POTENTIAL ADVERSE EFFECTS OF LONG TERM OPIOID USE

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1. INTRODUCTION

1.1 What Are Opioids?

Opioids are a family of analgesic medications, which are used primarily in the treatment and management of acute or chronic pain. They are usually prescribed by a medical practitioner in cases of moderate to severe pain and less commonly, as a treatment option for controlling coughs and diarrhea.

1.2 Types of Opioid Medication

There are many different types of opioid medication and they are available in various strengths. The type of opioid drug prescribed to a patient is usually dependent upon the characteristics and nature of the pain they are experiencing. Opioids can come in various forms including tablets, solutions, elixirs, suppositories and patches. Common types of prescriptions opioids include the following:

Codeine	Weak Opioid Analgesic Medication
Tramadol	Moderate Opioid Analgesic Medication
Morphine	Strong Opioid Analgesic Medication

1.3 How Do Opioid Analgesics Work?

Opioid analgesics suppress the perception and emotional response to pain by attaching themselves to receptors (a type of protein) mainly in the brain, spinal cord and gastrointestinal tract called opioid receptors. From here they can reduce the pain signals sent from the nervous system to the brain.

1.4 Adverse Side Effects of Opioid Medication After Prolonged Use

Prolonged use of opioid analgesics can produce undesirable side effects. These include the following:

- Gastrointestinal Effects
- Respiratory Effects
- Cardiovascular Effects
- Central Nervous System Effects
- Musculoskeletal Effects
- Endocrine System Effects
- Immune System Effects
- Addiction & Misuse

As previously mentioned, opioids bind themselves to receptors within various parts of the body in order to inhibit pain signals. Unfortunately, a consequence of this, is that opioids are not limited to inhibiting pain signals but can also inhibit and interfere with other important functions, as outlined above. These unwanted side effects will be discussed in more detail in the following section.

2. ADVERSE EFFECTS OF LONG TERM OPIOID USE

2.1 Gastrointestinal System

2.1.1 Nausea & Vomiting

The Chemoreceptor Trigger Zone (CTZ) is an area of the brain that detects noxious chemicals that do not belong in the blood. Opioids stimulate the CTZ and cause it to send signals to the Vomiting Centre (VC) in the brain. The VC then initiates a vomiting reflex in order to get rid of the detected noxious chemicals. This process causes nausea, vomiting and abdominal discomfort. Increased vomiting, secondary to opioid use can lessen the effect of opioid medication as large quantities of the drug are expelled from the body during vomiting.

2.1.2 Gastroesophageal Reflux

Opioid analgesics have the ability to negatively impact stomach and bowel function. One of the negative effects opioids can have on stomach function is Delayed Gastric Emptying, where the stomach takes too long to empty the food inside of it. Symptoms of Delayed Gastric Emptying include heartburn, acid reflux, upper abdominal pain and fullness in the stomach.

2.1.3 Constipation

Opioids bind to specific receptors in the gastrointestinal tract. This can result in reduced bowel motility, which delays defecation and leads to the dehydration of faeces through increased water reabsorption. Opioid induced constipation is usually accompanied with other undesirable effects such as

bloating, rectal bleeding, straining, abdominal pain and in extreme cases, rectal tearing and anal fissures.

2.2 Respiratory System

2.2.1 Central Sleep Apnoea (CSA)

CSA occurs when the brain fails to transmit signals to the breathing muscles. Opioids have the ability to affect the brain's control over breathing function, which can result in periods during sleep where breathing becomes irregular or stops temporarily.

2.2.2 Respiratory Depression

The Respiratory Centre in the brain stem sends signals down the spine to the muscles involved in breathing and causes them to contract and relax automatically. This ensures regular respiratory patterns and appropriate lung volume, also known as tidal volume. Respiratory Depression or Hypoventilation occurs when the respiratory rate falls too low to provide sufficient ventilation of the lungs. Long-term use of opioid medication can cause changes in respiratory pattern as well as a decrease in tidal volume, leading to Respiratory Depression.

2.3 Cardiovascular System

2.3.1 Myocardial Infarction

Myocardial Infarction, commonly known as a Heart Attack, occurs when one of the coronary arteries responsible for supplying the heart with oxygenated blood becomes blocked for a prolonged period of time, causing the heart tissue to die. Opioids can cause Atrial Fibrillation (AF). This is an abnormal or irregular heart rhythm. AF increases the risk of many heart conditions

including Hypertension, Coronary Artery Disease, Heart Failure and Heart Disease and Myocardial Infarction.

2.4 Central Nervous System

2.4.1 Sedation/Drowsiness

As opioids have multiple inhibitory effects on cerebral activity, they are known to cause drowsiness and in some cases, sedation. This side effect can also cause communication impairment and incapacities. As tolerance of the opioid medication increases, these side effects tend to lessen.

2.4.2 Cognitive Impairment

Long-term use of opioids can cause thinking disturbances and affect the ability to react. One example of this is Cognitive Impairment. Cognitive functioning is the acquisition, processing and storage of information by the brain. If this is adversely affected, it can lead to decreased attention span, disorientation, restlessness, hallucinations and delirium.

2.4.3 Hyperalgesia

Hyperalgesia is an abnormal heightened sensitivity to pain. Opioid Induced Hyperalgesia (OIH) is the paradoxical response to opioid medication, whereby the desired analgesic effect of the drug, which decreases the perception of pain, is reversed. This leads to an increase in pain perception and the inefficiency of the medication.

2.4.4 Tolerance

Over time, a tolerance can be built up to opioid analgesic medication. This usually leads to increasing doses of the drug in order to achieve the desired pain relief. Unfortunately, increasing doses of opioid analgesics usually correlate with an increasing risk of unwanted side effects.

2.5 Musculoskeletal System

2.5.1 Osteoporosis

Osteoporosis is a condition that causes a reduction in bone density leading to an increased risk of bone brittleness and fragility. One of the ways that prolonged use of opioid analgesics are thought to induce osteoporosis is through the inhibition of osteoblast function. Osteoblasts are cells responsible for synthesizing new bone, thus maintaining healthy bone density. Opioids bind to receptors on the osteoblasts and can cause decreased synthesis of new bone, resulting in decreased bone density.

2.5.2 Myoclonus

Myoclonus is the uncontrollable twitching and jerking of the muscles. The exact cause for opioid induced Myoclonus is unclear, though it is thought to be caused by the inhibition of Glycine. Glycine is an inhibitory neurotransmitter, which is responsible for balancing and calming the signals sent between nerve cells in order for the body to function. Inhibition of Glycine would decrease it's inhibitory effects and can result in Myoclonus.

2.6 Endocrine System

2.6.1 Hypogonadism

Hypogonadism is the reduction or absence of hormone secretions. It leads to infertility, lack of libido and other sexual problems. In women, this can present as early menopause and amenorrhoea and in men, it can cause erectile dysfunction and delayed ejaculation. Opioids can induce Hypogonadism by binding to receptors within the Hypothalamus and decreasing the levels of Testosterone in men and Oestrogen in women.

2.7 Immune System

2.7.1 Immunomodulation

The immune system is a collection of cells, tissues and organs that protect the body from disease and infection. It detects and targets foreign and unwanted bacteria and viruses and prevents them from attacking the body's healthy tissue. Opioids can produce immune modulation and suppress the immune system's ability to fight off infection in the host environment.

2.8 Addiction & Misuse

2.8.1 Dependency

Chronic opioid use can cause abnormal brain changes, which lead to addiction and dependency. This is due to the intense cravings that can occur after using the drug for extended periods and this can develop into compulsive use and the experience of withdrawal symptoms. Withdrawal symptoms are both emotional and physical and can include anxiety, insomnia, depression, sweating, palpitations and nausea. These symptoms can strengthen opioid dependency, as the drug is often taken in order to avoid the experience of withdrawal.

2.8.2 Recreation

Opioids are prescribed to relieve pain. They release a chemical in the brain called Dopamine, which, particularly in the absence of pain, can result in feelings of pleasure. This can encourage the repeated abuse of the drug in order to achieve this effect for recreational purposes.

3. SUMMARY

3.1 Opioids are efficient analgesic medications prescribed by a medical practitioner for their pain relieving effects.

3.2 They work by binding themselves to various opioid receptors, which are mainly found in the brain, spinal cord and gastrointestinal tract but are not limited to this and can be found in other locations around the body. They then inhibit the pain signals sent by the Central Nervous System to the brain in order to decrease pain perception.

3.3 Unfortunately, just as opioids can manipulate the pain signalling pathways, they can also affect and modulate other functions within in the body.

3.4 While many patients are able to use opioids for prolonged periods of time without experiencing any adverse outcomes, long-term use of opioids in others can produce some of the aforementioned undesirable side effects.

3.5 These side effects will usually subside with manipulations to the dosage and type of opioid analgesic medication being taken.

4. SUMMARY/STATEMENT REGARDING OPIOIDS

4.1 Opioids/narcotics are strong analgesics used with great care for cancer and non-cancer pain.

4.2 Not all opioids and their formulations behave the same. They are all potentially harmful in long term use and/or high dose use.

4.3 Long term opioids can cause; tolerance, dependence, addiction, urinary retention, constipation, accidental overdose, withdrawal, cognitive impairment, hypotension, respiratory depression, poor sleep, immune depression, sexual dysfunction, weight gain, nausea, vomiting, blurred vision and other drug interactions

4.4 Long term use of opioids should be considered with great care and it is effectively a compromise as eventually it will cause harm/or stop working for a given dose. Patients are held entirely reasonable for their actions when driving with these medications on board, hence if you are feeling drowsy you should not drive or operate machinery.

4.5 These drugs do interact with many other agents such as Benzodiazepines so great care should be taken in concurrent use. Ask for specific guidance from your Health Care Practitioner.

4.6 The prescriber will retain the right to stop or refuse to prescribe Opioids and other potentially mind altering medication, if he or she deems appropriate due to clinical reasons and/or suspicion of prescription drug misuse.

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