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A REVIEW ON SUSTAINED RELEASE MATRIX TABLET FOR MUSCLE RELAXANT

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ABSTRACT

Skeletal muscle relaxants (SMRs) consist of a heterogeneous group of medications with a side effect profile of concern. The aim of this paper was to review the evidence of use of SMRs in the treatment of sports injuries. However, there is little consensus on a proper diagnosis and optimal treatment strategy for these patients. Low back pain is a common problem worldwide causing deterioration of health and quality of life. Low back pain is often associated with muscle spasm. We investigated the combined effect of muscle relaxants and pain killers for low back pain. Patients are often prescribed these agents for the treatment of acute back pain, and many experience relief within several weeks of starting therapy. However, these medications (reviewed in this article) are controversial alternatives that carry risks of adverse effects and increased cost.

KEYWORDS -Skeletal muscle relaxants, low back pain, Advance effect, et.

INTRODUCTION

For the past three decades, low back pain has consistently been ranked among the top five most common reasons for physician visits in the United States .We investigated the combined effect of muscle relaxants and pain killers for low back pain. Low back pain (LBP) is a common problem with global lifetime prevalence of approximately 38.9%. The highest incidence of LBP is reported in the third decade of life with increasing prevalence until 60–65 years.

The American Pain Society and the American College of Physicians published guidelines in 2007 for low back pain, recommending acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs) as first-line treatment for most patients. Patients are often prescribed these agents for the treatment of acute back pain, and many experience relief within several weeks of starting therapy. For optimal effect, high doses of NSAIDs and muscle relaxants are required. At such high doses, NSAIDs cause gastric intolerance while centrally acting muscle relaxants are associated with sedation, mental confusion, dizziness, weakness, and impairment of coordination. Thus, an ideal fixed dose combination. In a double-blind study in 53 outpatients with painful skeletal muscle spasm, chlorzoxazone was found to be significantly more effective than diazepam with fewer side effects. Given the frequency of use, the questionable role in the treatment of back pain, and the potential for misuse, it is imperative for clinicians to be aware of the facts regarding commonly used muscle relaxants in the United States. Higher effectiveness for short-term pain relief has been reported with the addition of skeletal muscle relaxant to paracetamol or an NSAID than with the analgesics alone. Currently, no experience has been published for the effectiveness of chlorzoxazone and ibuprofen in the treatment of LBP in the Indian population. Hence, the present study was done to compare the efficacy and safety of the FDC of chlorzoxazone and ibuprofen versus ibuprofen alone in patients with acute LBP clinically suspected to be associated with muscle. In a double-blind study in 53 outpatients with painful skeletal muscle spasm, chlorzoxazone was found to be significantly more effective than diazepam with fewer side effects.

Spasticity from the upper motor neuron syndrome (a complex of signs and symptoms that can be associated with exaggerated reflexes, autonomic hyperreflexia, dystonia, contractures, paresis, lack of dexterity, and fatigability, in addition to spasticity) can result from a variety of conditions affecting the cortex or spinal cord.[1] Some of the more common conditions associated with spasticity include multiple sclerosis,[2] spinal cord injury.

Skeletal muscle relaxant

Skeletal muscle is highly vascularized and innervated, and embedded with components of the metabolic and regulatory machinery, supporting efficient energy production and cellular homeostasis. Each myofiber represents a muscle cell with its basic cellular unit, the sarcomere. Skeletal muscle is one of the three significant muscle tissues in the human body. Each skeletal muscle consists of thousands of muscle fibers wrapped together by connective tissue sheaths. The neuronal innervation of a skeletal muscle typically comprises sensory

nerve fibers, motor nerve fibers, and the neuromuscular junction. The nerve fibers are composed of myelinated as well as non-myelinated nerve fibers. Skeletal muscle is one of the three significant muscle tissues in the human body. Each skeletal muscle consists of thousands of muscle fibers wrapped together by connective tissue sheaths. The individual bundles of muscle fibers in a skeletal muscle are known as fasciculi. The outermost connective tissue sheath surrounding the entire muscle is known as epimysium.

Structure and function

The primary functions of the skeletal muscle take place via its intrinsic excitation-contraction coupling process. As the muscle is attached to the bone tendons, the contraction of the muscle leads to movement of that bone that allows for the performance of specific movements. The skeletal muscle also acts as a storage source for amino acids that different organs of the body can use for synthesizing organ-specific proteins. The stem cells which differentiate into mature muscle fibers are known as satellite cells which can be found between the basement membrane and the sarcolemma (the cell membrane surrounding the striated muscle fiber cell). The skeletal muscle also provides structural support and helps in maintaining the posture of the body. The skeletal muscle also acts as a storage source for amino acids that different organs of the body can use for synthesizing organ-specific proteins. The skeletal muscle also plays a central role in maintaining thermostasis and acts as an energy source during starvation.

Action

Depolarizing blockers typically produce fas ciculations lasting a few seconds before inducing flaccid paralysis, but fasciculations are not prominent in well-anaesthetized patients. Additionally, it is also associated with the diaphragmatic, esophageal, and eye muscles. Thus, skeletal muscle serves a variety of purposes, including moving of the body, breathing, and swallowing. Skeletal muscle fibers are striated, multinucleated cells ranging from 10 to 100 micrometers in diameter and many centimeters long. The nuclei are located in the cell's periphery, adjacent to the sarcolemma. Each muscle fiber is composed of several hundred to several thousand myofibrils. Myofibrils are composed of actin (thin filaments), myosin (thick filaments), and support proteins.

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MATRIX TABLET

A matrix system consists of active and inactive ingredients that are homogeneously dispersed and mixed in the dosage form.In a matrix system the drug is dispersed as solid particles within a porous matrix formed of a hydrophobic polymer (such as wax, polyethylene, polypropylene, and ethyl cellulose) or hydrophilic polymer (such as hydroxy propyl cellulose, hydroxy propyl methyl cellulose, methylcellulose, sodium carboxy methylcellulose, alginates and scleroglucan). In this sense, the term "matrix" indicates the three dimensional network containing the drug and other substances such as solvents and excipients required for the specific preparation. Matrix drug delivery systems release the drug in continuous manner.

Sustained release matrix drug delivery system

The term sustained release has been constantly used to describe a pharmaceutical dosage form formulated to retard the release of a therapeutic agent such that its appearance in the systemic circulation is prolonged and its loading dose, polymer solubility of drug and its diffusivity in the polymer matrix and the porosity of the release unit plasma profile is sustained in duration. The matrix device, as the name implies, contains a substance dispersed in the same manner throughout the polymer matrix. In the model, the outer layer exposed to the bath solution dissolves first and then disperses out of the matrix.

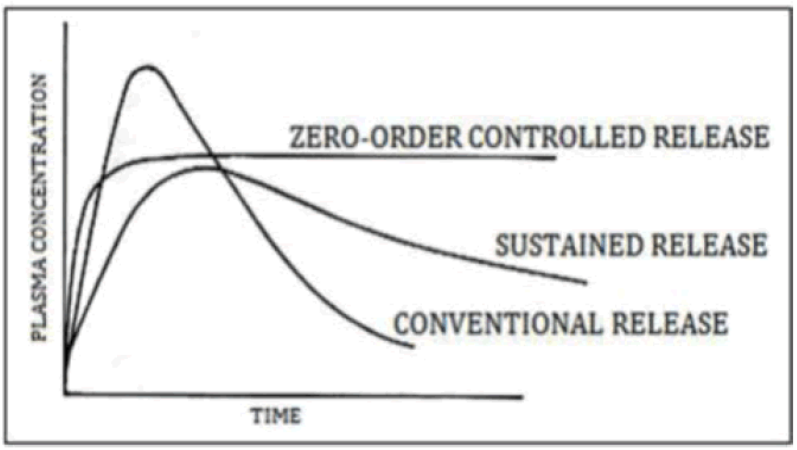

Figure 1. Plasma drug concentration vs. time profile for oral conventional dosing and single oral dose of sustained and controlled release formulation

Oral sustained release drug delivery system

Stable release, continuous action, extended action, controlled release, extended action, depot words used to identify drug delivery systems are designed to achieve a long-term therapeutic effect by continuing drug delivery over time after single dose administration. In the case of oral administration this time is measured in hours and in the case of injections this time varies from days to months. Most dosage form for continuous release follows the method of distribution, dispersion or combination of both, to produce a slow release of the drug at a predetermined rate.

Classification of sustained release matrix tablet

The methods used to achieve sustained release of orally administered drugs delivery systems are as follows.[12]

• Diffusion System
• Reservoir Device
• Matrix Device
• Dissolution System
• Osmotic System
• Ion-exchange Resin
• Swelling and Expansion System
• Floating System
• Bioadhesive or Bucoadhesive or Mucoadhesive system

The matrix device, as the name implies, contains a substance dispersed in the same manner throughout the polymer matrix. In the model, the outer layer exposed to the bath solution dissolves first and then disperses out of the matrix.

Advantages of matrix tablet

Easy to manufacture.
Versatile, effective and low cost.
Can be made to release high molecular weight compounds.
The sustained release formulations may maintain therapeutic concentrations over prolonged periods.
The use of sustain release formulations avoids the high blood concentration. Sustain release formulations have the potential to improve the patient compliance. Reduce the toxicity by slowing drug absorption

Disadvantages of sustained release matrix tablet

The drug release rates vary with the square root of time. Release rate continuously diminishes due to an increase in diffusional resistance and/or a decrease in effective area at the diffusion front. However, a substantial sustained effect can be produced through the use of very slow release rates, which in any applications are indistinguishable from zero order.

Manufacturing technique of matrix tablet

Direct compression

Powders or granules compressed directly into tablets without alteringthe physicality.

Dry granulation

It is of two types, slugging and roller compaction. Inslugging method, granule is recompressed and slugs are crushed to produce granules. Whereas in roller compaction, powder is recompress with pressure rolls.

Wet granulation

It involves massing of drygranule blends in a volatile fluid, wet sizing then drying and followed by dry screening. Steam granulation. Steam is used as a binder for granulation instead of water. It uniform layer distributes and diffuses into the granules. The granules become rounded with more surface area and hence enhance drug dissolution rate from granules.

Melt granulation

Moldable binders are used for granulation, which melts

at 50-80 ˚C. Dry granules collected by cooling it to ambient temperature.

Freeze granulation

It involves spraying droplets of slurry into liquid nitrogen and the drops are then immediately frozen into granules followed by drying process, i.e. lyophilisation.

Polymer used in matrix tablet

A) Soluble polymers

Polyethylene glycol (PEG), polyvinyl alcohol (PVA), Polyvinylpyrrolidone (PVP), Hydroxypropyl methyl cellulose (HPMC)

B) Hydrogels Polyhydroxyethylemethylacrylate (PHEMA),
Cross-linked polyvinyl alcohol (PVA), Crosslinked polyvinyl pyrrolidone (PVP), Polyethylene oxide (PEO), Polyacrylamide (PA).

c) Biodegradable polymers Polylactic acid (PLA), Polyglycolic acid (PGA), Polycaprolactone (PCL), Polyanhydrides, Poly ortho esters.

d) Non-biodegradable polymers
Polyethylene vinyl acetate (PVA), Polydimethylsiloxane (PDS), Polyether urethane (PEU), Polyvinyl chloride (PVC), Cellulose acetate (CA), Ethyl cellulose (EC)

Evaluation of sustained release matrix tablet

• Weight Variations: Twenty pills are measured individually and combined, calculated by the average weight of the pills.
• Hardness: Strength tests are performed on tablets in each group using a Monsanto hardness tester and average values are calculated.
• Friability: Pills tested for elasticity using a Roche friabilator, around 25rpm 4min.
• Size: The size of the tablets is determined using a micrometer screw gauge.
• Content Uniformity: Using a visible UV spectrophotometer obtained the value of a drug using a curve measuring method.
• Kinetic Studies
• In Vitro Dissolution Study: Drug release research is usually based on the Rotating Paddles apparatus. In particular the buffer is used as a scattering point. The bath temperature is maintained at 370C and the required sample of the soluble area where the drug release is taken at normal time and then returned to the same local area.
• In-Vivo Methods Once a satisfactory in-vitro profile is achieved, it becomes necessary to conduct invivo testing and establish in-vitro in-vivo relationships. The different methods of in-vivo testing are.
• a. Clinical response
• b. Blood level data
• c. Urinary excretion studies
• d. Nutritional studies.
• e. Toxicity studies
• f. Radioactive tracer techniques

Design consideration of dosage form

1) Biological factor

a. First-pass effect

Drugs with a significant first-pass impact show a delayed release rate. The bioavailability is impacted by this delayed release rate.

b. Half-life

A drug's half-life is a measurement of how long it stays in the body. A excessively high concentration of medicine may be present in the dosing method if the substance has a short half-life of less than 2 hours.

c. Adverse effects

Extending the medication release could result in undesired side effects.

d. Absorption and solubility

absorbency and soluble both are related. Drugs that are less water soluble can reduce the effectiveness of absorption overall.

e. Metabolism

Drugs that are extensively processed either in the intestine's lumen or tissue prior to absorption may have decreased bioavailability when taken in slower releasing dose forms.

2) Physiochemical factor

A. Drug stability

medicine leakage in the digestive system due to acidic digestion and/or acidic breakdown is a crucial factor in oral dose formulations. Drugs degrade in solid states much more slowly than they do in suspended or solution states.

B. Partition Coefficient

It refers to how much medicine is present compared to the water phase, in the organic phase. Because They won't be leaving the phospholipid membranes through partitioning once they enter it, drugs with greater partition co-efficients are not suited for oral SRDDS. By using the formula, it may be determined.

K= Co / Cw Co = Conc. at eqm. in the oil phase.

Cw = Conc. in water phase at equilibrium.

CONCLUSION

The conclusion of the discussion above is that the matrix tablets are useful in overcoming patient compliance issues and dosage form efficiency issues that are related to conventional dosage forms' inability to produce the required therapeutic response. Along with other advantages, cost-efficient and a single or every day intake are the pluses. The composition of long-lasting matrices pills, their benefits and drawbacks, and the different polymers employed to create a method were the main topics of this review paper. As a result, the dosage form design is being optimised for sustained release matrix tablets.

By the above discussion, it can be easily concluded that sustained-release formulation are helpful in increasing the efficiency of the dose as well as they are also improving the patient's compatibility. More over all these comes with reasonable cost. The dosage form is easy to optimize and very helpful in case of the antibiotics in which irrational use of the same may result in resistance.

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