various parts of the brain (in particular the limbic system).⁴

Evidence suggests:

- All effective antipsychotics block D2 receptors
- Differential blockade of other dopamine receptors (eg D1) may influence therapeutic and adverse effects
- Antagonism of other receptors may influence antipsychotic activity, eg 5HT2 antagonism with some agents.

Pharmacodynamics

1. CNS:
 - Sedative - hypnotic
 - Antipsychotic
2. Antiemetic
3. Respiratory
 - There is no significant respiratory depression
4. Myocardial effects
 - There are no significant myocardial depressant effects

Pharmacokinetics

Absorption:

- Droperidol can be given **IV** or **IM**. There is no oral form

It is rapidly absorbed following intramuscular administration

The onset of action is from three to ten minutes following intravenous or intramuscular administration.

The full effect, however, may not be apparent for 30 minutes.

The duration of the sedative and tranquillizing effects of droperidol generally is two to four hours.

- Droperidol has a faster onset of action and a shorter duration of action than intramuscular haloperidol.

Distribution:

- Protein binding is extensive
- The distribution phase half-life for plasma is ten minutes.

The terminal plasma elimination phase half-life is about 130 minutes

Metabolism and excretion:

- Droperidol is metabolized by the liver and metabolites are excreted in both bile and urine.

Indications

These include:

1. Acute agitation associated with an acute psychotic episode (such as schizophrenia or drug induced psychosis) or mania:

- Note that droperidol is now preferred over the more traditional **haloperidol** for acute behavioural emergencies because it is **more sedating**, has a **quicker onset of action**, a **shorter half-life** and is **less cardiotoxic** than haloperidol.

Although **midazolam** (alone or in combination with an antipsychotic agent) is commonly used for acute behavioral emergencies, droperidol has a number of advantages to it.

In comparison with intramuscular midazolam, the DORM study ⁵, showed that droperidol resulted in a similar security-duration

requirement, required less additional sedation, and had a lower rate of adverse effects.

It also had a more predictable response compared to midazolam according to the Altered Mental Status Scale, with rapid and then persistent sedation but not over sedation.

Additionally it has been shown that there is *no* evidence of significant increased risk for QT prolongation or of arrhythmias with the usual doses employed in the Emergency Department.⁶

2. Anti-emetic:

- Droperidol is frequently given intravenously in small doses at the end of anaesthesia to prevent vomiting.
- It can also be used to treat vomiting that has not responded to other standard antiemetic drugs.

3. Alcohol withdrawal:

- For severe psychotic symptoms when oral administration is not possible.

4. Occasionally for persistent migraine.

Contraindications & Precautions

These include:

These include:

1. Known hypersensitivity to droperidol.
2. Caution with other CNS depressants, including alcohol, (synergistic sedation)
3. Caution with other agents of conditions that prolong the QT interval
4. Hypotension
5. Renal impairment
 - Dose should be reduced.
6. Parkinson's disease:
 - Antipsychotics used in Parkinson's disease may aggravate the condition and may oppose the action of the dopamine agonists used to treat it.

Quetiapine or clozapine may be more suitable.

7. Hepatic

- Use with caution in severe hepatic impairment; consider dose reduction.

Pregnancy

Droperidol is classed as a **group C** drug in pregnancy.

Group C drugs are those which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Specialised texts should be consulted for further details.

There is limited safety information available following the use of droperidol during pregnancy.

Droperidol has been used in the treatment of hyperemesis gravidarum and the prevention of postoperative nausea and vomiting during and after caesarean sections.

Maternal use of droperidol has **not** been associated with adverse maternal and neonatal outcomes.⁷

If droperidol is the medicine of choice, use the lowest effective dose during pregnancy and monitor maternal wellbeing and fetal development.

Studies regarding the long term behavioural and cognitive outcomes of children following exposure to droperidol in utero are limited

Ultimately the decision to use droperidol becomes a consideration of risk versus benefit.

On current knowledge one-off doses are unlikely to cause harm to the fetus. In the ED setting the benefits to a seriously disturbed and psychotic pregnant patient are very likely to outweigh any theoretical risk to the fetus.

Breastfeeding:⁷

Published information following the use of droperidol during breastfeeding has not been located.

A single dose or short term use of droperidol as an adjunct to anaesthesia is unlikely to pose harmful effects to the breastfed infant.

The decision to breastfeed while on droperidol therapy should be made in consultation with a psychiatrist and neonatal care provider.

In women who choose to breastfeed their healthy full-term infant while taking droperidol, closely observe the infant for adverse effects such as drowsiness, poor feeding and sleeping pattern changes.

Inform neonatal care providers immediately if any adverse effects are noted in the breastfed infant.

Adverse Effects

1. CNS:

- Sedation
 - ♥ Has synergistic effects with other CNS depressants, including alcohol.
- Extrapyrimal reactions:
 - ♥ Although it has less propensity to cause these compared to haloperidol.

See chlorpromazine (in Drugs folder) for description of extrapyramidal effects.

2. CVS:

- Hypotension
- Prolonged QT:
 - ♥ Note however that there is no convincing evidence for a causal relationship between **therapeutic** droperidol administration and life-threatening cardiac events, when droperidol is used appropriately.^{1,5,6}

3. Neuroleptic malignant syndrome.

Dosing

Acute Behavioural Emergencies in younger patients:

Acute medical settings are considered to be settings in which cardiorespiratory resuscitation resources are *immediately* available and staff are highly trained and experienced in their use.

The intravenous route is generally preferred for achieving **rapid** tranquilisation, if necessary to the point of sedation, because it allows titration of the dose and provides a more immediate effect.

If a patient cannot be physically restrained to the point where an intravenous line can be established without risk of harm to staff members, then initial intramuscular medication is appropriate.

In all cases, undertake close post-medication monitoring.

Give:

- **Droperidol IM dose: 2.5-10 mg.**¹

This can be repeated after at least 20 minutes, titrated to clinical response, up to a maximum of 20 mg in 24 hours.

OR

- **Droperidol IV:**¹

2.5 to 5 mg IV, repeated every 3 to 4 minutes, titrated to clinical response, up to a maximum of 20 mg.

For persistent/ resistant migraine:

For persistent/ resistant migraine:¹

- Give 1.25 to 2.5 mg IM, 12-hourly for up to 48 hours

As anti-emetic::

- Droperidol is often given intravenously in small doses (**0.625 mg or ¼ of the 2.5 mg per 1 ml ampoule**) at the end of anaesthesia to prevent vomiting.
- It can also be used more generally as an anti-emetic for intractable vomiting:

♥ **0.625 mg (or ¼ of the 2.5 mg per 1 ml ampoule) - 1.25 mg IV.**

It is **more effective** than metoclopramide or prochlorperazine, but may have a higher incidence of dystonic side effects.⁸

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