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Mini Review

Appraisal of Nanotechnology Application to Local Anesthesia (LA)

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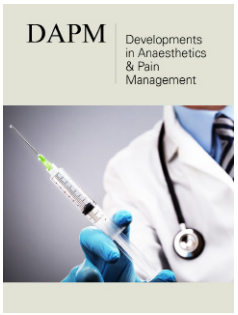

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Abstract

Numerous improvements have been made to the formulation of local anaesthetics, and practical use has been made of their effectiveness in producing long-lasting motor and sensory block. By providing analgesia for a longer period of time with a single dosage, sustained release formulations help to avoid the problems that frequently occur when using conventional analgesics. Additionally, it is claimed that controlled release of an anaesthetic agent lessens side effects, particularly cardiotoxicity, neurotoxicity, and tissue lesions, and prevents overdosing. The use of liposomal formulation and nanotechnology has produced highly effective pain management and rapid patient recovery.

Introduction

Due to its importance for both physical and mental health, pain has been referred to as "the fifth vital sign" since 1996. Multimodal analgesia is a notion that has been introduced to address the opioid epidemic that is occurring during traditional pain management [1]. One of the most popular and secure analgesics in multimodal regimens are Local Anaesthetics (LAs). However, its application is constrained by its short half-life (less than 24 hours) and potential toxicity (cardiac and neurological system dysfunction), which increase the urgency of finding ways to balance the negative effects and sustained analgesia [2]. Although disposable catheters with pumps are used to extend the time between LAs, there is still a chance of catheter dislodgment, infection, and trauma [3]. Catheter placement is also labor and time intensive. The above-mentioned are offset by extended-release and its mechanism of LAs (Table1); (Figure1). In order to provide low systemic toxicity, they are capable of constantly releasing a safe amount with a single administration (often injection without general anaesthesia [4]. Long-lasting nociceptive block can be obtained in the meanwhile [5]. Peripheral nerves are the first stops to perceive pain stimuli during pain transmission. It is reasonable to consider inhibiting pain from the very beginning, stopping downstream reactions and maladaptive changes of neuroplasticity which are more difficult to control [6]. Therefore, LAs become a perfect choice. LAs work on peripheral nerves via binding to intracellular domain of voltage-gated Na channel, inhibiting influx of Na+, resulting in the blockade of depolarization. LAs are constituted with three chemical groups: a hydrophilic amino group (mostly tertiary amines), a lipophilic benzene ring, and a linker which can be an amide or an ester, determining LAs' classification [7].

Table 1: Advances of nano-structured extended-release local anesthetics.

Local Anesthetic	Class/Chemical Linkage
Lidocaine	Amide
Bupivacaine	Amide
Ropivacaine	Amide
Prilocaine	Amide
Mepivacaine	Amide
Articaine	Ester
2-Chloroprocaine	Ester
Tetracaine	Ester
Procaine	Ester

Amide-type LAs are the most commonly used, including bupivacaine, ropivacaine, lidocaine, and mepivacaine. Ester-type LAs involve chloroprocain, procaine, and tetracaine [8]. The earliest points of transmission for pain sensations are peripheral nerves. It makes sense to think about blocking pain right away in order to prevent downstream effects and more difficult-to-control maladaptive alterations in neuroplasticity [9]. LAs are a wonderful choice as a result. By attaching to the intracellular region of the voltage-gated Na channel and blocking the influx of Na^+, LAs limit depolarization in peripheral neurons [10]. Three chemical groups make up LAs: a lipophilic benzene ring, a hydrophilic amino group (most commonly tertiary amines), and a linker that can either be an amide or an ester. The most popular LAs are those of the amide type, such as bupivacaine, ropivacaine, lidocaine, and mepivacaine [11]. Chloroprocain, procaine, and tetracaine are components of ester-type Las (Figure 1).

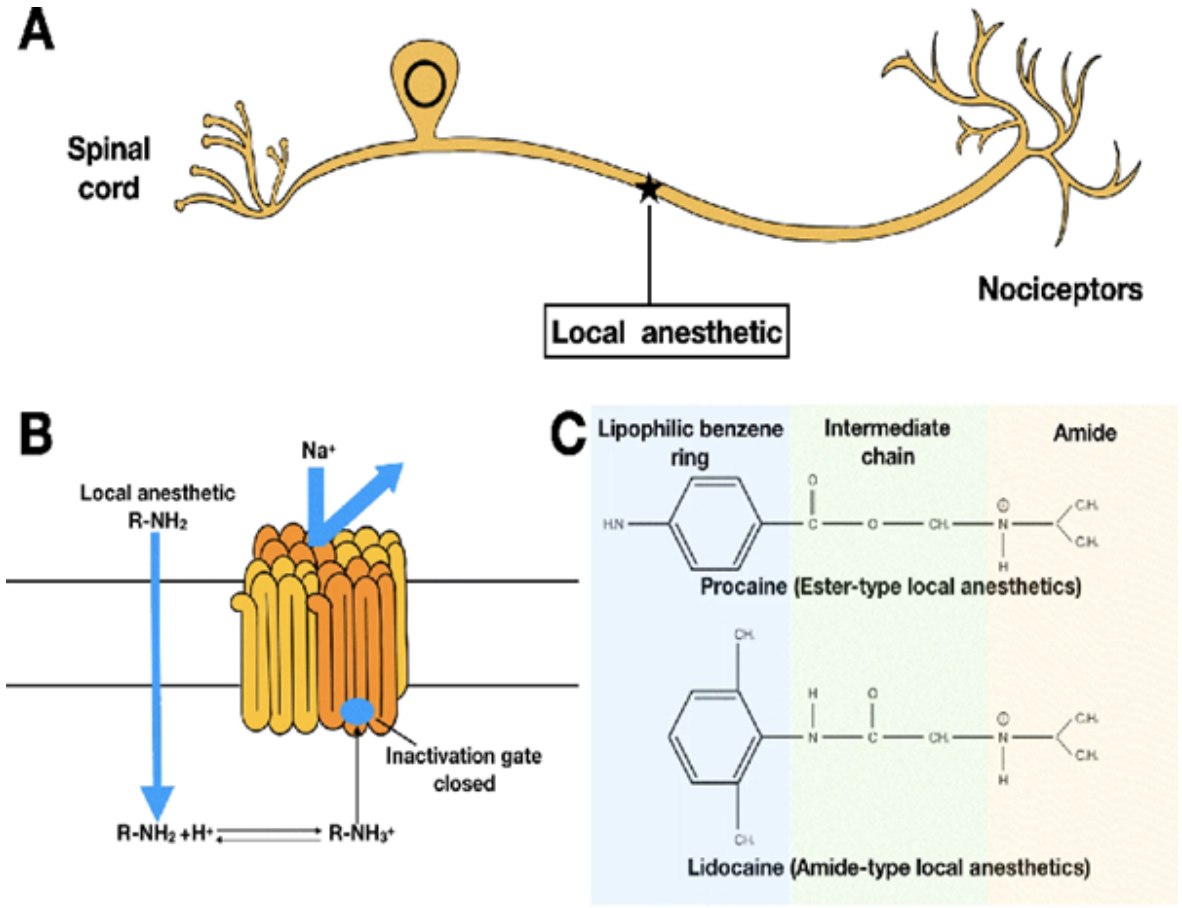

Figure 1: Extended-release and its mechanism of Las.

LAs have a significant role in multimodal analgesia. Its utilisation is constrained by a short duration and unfavorable side effects, which leads to the development of extended-release LAs [12]. Due to their similar size to the physiological environment, nano-structured DDSs exhibit greater biocompatibility and biodegradation compared to micro-structured DDSs [13]. Liposomes, a class of nanocarriers, have the first success in producing super-long-lasting LAs that can release bupivacaine for up to 72 hours *invivo*. Additionally, liposomes enhance the safety of LAs under emulsion protection [14]. However, liposome's instability makes it difficult to store and co-administer with additional free LAs. Polymersomes have a more favourable profile than liposomes, with higher stability and longer release. Additionally, the electrospinning process and the stimuli-responsive characteristic give polymersomes greater flexibility in

their form and release behavior [15]. Combining nanocarriers is an alternate method of improving flaws and enhancing strengths to materials and industrial processes. The stage is now set for hybrid nanocarriers, which not only enhance the release profile but also expand the range of administration methods, such as the transdermal route [16]. Future extended-release formulations for varied analgesic needs may be more precise and regulated thanks to the ever-growing versatility of nanocarriers.

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