

***Title of Lecture: Analgesics***

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***Refer to slide no. : 9 (****CNS Pharmacology)* ***[27-42]***

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There are 3 major effects for NSAIDs (non-steroidal anti-inflammatory drugs)

* Analgesics
* Antipyretics
* Anti-inflammatory

They are more potent in comparison to paracetamol and aspirin. Aspirin is considered an NSAID.

Analgesics are classified into non narcotic and narcotic based on whether the analgesics produce an addiction or not.

The non narcotics don’t lead to addiction. They are effective in mild to moderate pain since are not strong analgesics, but they have a good antibiotic and anti-inflammatory action.

Narcotics are good and widely used in the management of severe pain. They are not used in the management of mild to moderate pain.

Pain is classified into mild, moderate and severe.

Morphine is narcotic.

Person with a headache and goes to a pharmacy, will the pharmacist give him morphine even if he can? No.

Yes, it will treat the headache but because narcotic analgesics usually lead to addiction. They have no anti-inflammatory effect and so they cannot be used in inflammatory treatment.

A person with a trauma, pain is caused by prostaglandins. Narcotics have no effect on prostaglandins, and so no anti-inflammatory or antipyretic effect.

Starting with NSAIDs requires the understanding of the synthetic machinery of the major mediators of inflammation, prostaglandins and leukotriens.

Starting material is phospholipids, already present in our cells. It is converted into a 20-carbon fatty acid, Arachidonic acid by phospholipase A enzyme.

Arachidonic acid undergoes two pathways:

1. The cyclooxygenase/ prostaglandin synthase enzyme
2. Lipooxygense.

Lipooxygenase produces a number of leukotriens, which have many numbers (leukotriens 3,4…etc).

Combination of leukotriens is known as slow reacting substanceof anaphylaxis.

Prostaglandins are produced through cyclooxygenase, many none stable intermediates and then more stable prostaglandins are produced.

Again, both prostaglandins and leukotriens are involved in inflammation along with other substances mentioned in the pathophysiology of pain such as serotonin. Serotonin is a major neurotransmitter that transfers the signal to the spinal cord and then to the thalamus.

Production of prostaglandins and such mediators of inflammation are defensive mechanisms to counter act the effects of inflammation. They are responsible for the messaging of pain, redness, hotness.

Suppose we have a trauma, they will travel to the site of injury in many quantities to decrease the severity of the injury. Now after the injury there is pain and we have to relieve it by many ways, like sub-specific inhibition of synthesis. Inhibition of the mediators will relieve the pain. It had done its job; counteracted the inflammation, but we have some pain and this can be relieved by analgesics.

This process could be continuous even if there is no injury or trauma, but there is a pathophysiological defect related to the immune system.

We have a stimulus running inside the body like arthritis or vasculitis, these are autoimmune diseases, certain antibodies that are defected giving them a continuous problem.

Usually in trauma, after a day or two with analgesics there’ll be no more pain. But people with arthritis have persistent injury and they have to take medications for life.

A person with some irritation on the nerves, as in disk disease where there’s a defected or dislocated cartilage of the vertebrae pressing on the nerves causing persistent irritation. This irritation is basically production of certain prostaglandins, relieved by analgesics.

Slow reactive substance of anaphylaxis is substance responsible for the broncho-constriction in patients with anaphylaxis and bronchial asthma. People think it’s because of histamine, antihistamines are not beneficial for asthma patients, on the contrary they are considered harmful for asthma patients since they dry the secretions. They have an anticholenergic action.

Since the slow reactive substances of anaphylaxis are harmful to asthma patients we give him an inhibitor for the lipooxygenase, phospholipase A2 inhibitors, or leukotriens antagosnists and all are available.

NSAIDs are absolutely contraindicated in bronchial asthma patients except phospholipase inhibitors like cortisol. They are indicated in cases known as steroid-dependant bronchial asthma, not only effective, they’re indicated but as a last resort.

NSAIDs increase side effects, but not as severe as steroids. Steroids are major blockers, anyone who takes them will benefit except a patient with peptic ulcer.

So phospholipase A2 inhibitors are to be used in the management in the management of bronchial asthma.

Prostaglandins are of many types and numbers. A lot of them contract the uterus, some produce broncho constriction, some produce broncho-dilatation, a lot produce vasoconstriction and enhancement of platelet aggregation, and others cause vasodilatation and inhibit platelet aggregation.

Prostaglandins are protective to the stomach, duodenum and the GI. They protect the stomach from the acidity by inhibiting acid secretion and they provide a mucus layer with huge numbers of prostaglandins which is what protects against digestion of the stomach. Ulcer is basically a defect in the mucus layer causing an injury and since the acidity is high, they’re will be irritation, pain and bleeding and so on.

Evidence of this fact: anti-inflammatory NSAIDs given to patients or normal person will cause irritation because they interefere with the prostaglandin secretion. All NSAIDs are not devoid of this irritation to GIT, majorly by interfering with the prostaglandin synthesis.

Anti-inflammatory agents:

Steroidal and non steroidal. Steroidal maybe used in bronchial asthma while the non-steroidal are contraindicated for asthma patients.

Peptic ulcer patient: phospholipase inhibitors, steroidal and non-steroidal agents are completely contraindicated.

Never give steroidal NSAIDs to a patient who had peptic ulcer since prostaglandins are important for protecting the stomach.

Some prostaglandins have good effects and other lead to pain, inflammation and are mainly harmful. When we have harmful prostaglandins then ideally, we should inhibit their synthesis (achieved by steroids, phospholipase inhibitors and NSAIDs) or use an antagonist.

If useful and protecting the stomach we use a specific agonist, synthetic analogues. They are used in cases of peptic ulcers in which steroidal or non steroidal drugs were used and inhibited the synthesis of prostaglandins.

Prostaglandins are used in delayed parturition, given as vaginal tablets; they’re gentle on the uterus. After application, wait and look for the contractions, if they haven’t occurred then there’s no choice but to use oxytocin which has severe side effects (e.g. uterus rupture)

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