Pharmacology

Theoretical

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**L.12**

Central nervous system agents

Central nervous system agents are drugs that affect the central nervous system i.e. the brain and the spinal cord, and produce a response that could be used to alleviate or treat a particular medical condition.

Central nervous system agents can be used as analgesics, anesthetics, anti-emetics, anti-convulsants, and have many more therapeutic uses.

**Analgesics**

***Nonsteroidal anti-inflammatory agents ===========================***

Overview

Inflammation is a normal, protective response to tissue injury caused by physical trauma, noxious chemicals, or microbiologic agents.

Inflammation is the body's effort to inactivate or destroy invading organisms, remove irritants, and set the stage for tissue repair.

When healing is complete, the inflammatory process usually stoped .

All nonsteroidal anti-inflammatory agents (NSAIDs) differ in structure but they all have similar

1. antipyretic,
2. anti-inflammatory and
3. analgesic properties.

NSAIDs work by blocking the cyclo-oxygenase (COX) enzyme, so inhibit production of prostaglandins and thromboxanes, which are produced as part of the inflammatory response.

There are two types of COX enzymes, COX-1 and COX-2.

COX-1 is expressed in most tissues, including platelets.

COX-2 is induced in inflammatory cells when they are activated and the primary inflammatory cytokines (interleukin-1 and tumor necrosis factor alpha). COX-2 enzyme is responsible for production of mediators of inflammation.

Most NSAIDs are inhibitors of both isoenzymes.

 The anti-inflammatory action of NSAIDs is mainly due to inhibition of COX-2, and their unwanted side effects are largely due to inhibition of COX-1.

Salicylates ( aspirin ) -------------------------------------

Aspirin is the prototype of traditional NSAIDs and was officially approved by the FDA in 1939.

 It is the most commonly used and is the drug to which all other anti-inflammatory agents are compared.

Actions:

The NSAIDs, including aspirin, have three major therapeutic actions

 they reduceinflammation (anti-inflammation),

 pain (analgesia),

 and fever

However, not all NSAIDs are equally potent in each of these actions.

A - Anti-inflammatory actions:

B - Analgesic action:

C - Antipyretic action:

D - Gastrointestinal effects:

E - Effect on platelets:

 **Therapeutic uses:**

1 - Anti-inflammatory, antipyretic, and analgesic uses: The salicylic acid derivatives are used in the treatment of gout, rheumatic fever, osteoarthritis, and RA. Commonly treated conditions requiring analgesia include headache, arthralgia, and myalgia.

2 - External applications: Salicylic acid is used topically to treat corns, calluses, and warts.

3 - Cardiovascular applications: Aspirin is used to inhibit platelet aggregation.

Adverse effects:

1- Gastrointestinal: The most common GI effects of the salicylates are epigastric distress, nausea, and vomiting. Microscopic GI bleeding is almost universal in patients treated with salicylates.

2 - Blood: The irreversible acetylation of platelet cyclooxygenase reduces the level of platelet TXA2, resulting in inhibition of platelet aggregation and a prolonged bleeding time. For this reason, aspirin should not be taken for at least 1 week prior to surgery.

3 - Hypersensitivity: Approximately 15 percent of patients taking aspirin experience hypersensitivity reactions.

**4 - Reye's syndrome:** Aspirin and other salicylates given during viral infections has been associated with an increased incidence of Reye's syndrome, which is an often fatal, fulminating hepatitis with cerebral edema.

 This is especially encountered in children, who therefore should be given acetaminophen instead of aspirin when such medication is required to reduce fever. Ibuprofen is also appropriate

5 - In pregnancy: Aspirin is classified as FDA pregnancy category C risk during Trimesters 1 and 2 and category D during Trimester 3. Because salicylates are excreted in breast milk, aspirin should be avoided during pregnancy and while breast-feeding.

**B. Propionic acid derivatives ----------------------------------------**

Ibuprofen

Ketoprofen

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All these drugs possess anti-inflammatory, analgesic, and antipyretic activity; additionally, they can can alter platelet function and prolong bleeding time.

They have gained wide acceptance in the chronic treatment of RA and osteoarthritis, because their GI effects are generally less intense than those of aspirin.

**C. Acetic acid derivatives ----------------------------------------------**

Indomethacin

Sulindac

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All have anti-inflammatory, analgesic, and antipyretic activity. They act by reversibly inhibiting cyclooxygenase.

They are generally not used to lower fever.

**D. Oxicam derivatives -------- ------------------------------------**

Meloxicam

Piroxicam

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They have long half-lives, which permit once-daily administration,

**E. Fenamates---------------------------**

Mefenamic acid ( ponstan capsules)

**F. Heteroaryl acetic acids-------------------------------------**

Diclofenac ( voltarine )

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approved for long-term use in the treatment of RA, osteoarthritis, and ankylosing spondylitis.

 Diclofenac is more potent than indomethacin or naproxen.

**G. Celecoxib --------------------------------**

Celecoxib

**Acetaminophen ------------------------------**

Pracetamol

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Acetaminophen inhibits prostaglandin synthesis in the CNS.

This explains its antipyretic and analgesic properties.

Acetaminophen has less effect on cyclooxygenase in peripheral tissues, which accounts for its weak anti-inflammatory activity.

 Acetaminophen does not affect platelet function or increase blood clotting time.

Therapeutic uses

Acetaminophen is a suitable substitute for the analgesic and antipyretic effects of aspirin for those patients with gastric complaints, those in whom prolongation of bleeding time would be a disadvantage, or those who do not require the anti-inflammatory action of aspirin.

 Acetaminophen is the analgesic/antipyretic of choice for children

Adverse effects

With normal therapeutic doses, acetaminophen is virtually free of any significant adverse effects.

This agent should be avoided in patients with severe hepatic impairment. Periodic monitoring of liver enzymes tests is recommended for those on high-dose acetaminophen.

**Narcotic analgesics**

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Narcotic analgesics are drugs that relieve pain, can cause numbness and induce a state of unconsciousness.

narcotic analgesics reduce neuronal excitability in the pain carrying pathway.

Morphine and its analogues, and some synthetic derivatives are classed as narcotics analgesics.

Narcotic analgesics are used to relieve acute and chronic, severe pain.

Some narcotics are more potent than others.

 They also have the tendency to cause tolerance and dependence.

**Morphine ----------------------------------**

Morphine is an opioid pain medication. An opioid is sometimes called a narcotic.

Morphine is used to treat moderate to severe pain. Short-acting formulations are taken as needed for pain.

The extended-release form of this medicine is for around-the-clock treatment of pain. This form of morphine is not for use on an as-needed basis for pain.

Morphine is not for treating short-term pain just after surgery unless you were already taking morphine before the surgery.

Morphine Side Effects

**Nervous system -----------------**

Central nervous system side effects may be either depressant or excitatory.

drowsiness and sedation.

**Respiratory--------------------**

Respiratory side effects including respiratory depression

respiratory depression can be treated with the opioid antagonist naloxone.

**Gastrointestinal --------------------------**

Gastrointestinal side effects including nausea, vomiting, dyspepsia, constipation, dry mouth, increased gastroesophageal reflux, intestinal obstruction, and increased biliary pressure have been reported

**Cardiovascular side effects** including hypotension

**Addiction --------------------**

Tramadol

Tramadol is a narcotic-like pain reliever.

Tramadol is used to treat moderate to severe pain.