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Pharmacological Activity of Emergency Drug Morphine

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ABSTRACT

When taken orally or intravenously, morphine works well as an analgesic. However, after oral administration, first-pass metabolism in the liver and gut wall reduces the amount of morphine that reaches the systemic circulation. Additionally, a functioning gastrointestinal tract is necessary for the absorption of morphine taken orally. This restricts the amount of oral morphine used following surgery. The buccal route of morphine administration can solve both of these issues. It has been demonstrated that administering morphine via the buccal route is an effective way to relieve pain following elective orthopedic surgery. The pharmacokinetic findings from this investigation have been called into doubt, though. Fisher, Fung, and Hanna came to the conclusion that administering morphine by buccal route produced significant inter-individual variability in the concentration time profiles and, generally, lower morphine plasma concentrations than those previously observed; this may have been caused by a significant variation in the duration of tablet persistence on the buccal mucosa. This medication is prescribed because it is safe and effective at the dose prescribed for your mother's type of pain. When used in this type of severe pain, monitored and reviewed carefully as we have agreed upon, and used as per instructions given to you here on this prescription, we ensure that her pain is relieved to a milder level and nothing untoward happens to her. However, the medication can cause dangerous adverse effects if used without due caution.

Keywords: Morphine, gastrointestinal tract, pharmacokinetic, metabolism.

Introduction

Parenteral acetaminophen (propacetamol) and an NSAID (like ketoprofen) are frequently used for postoperative analgesia following a Caesarean section. However, they are typically ineffective, which makes opioid analgesia necessary. Although many different opioid administration schedules have been suggested, perispinal morphine is one of the most popular. After a single injection given during perispinal anesthesia, this hydrophilic and long-acting medication can continue to work for several hours. Perispinal morphine may cause side effects (such as nausea, vomiting, and pruritis) and respiratory depression; however, the risk is reduced at lower dosages. For perispinal morphine, there are two possible administration methods: intrathecal (i.t.) injection or epidural (ED). The type of anesthesia used (spinal or epidural) frequently influences the choice, but the new method of combined spinal-epidural anesthesia allows for either method of morphine administration. There isn't any conclusive data that favors one method over another. Prior research has demonstrated that 18 hours of postoperative analgesia can be achieved with 3 mg of ED morphine (administered alone) without the risk of respiratory depression and that 0.1 mg of i.t. morphine (in addition to ketorolac) can produce analgesia for the same amount of time. In terms of 24-hour morphine consumption, these two doses seem to be comparable when given without the addition of any more analgesic medications. Thus, they were deemed to be equally potent for the purposes of the current investigation. The purpose of this study was to compare these two protocols; however, in order to provide additional analgesia through intrathecal sufentanil, parenteral acetaminophen, and ketoprofen, the morphine dosages were decreased to 2 and 0.075 mg, respectively. Thus, the purpose of the research was to evaluate the effects and safety of 2 mg of ED morphine and 0.075 mg of intrauterine morphine following a cesarean section in relation to initial intrauterine sufentanil and subsequent parenteral acetaminophen and ketoprofen.

Figure 1: Picture of Morphine vial

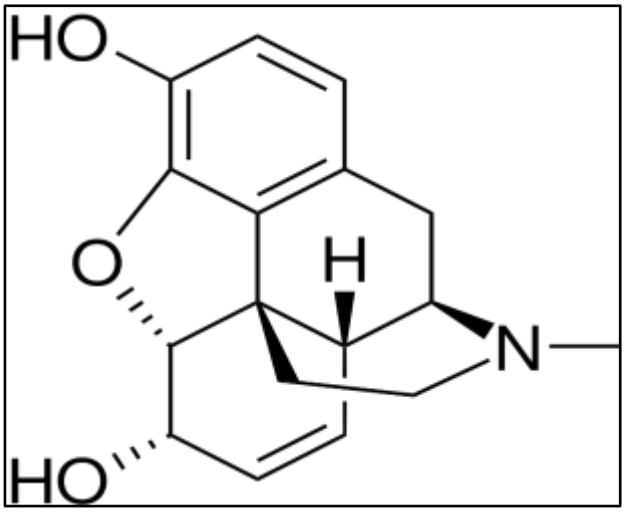

Figure : Chemical Structure of morphine

Synthesis of Morphine

The investigation into the complete synthesis of morphine has continued unabated for the past ten years. To create the structural framework of morphine, many synthetic approaches and natural reactions were employed. Over the past ten years, Metz et al. have been investigating the use of commercially available isovanillin as the starting material for the complete synthesis of morphine. Isovanillin was used by Metz et al. in 2011 to accomplish four contiguous stereocenters using intramolecular nitrone cycloaddition. According to their most recent study, establishing the benzoic quaternary would need the Heck cyclization reaction.

For Fukuyama, the asymmetric total synthesis of (-)-morphine was thoroughly investigated. 2010 saw the discovery by Fukuyama and colleagues that the Suzuki-Miyaura coupling reaction and enzymatic resolution may be employed as crucial steps in the cyclohexenol unit's synthesis. In order to build the morphine skeleton in 2017, they streamlined the entire synthesis process without the need of protective groups. Aside from Metz et al. and Fukuyama et al., other groups have also made innovations and improvements to the morphine total synthesis pathway. To produce the stereoselectivity of morphine precursors, Chida and colleagues (2013) presented a sequential [3,3]-sigmatropic rearrangement of allylic vicinal diols in a single pot process. That same year, Fan et al. employed a novel method for the formal synthesis of morphine by installing functional groups by the mean of SmI2-promoted reductive coupling/desulfurization and tandem alcoholysis/oxa-Michael addition using the Hudlicky intermediate. The important step to stereoselectively completing the whole synthesis of morphine in 2014 was the catalytic hydrogenation and Grewe cyclization, which was accomplished by Opatz and colleagues using Noyori asymmetric catalyst. Martin D. Smith et al. (2016) used photo-induced cyclization of o-aryl butyrolactone to produce the furan ring in morphine, then ene–yne–ene ring closure metathesis imposed the tetracyclic morphine core. predecessors. In 2019, morphine complete synthesis research made a lot of progress. When compared to other groups that employed chiral precursors or intermediates, Chang-Sheng et al. found that spiropyrrolidine, an organ catalyst, could react with achiral substrates through an asymmetric catalytic process to generate quaternary carbon constructions. A nine-step formal synthesis of (±)-morphine was described by Louis Barriault et al. This synthesis used the Diels−Alder/Cloisen/Friedel−Crafts sequential reaction to produce a single pot reaction without protective groups, which greatly decreased the complexity of the entire morphine synthesis. While some amazing work has been done in the last ten years, the synthesis approach and key-step investigation used by academics have changed.

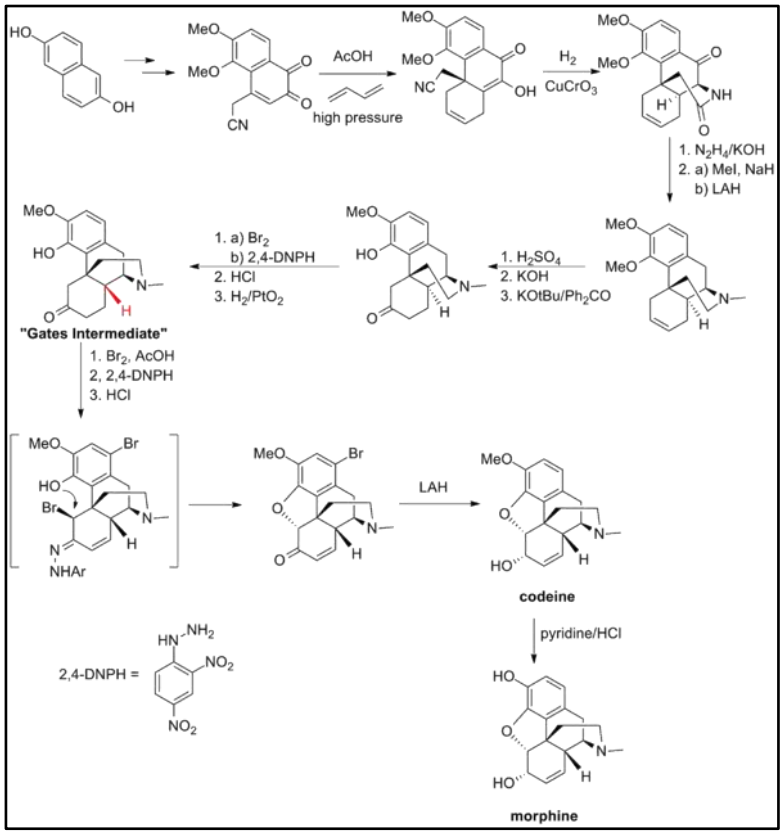

Figure : Synthesis procedure of morphine.

SAR of Morphine

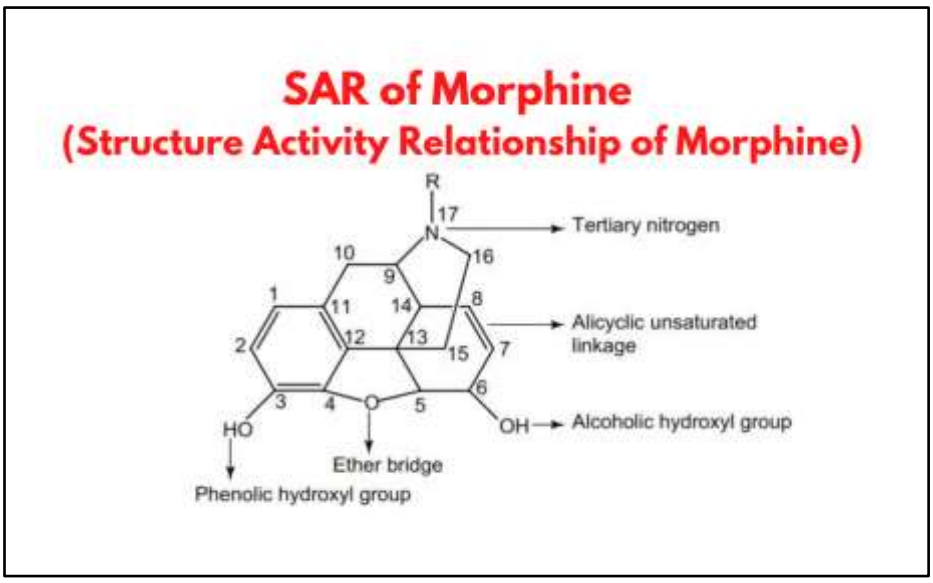

Figure : SAR of Morphine

Mechanism Action

When comparing various opioid analgesics, morphine is regarded as the standard. Similar to other drugs in this class, morphine binds to mu, kappa, and delta opioid receptors. The majority of this medication's analgesic effects are caused by binding to the mu-opioid receptor in the peripheral and central nervous systems (PNS and CNS, respectively). Morphine's overall impact is to reduce nociceptive transmission by inhibiting the nociceptive afferent neurons of the PNS and activating the descending inhibitory pathways of the CNS.

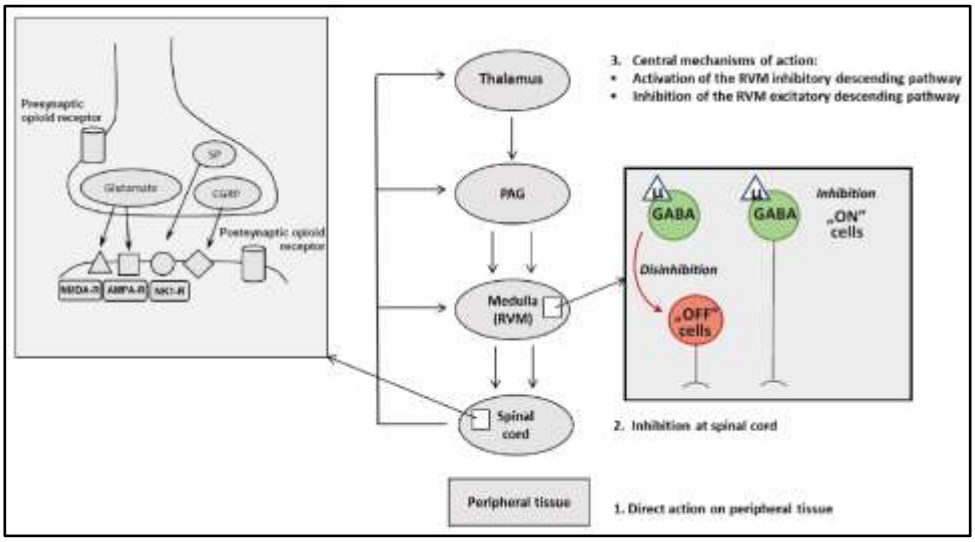

Figure 2: Mechanism of action of Morphine.

Pharmacokinetics

Oral, intravenous, rectal, subcutaneous, spinal injection (e.g., epidural), inhalation, and snorting are among the ways that morphine can be given. Merely 40 to 50 percent of the drug's absorbed dose reaches the neurological system due to extensive first-pass metabolism in the liver. The kidneys digest the majority of the morphine, which is then excreted from the body as urine.

Administration

The administration of morphine can happen via a number of vehicles. The most common ways to administer it are orally (PO), intravenously (IV), epidural, and intrathecal. Both immediate-release and extended-release oral formulations are available for the treatment of both acute and chronic pain. More intense and poorly controlled pain may be addressed using intrathecal, epidural, and IV formulations administered once or repeatedly. The amount of infusion that a patient receives can vary greatly and is primarily determined by how naive or tolerant they are to opiates. It's interesting to note that intramuscular (IM) administration of IV morphine formulation is also prevalent. Additionally, morphine is offered as a suppository. A lot of people use and abuse morphine. People have therefore discovered ways to insufflate, or snort, the drug. Additionally, morphine is offered as an oral solution that can be applied sublingually. The use of sublingual morphine in palliative care is quite common.

Morphine Dosage

When administering intramuscular morphine sulfate for pain management, doses ranging from 100 to 150 mcg/kg can be given every two hours. The amount of morphine required for anesthesia and procedures depends on how long the procedure will take and how much discomfort is expected.

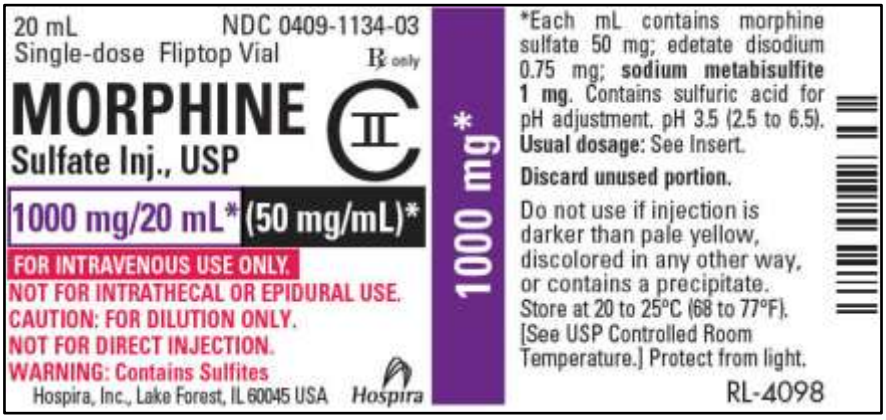

Figure 3: Administration of Morphine.

Adverse Effects

Constipation is one of the most typical side effects of morphine use. The myenteric plexus's mu-opioid receptors are stimulated to produce this action, which lowers peristalsis and prevents stomach emptying. Urinary retention, nausea, vomiting, and depression of the central nervous system are other frequent adverse effects. One of the more dangerous side effects of opiate usage that is particularly crucial to watch out for in the postoperative patient group is respiratory depression.[9] Dizziness, sedation, and lightheadedness are further adverse effects that have been recorded. Because patients frequently experience nausea and vomiting, morphine is frequently administered in emergency rooms together with an antiemetic, like ondansetron. When patients present with right upper quadrant pain and some doctors fear possible biliary tract pathology, they will not prescribe morphine due to the potential for euphoria, dysphoria, agitation, dry mouth, anorexia, and biliary tract spasm. According to reports, morphine can also have an impact on the circulatory system, leading to flushing, bradycardia, hypotension, and syncope. It's also crucial to remember that individuals may develop edema, urticaria, pruritis, and other skin rashes.

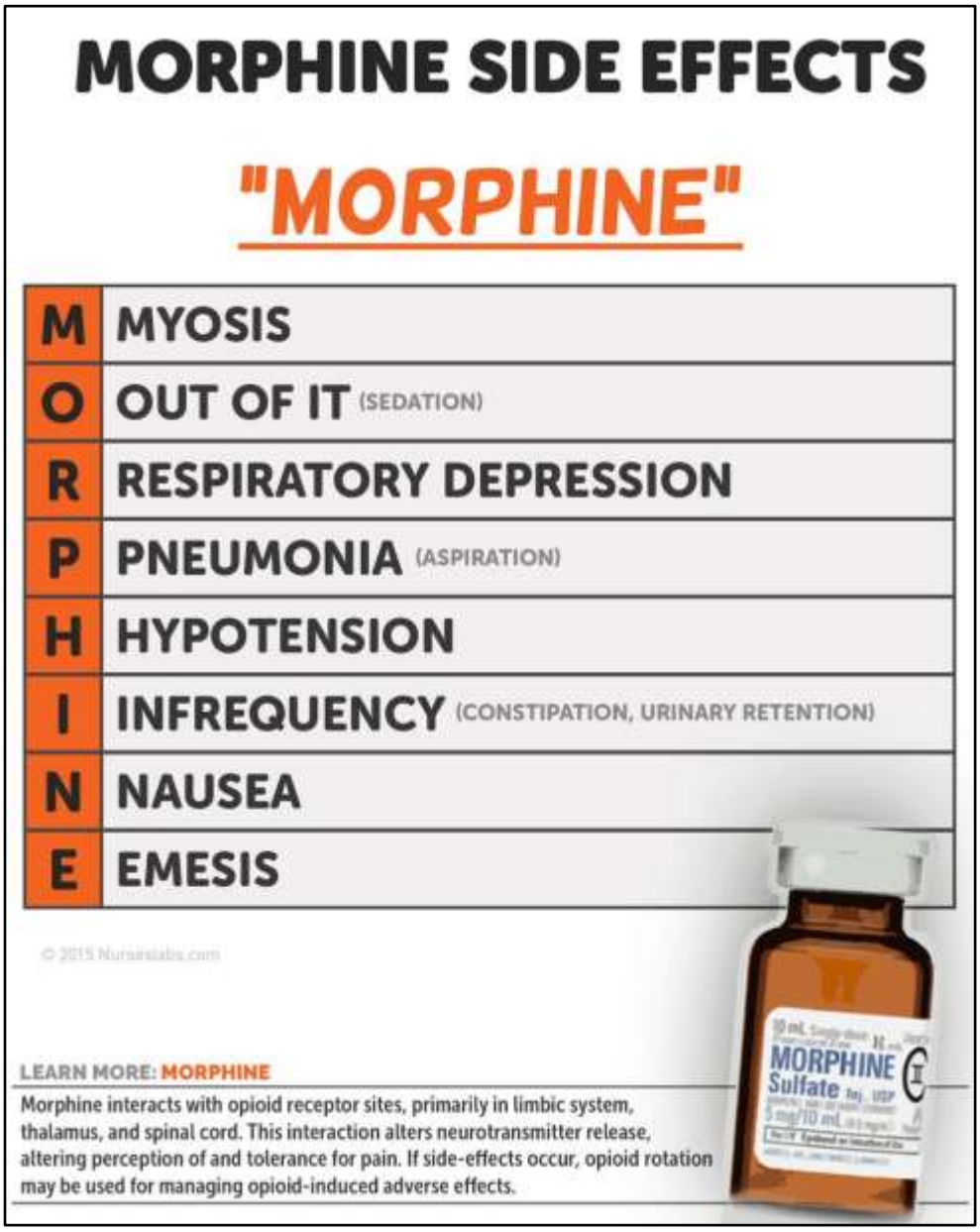

Figure 4: Adverse reactions of morphine.

Contraindication

When taken as directed, morphine is a very helpful drug. However, there may be very specific circumstances in which this medication should not be used. Since morphine might further reduce the respiratory drive, extreme vigilance is required in cases of severe respiratory depression and asthma exacerbation. Morphine should also be avoided in situations where there has been a prior hypersensitivity reaction and stopped right away if there is an active reaction.

When taking monoamine oxidase inhibitors (MAOIs) together with morphine, caution is also required because of the synergistic impact of both drugs. The patients may subsequently experience severe hypotension, serotonin syndrome, or worsening respiratory depression as a result of this combination. Another significant contraindication is GI blockage. Many people also believe that giving opioids to someone who has a history of substance abuse is contraindicated, particularly if the patient has a history of opioid abuse. While there is much debate on this subject, most medical professionals concur that pain needs to be managed. Nonetheless, the majority will concur and admit that opioid analgesics are not the only option.

Conclusion

This article, in general, presents five synthetic pathways of morphine from various researchers and provides a thorough analysis and discussion of the yield-reaction connection, green chemistry applications, and industrial production viability. Smith suggested the least steps synthetic route with the highest yield in terms of the correlation between the reaction steps and the overall yield. From the standpoint of green chemistry, each researcher's trend and direction should be to build an environmentally sustainable and friendly morphine synthesis method. Realizing that morphine manufacturing has become industrialized is a challenge for all researchers. However, Smith's optimal technique for the entire synthesis of morphine is rather well-known, regardless of the application of green chemistry or the viability of industrial production. As a result, Smith's entire synthetic morphine approach is superior. The potential for growth in morphine total synthesis is enormous, notwithstanding the obstacles and hurdles. The synthetic pathway becomes more environmentally benign, especially with the application of green chemistry, which may open up the door to industrial production.

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