Nanotechnology in Pain Management

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Abstract

Pain is the most common reason for people to seek medical care in the United States and it is a significant economic burden. Pharmacotherapy is the first line of approach in its management. Having said so medications do come with a wide range of side effects and abuse or over use potential. This instigates the need to develop effective as well as safe drugs. This is where nanotechnology holds a key and has attracted different industries including the pharmaceuticals. Nanotechnology is conducted at a nanometer scale and can help design drugs at a molecular scale. Designed at that scale, drugs with unique properties such as high bioavailability, receptor specificity, long duration of action and less systemic toxicity have evolved. While nanotechnology-devised smart drugs already exist in the market that can surprise us, many are in the pipeline. As the challenges posed by pain are colossal there is a need for consistent development of safe and effective pain medications, and that can something be accomplished by nanotechnology in our near coming future.

Introduction

Pain management is a known significant challenge in the United States involving nearly 100 million patients and costing at least $560-$635 billion every year. In the efforts to find new, effective and safer modalities to treat pain, a science, engineering, as well a technology conducted at nanoscale has started finding its inroads into the system.

Its desirable attribute of designing and developing drugs with targeted delivery has made it a great fit for pharmacological pain management.

The field of medicine is a constant evolution that necessitates exploration of new roads in both diagnostic and therapeutic aspects of this field. One ever-growing interest exists in the research and development of more precise and effective ways in treatment modalities. Pain is the most common reason for people to seek medical care in the United States, with an estimated one-third of its population (100 million people) affected, exceeding diabetes, heart disease, stroke and cancer combined. Being a significant economic burden, costing the society at least $560-$635 billion annually, it is crucial that we continue to strive for newer, effective, and safer modalities to treat pain [1]. This is where we believe nanotechnology holds the future for a more effective drug delivery system to treat pain. The concept of nanotechnology was first propounded by Nobel Laureate Richard Feynman in 1959.

Nanotechnology is defined as science, engineering, and technology conducted at nanoscale. It is the study and application of nanometer technology that can be used across the different realms of science such as: chemistry, biology, physics, material science, engineering, as well as the pharmaceutical industry. The pharmaceutical industry has been showing interest in using nanotechnology to develop highly specific medical intervention, both diagnostic and therapeutic, at the molecular scale (i.e. size below 1000 nm) for curing diseases or repairing damaged tissues, which refers to nanomedicine, a sub-discipline of this technology. It is being used to produce drugs with novel and effective delivery systems that hold much promise. Such drugs can be called as “smart drugs” because by being more specific in targets or delivery, they can be more effective while having decreased systemic side effects and increased safety. The pharmaceutical structure of these novel drugs increases their biocompatibility, further improving safety and reducing adverse effects. Lastly it is their pharmacokinetics, which is much improved to primitive methods that keeps pharmaceutical industries extremely interested. Some of these properties include small size, surface charges, and hydrophobicity that increase absorption, resulting in an overall more bioavailable substance. These nanoparticles can enter human cells via cell-mediated endocytosis; a unique ability achieved by coating particles with hydrophobic polymers, thus avoiding their rapid natural removal entertained by human body. The outer surface of these molecules can be altered with specific proteins or antibodies to aid in binding or interacting with specific tissue, again increasing target selectivity and decreasing systemic effects [2].

With so many desirable attributes of nanotechnology, and pharmacotherapy being the first line of approach in pain management, it makes a good fit in designing effective drugs to treat pain. Currently opioids are the most commonly used drugs. Pain being mostly chronic, patients not responding to basic NSAIDs end up relying on opioids for relief, which is although effective, does not come without a cost. There are a whole slew of side effects included in opioids packages including constipation, drowsiness, and nausea and vomiting; but
there are more than the se that range from urinary retention, postural hypotension, respiratory depression, as well as other CNS related disorders that a majority of patients experience [3]. “Smart drugs” from nanotechnology are targeting specific with high binding capability, higher membrane permeability, longer duration of circulation in blood and action. These features are particularly attractive while treating pain; as such nano drugs can be effectively used for longer-term with minimal side effects and decreasing opioids use. They can also be designed to provide a controlled release of substance, which can lead to better patient compliance, reduced oral pill intake, and decreased incidence of abuse of prescription pain medications. These medicines can be controlled via an implantable device that delivers long acting medications, at fixed dose, over a fixed period to maintain constant therapeutic levels, thereby improving efficacy and safety. Lastly, these smart drugs are designed to be highly soluble, thus decreasing bio toxicity. All these features make nanomedicine a likely discipline to pursue to effectively treat pain.

Among the standard drugs used to treat pain, quite a few have been developed using nanotechnology holding the promises of a smart drug. Such analgesics that are FDA approved and marketed are NSAIDs such as diclofenac, and opioids such as morphine, fentanyl, and oxycodone. Diclofenac submicron particle capsule has been indicated for mild to moderate acute pain in adults at low doses [4-6]. Data from 4 randomized control trials in patients undergoing surgical procedures approved a single-injection, extended release, epidural morphine sulfate formulation for postoperative pain. The formulation showed better effects when compared to controls receiving either conventional epidural morphine or placebo [7]. An oral, extended release, once-daily formulation containing a mixture of immediate-release and extended-release morphine sulfate for moderate to severe around-the-clock pain without any alternatives was approved following studies that revealed comparable analgesic efficacy and stronger pharmacokinetic profile when compared to controlled release morphine sulfate [8-9]. Nanotechnology designed oral transmucosal fentanyl citrate; fentanyl sublingual tablet and fentanyl nasal spray are being used for acute and chronic moderate to severe pain is comparable with a fentanyl sublingual tablet and fentanyl nasal spray are being used for breakthrough cancer pain in those who are already receiving and tolerant to opioids therapy following proven results from several clinical trials [10-17]. Pharmacokinetic and pharmacodynamic profile of a newly approved tablet formulation of immediate-release oxycodone for acute and chronic moderate to severe pain is comparable with a regularly developed immediate-release oxycodone [18]. Oromucosal liquid approval for oral pain due to various lesions followed the immediate and clinically significant results that found no difference while comparing CAM2028-control and CAM2028-benzylamine [19]. Furthermore, some nanotechnology designed NSAIDs such as indomethacin, meloxicam, naproxen, celecoxib ibuprofen are in pipeline at different stages and are expected to be approved and marketed soon [20-23].

With pain being a comorbidity that significantly affects quality of life, inflicting an enormous economic burden both on health system and society, the challenge is colossal. Nanotechnology offers the potential of developing novel and effective drug delivery systems that will effectively treat pain, emphasizing on the beginning of a new era in pain management.

References


