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CARFENTANIL–SYNTHETIC OPIOID ANALGESIC: A REVIEW

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INTRODUCTION

Carfentanil is a synthetic opioid agonist which is one of the most potent opioids analgesics in opioids drugs. It was discovered and developed by Janssen Pharmaceutical in year 1974 and it was an analog of the opioid analgesic fentanyl. The potency was estimated to be approximately ten thousand times more potent than morphine.

Carfentanil is a powerful derivative of Fentanyl and is a synthetic narcotic analgesic produced from Morphine. This drug is not approved for human use in any dose, it's typically used in veterinary medicine to sedate large and big animals.

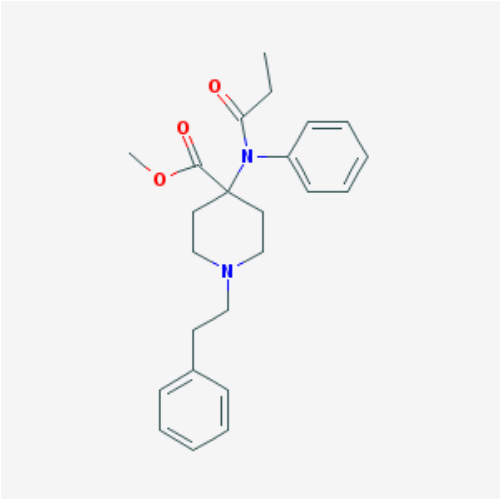
Carfentanil binds strongly with μ opioid receptor and acts as a comparative agonist. Opiate analgesic drugs act on G-protein receptors and regulate both positive and negative of syneptic transmission via G-protein that activate effector proteins. Carfentanil induce similar effects of analgesia as other opioids, however due its high potency it will induce side effect such as sedation that is why it used as a tranquilizer for large animals.

CHEMISTRY

Carfentanil is an opioid analogue that have monocarboxymethyl group in the fourth position of the piperidine ring of fentanyl. Carfentanil is a white granular or crystalline powder which shows a clear solution in water, and it also soluble in chloroform and other organic solvent and sparingly soluble in water but it shows highly solubility in water in hydrochloride and citrates forms. It has high lipophilicity, which allows greater penetration through the blood-brain barrier which shows its high potency.

Carfentanil acts on the μ-receptor in the central nervous system. Carfentanil stiμlates the exchanges of GTP for GDP on the G-protein complex inhibits the adenylate cyclise which results in a decrease in intracellular cAMP and leads the reduction in release of neurotransmitters substance. The analgesic activity of Carfentanil is due to its stiμlation to the opening of G-PC (G- protein coupled receptor inwardly regenerated potassium channels and blocks the opening of N-type voltage gated calcium channels resulting in hyperpolarization and reduced neuronal votability.

Molecular structure



Molecular forμla: C24H30N2O3

Molecular weight: 394.515 g/mol

Melting point: 152-190°C

Boiling point: 508°C

Synonym: - 4- carbomethoxy fentanyl

IUPAC name:- Methyl 1 – (2-pheneylethyl)-4- [phenyl (profanely) Amino] Pepperdine 4 – carboxylate

Solubility: Carfentanil is the white colour crystalline powder which soluble in chloroform diclorομethene and ethyl acetate and sparingly soluble in water but it shows

highly solubility in water in hydrochloride and citrates forms.

PHARMACODYNAMICS/MECHANISM OF ACTION

Carfentanil acts on the μ (Little action on kappa and delta) opioid receptors as an agonist. It will show similar effects of analgesia as other opioids. It will also induce strong side effects like other opiods such sedation. That why it is used as a tranquilizer for large animals.

Carfentanil acts predominately with the opioid μ-receptor. These μ-receptors are distributed in the brain, spinal cord, and other many different tissues. It exerts its principal pharmacological effects on the central nervous system. Its therapeutic actions are analgesia and sedation. Carfentanil additionally depresses the respiratory system, depresses the cough reflex center, and constricts the pupils.
Competitive agonist activity show by the carfenanil due to it's affinity of μ opioid receptor. Generally morphine receptor attached with G- protein receptor and show both positive and negative regulators of synaptic congugation via G-proteins that activate effector proteins. Carfentanil binds with the opioid receptor to increase the stimulation the exchange of GTP to GDP on the G-protein complex. As the effective system is adenylate cyclase and cAMP located at the inner most surface of the plasma membrane, opioids decrease intracellular cAMP by decreasing inhibition of adenylate cyclise and act as the release of sensetive neurotransmitters. The Opioid analgesics also act by inhibiting the release of vasopressin and somatostatin. Opioids analgesics also close N-type voltage-operated calcium channels (OP2-receptor agonist) and open calcium-dependent rectifying potassium channels (OP3 and OP1 receptor agonist). This acts as hyperpolarization and reduced neuronal excitability.

PHARMACOKINETICS

Carfentanil recorded pharmacokinetic with models as elimination half –life 5-6 hours and non Carfentanil metabolite gave elimination half-life as 11-12 hours.

Route of Administration:

The very preferred route of administration of Carfentanil to anesthetize the large animals is intraμscular via a dart, and the dose range between 0.005 and 0.020 mg per kilogram of body weight. Carfentanil have high potency it also can be easily absorbed through the skin or inhaled.

Medicinal uses:-

Analgesia

The analgesic activity of carfentanil depends on its blood plasma drug level and dose. This indicates for the relief of mild to severe pain.

Acute pain

Opioids are the most effective agents for the treatment of acute and severe pain for short terms relief and it also controls to severe acute pain treatment. They have also been found to be important in treatment of rheumatoid arthritis and Cancer pain.

Central Nervous System (Tranquilizer)
Carfentanil induce similar effects of analgesia as other opioids , however due its high potency it will induce side effect such as sedation, that is why it used as a tranquilizer for large animals.

Side effects

Carfentanil has the following side effects.

More common:

- euphoria & drowsiness
- Restlessness
- Sweating
- Runny nose
- Insomnia
- Difficulty concentrating
- Depression
- Mscle aches
- Anxiety
- Heart failure, weak or absent pulse
- Cardiac arrest
- Disorientation
- Pinpoint pupils
- Nausea or vomiting
- Clammy Skin

- Sedation
- Death

Side Effects: Post Treatment

- Restlessness
- Weakness
- Stomach cramps
- Speech disorder

Carfentanil drug Interaction

Carfentanil may interact with:

- The analgesic activity of Carfentanil is enhance due to the two important chemical classes present in it like Phenethylamine and Amphetamine
- The severity of adverse drug effects can be increased when Carfentanil is administered with 5-methoxy-N,N-dimethyltryptamine.

Carfentanill and Acepromethazine

The risk of hypotension and CNS depression can be increased when Carfentanil is administered with Aceprometazine.

Carfentanil Overdose

- Difficulties breathing
- Coma and Death
- Extreme sleepiness
- Difficulty thinking, talking, or walking
- Contraction of pupils

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