

What dose of methadone should I use?

Professor Derek Flaherty

BVMS, DVA, DipECVAA, MRCA, MRCVS

RCVS and European Specialist in Veterinary
Anaesthesia

SPC dose rates for Comfortan[®]

- dogs: 0.5-1.0 mg/kg SC, IM or IV
- cats: 0.3-0.6 mg/kg IM only



What dose should I use?

What am I aiming to achieve?

- **premedication**
 - sedation / pre-emptive analgesia
- **analgesia**

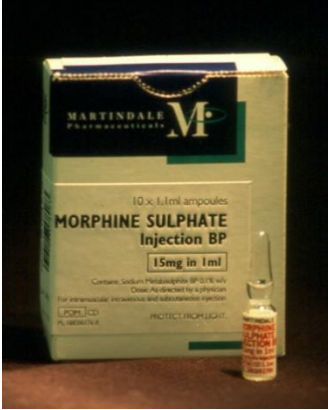
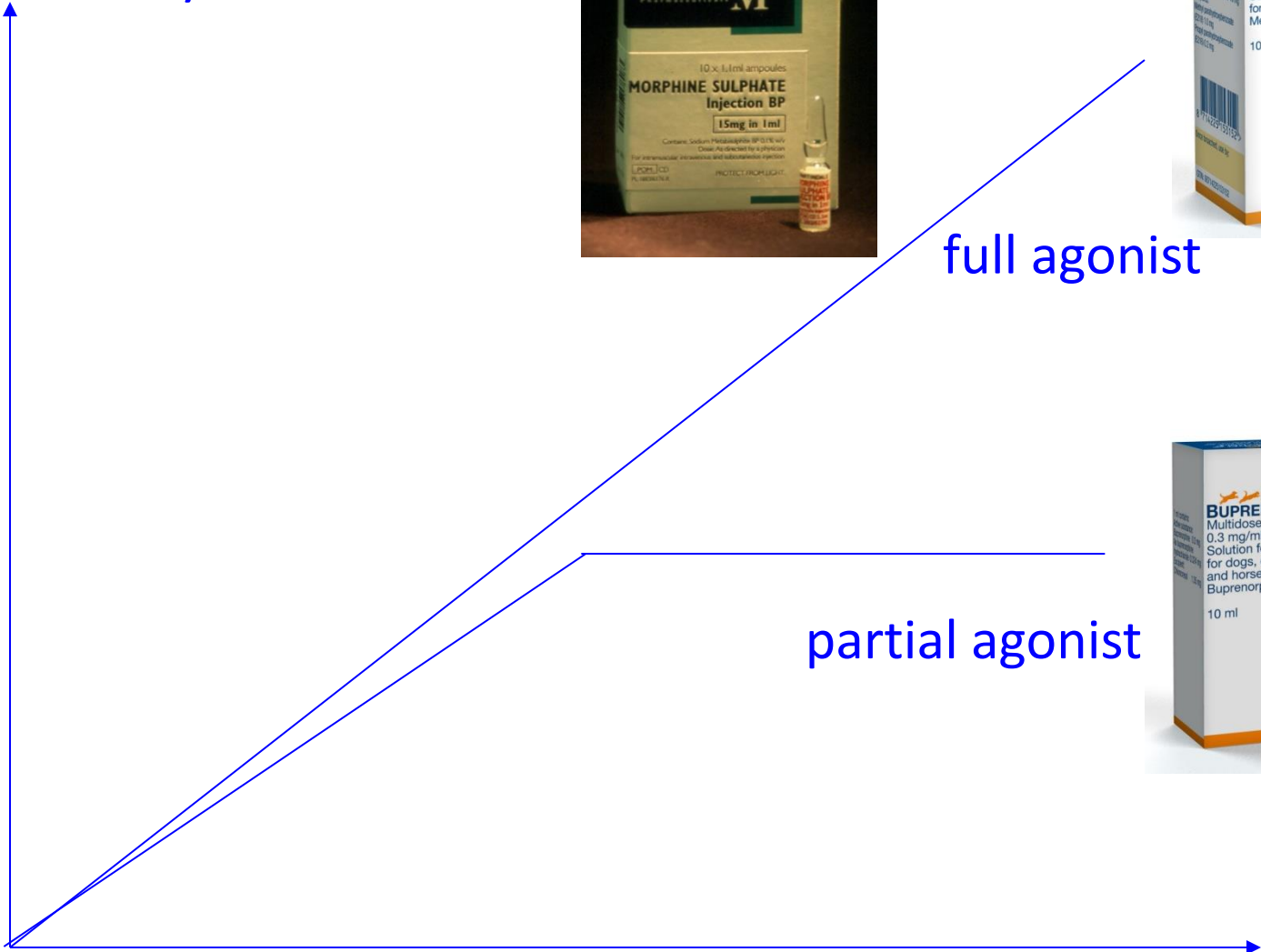


What dose should I use?

- being a full opioid agonist, methadone has an almost linear dose-response curve



analgesic efficacy



full agonist



partial agonist

dose

'Standard' premedication doses of methadone

- 0.2-0.3 mg/kg IM (in combination with a sedative / tranquillizer)
- SPC dose 0.5-1.0 mg/kg
- 0.2-0.3 mg/kg IM (in combination with a sedative / tranquillizer)
- SPC dose 0.3-0.6 mg/kg



What might alter these doses?

Many factors influence the most appropriate dose to administer:

- **temperament**
 - quiet animals likely to require lower doses than aggressive animals for sedation
- **health status**
 - sick animals require less than healthy animals
- **age**
 - geriatric animals likely to have more exaggerated effect and of greater duration

Example protocols – healthy dogs

- **ACP 0.03 mg/kg + methadone 0.3 mg/kg IM**
- **medetomidine 2-5 $\mu\text{g}/\text{kg}$ + methadone 0.2 mg/kg IM**
- **dexmedetomidine 2-3 $\mu\text{g}/\text{kg}$ + methadone 0.2 mg/kg IM**



Example protocols – healthy cats

- **ACP 0.05 mg/kg + methadone 0.3 mg/kg IM**
- **medetomidine 5-10 $\mu\text{g}/\text{kg}$ + methadone 0.2 mg/kg IM**
- **dexmedetomidine 5 $\mu\text{g}/\text{kg}$ + methadone 0.2 mg/kg IM**



Example protocols – aggressive dogs

- medetomidine 5 $\mu\text{g}/\text{kg}$ + methadone 0.5 mg/kg IM
- medetomidine 5 $\mu\text{g}/\text{kg}$ + methadone 0.5 mg/kg + ketamine 0.5 mg/kg IM
- medetomidine 10 $\mu\text{g}/\text{kg}$ + methadone 0.5 mg/kg \pm ketamine 0.5-1 mg/kg IM
- or dexmedetomidine at half the above medetomidine doses



**ketamine is off-licence
when used in these
protocols**

Example protocols – aggressive cats

- medetomidine 20 µg/kg + methadone 0.5 mg/kg IM
- medetomidine 20 µg/kg + methadone 0.5 mg/kg + ketamine 2-3 mg/kg IM
- or dexmedetomidine at half the above medetomidine doses



Route of administration

- **IV administration (dogs) will lead to faster and higher peak plasma concentrations**
 - increased sedation and analgesia
 - increased likelihood of side-effects
- **SC administration is likely to produce more variable onset and lower plasma concentrations**

SPC dose rates for Comfortan[®]

- dogs: 0.5-1.0 mg/kg SC, IM or IV
- cats: 0.3-0.6 mg/kg IM only

the upper end of these dose ranges should not be the primary starting point

i.e. the higher doses should only be reached following upwards titration from a lower dose



Methadone duration - dogs and cats

- averages 4 hours
- each animal is an individual
- do not be afraid to top-up sooner if the animal needs it
 - animals in pain are very difficult to overdose with opioids if titrated to effect



Re-dosing with methadone - dogs

If you require to 'top-up' with methadone:

- 0.1 mg/kg diluted in 0.9% NaCl to at least 1ml and administered slowly IV over approx. 2 min
- if insufficient effect, repeat above at 10 min intervals

or

- 0.2 mg/kg IM repeated at 20 min intervals, to effect

N.B. these doses are lower than those recommended on the Comfortan[®] SPC for analgesia

How quickly does methadone work?

- IV route → 10 min
- IM route → 15 min
- SC route → more variable



Re-dosing with methadone - dogs

- if you have reached a total cumulative dose of 0.6 mg/kg (IM or IV) and still have insufficient analgesia:
 - don't forget to be multimodal!
 - consider dysphoria
- ...before continuing with additional increments



Re-dosing with methadone - cats

- **Comfortan[®] is only licensed IM in cats**
- **lower dose range than dogs (0.3-0.6 mg/kg)**
- **∴ increment with 0.1-0.2 mg/kg IM (depending on initial dose) every 20 min to achieve desired effect**



Can methadone be given IV to cats?



- off licence
- lower doses should be used than those on the Comfortan[®] SPC
 - maximum of 0.2 mg/kg initial dose
 - can increment with 0.1 mg/kg slow IV every 10 min if required (up to total of 0.5 mg/kg)

Re-dosing with methadone – dogs and cats

- these incremental doses are suggestions only
- greater care (smaller increments) will be required if you've started with a relatively high dose



'Topping-up' during anaesthesia

- take care with the IV route, especially if the animal is anaesthetised (only licensed in dogs for this)
 - apnoea
 - severe bradycardia
- avoid these effects by using low doses IV in anaesthetised patients and titrating slowly
 - 0.1 mg/kg diluted in 0.9% NaCl to at least 1 ml and administered slowly IV over 5 min
- or give IM during anaesthesia

'Topping-up' during anaesthesia

- if administered IV to anaesthetised animals:
 - bradycardia → atropine 20 µg/kg IV
 - apnoea → IPPV until spontaneous ventilation resumes (turn down vaporiser)
 - avoid it in the first place!

How long can I continue methadone for?

- as long as the animal requires it!
- tolerance
 - increasing dose required over time to achieve the same effect
 - occurs rapidly with morphine
 - does not seem to occur with methadone
- dependence
 - common in humans (variable time to occur)
 - not recognised in animals

How long can I continue methadone for?

- as long as the animal requires it!
- long elimination half-life in humans → drug cumulation with repeated doses
- ? in dogs and cats
 - may need to reduce dose / increase dose interval if maintaining for > 24-48 hrs

Methadone doses - summary

A variety of factors will dictate the dose:

- degree of pain (already present or likely to occur)
- temperament
- health status
- route of administration

but...

being a full opioid agonist, methadone allows us to titrate dosing to achieve the desired effect

Methadone doses - summary

