



Smart Drug Delivery in Anesthesia: A Need or an Option?

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Dear Editor,

In many cases, medical interventions are associated with complications such as device calibration issues, abnormal patient reactions, medical errors, or adverse effects of the drugs used. The effectiveness and side effects of drugs and the use of accurate drug dosages have been of great interest. Since obtaining successful results in anesthesia is directly influenced by the dosage and administration of drugs, possible risks can seriously affect and divert the treatment process. Therefore, one of the most important concerns of therapists in this field is optimizing the drug delivery process, making it very important to provide suitable methods to improve the drug delivery system in anesthesia and reduce side effects.

Drug delivery is a set of measures to transfer drugs to the disease site with the help of systems, advanced technologies, and optimized formulations to ensure the safe and expected performance of the drug in the most appropriate way. Many traditional drug delivery methods face problems such as uncontrolled and non-specific drug distribution and systemic side effects. To overcome these limitations, targeted systems of controlled drug delivery in the specified area have been developed. One efficient method to increase the effectiveness of drugs and minimize adverse side effects is to controllably concentrate drugs in the desired area for a long time. These intelligent systems that control drug release increase the duration of drug action by reducing the frequency and increasing the concentration of the drug in a specified part of the tissue or organ. In addition, these smart drug delivery systems can help reduce toxicity and increase the safety

of drugs, prevent fluctuations in drug dosage, and improve drug performance (1).

In many cases, traditional drug delivery systems experience drug degradation before reaching the target area, weakening the drug's performance. All methods used for drug delivery aim to transfer the active medicinal compound to the target tissue with the highest possible concentration. Some methods, such as using microspheres and polymeric micelles for drug delivery, have advantages including reducing drug toxicity, increasing absorption rates, targeting specific areas, and reducing biochemical decomposition before reaching the destination. Other carriers used for drug delivery include porous silica nanoparticles, carbon nanotubes, monoclonal antibodies, some vitamins, liposomes, and micelles (2).

Liposomes are nanoscale vesicles with two phospholipid layers and are considered a suitable option for drug delivery due to properties such as non-cytotoxicity, biodegradability, and non-stimulation of host immune reactions. Most studies conducted on using liposomes for drug delivery aim at cancer treatment; however, liposomes can also enhance the performance of anesthetic drugs. Patient recovery is directly related to postoperative pain management. The use of many local anesthetics is limited due to their cytotoxicity and short-term effectiveness. One of the most important local anesthetics prepared with the help of a targeted drug delivery system is liposomal bupivacaine (3). The active persistence of this drug after a single administration for 96 hours at the maximum plasma concentration has been reported. However, achieving conclusive results requires phase 3 trials. Another example of smart drug delivery is the use of

epidural morphine DepoDur with the help of liposomes, which increases the performance of the drug and remains effective for pain relief up to two doses. Recently, pain control with the help of bupivacaine incorporated in liposomes in lumbar fusion surgery has been associated with successful results such as reducing hospitalization time, lowering health and treatment costs, increasing patient activity, and reducing drug dosage.

Solid lipids are another example of drug delivery systems that have been used to improve the performance of the benzocaine analog butamben and to minimize the toxicity of local anesthetics. The results of studies on this system showed a decrease in in vitro and cellular toxicity, an increase in analgesic power, and an increase in the solubility of butamben (4).

Mesoporous silica nanoparticles have special properties that have led to their widespread use in biomedical applications such as targeted drug delivery, stem cell research, and tissue engineering. These features include a proper surface-to-volume ratio, adjustable pore size, simple synthesis, biocompatibility, and proper surface performance. The exceptional properties of mesoporous silica nanoparticles, in cooperation with chemical compounds, polymers, and supramolecular structures, have made it possible to use them as targeted drug carriers with controlled drug release. Silica nanoparticles have good safety, biodegradability, and pharmacokinetics in laboratory conditions, which guarantees their use in clinical research. Among the applications of these nanoparticles in biomedical applications, we can mention photodynamic therapy, use in biosensors, targeted drug delivery in various types of cancer, biological imaging, and catalysis. The porous surfaces of silica nanoparticles have the ability to be doped with different compounds and can be directed to the desired tumor site under internal or external stimuli, releasing the drug cargo at the target point. This feature prevents premature release or waste of the drug in the desired treatment path. MSNs, as multi-potential nanocarriers, can be safely used in various clinical fields (5).

Although postoperative pain control is usually achieved with the help of local anesthetics, their use is challenging due to their short-term effectiveness. Recently, a drug delivery system based on hydrogel has been investigated. This hydrogel is temperature-sensitive, being liquid at room temperature and semi-solid after entering the body. Examination of drug transfer survival using this method showed that the durability of hydrogel was six times longer than that of levobupivacaine acid, resulting in reduced

postoperative pain, greater penetration of the anesthetic drug, and reduced spontaneous pain in the rats under investigation. Examining the performance of ropivacaine drug delivery with the help of hydrogels has shown that this method increases the release speed of the anesthetic drug and its duration of effect by 24 hours. In addition, temperature-sensitive hydrogels have less cytotoxicity and create a more lasting effect in the desired area. Mesoporous silica nanoparticles have also provided successful results in smart drug delivery (6).

The results of the above studies show that intelligent drug delivery and the development of necessary mechanisms in this field can play a significant role in the management of drugs used by anesthesiologists. Drug delivery systems have significantly evolved with the development of smart drug delivery. The intelligent drug delivery system, whether for multiple drugs or single drugs, offers positive features in pain treatment in terms of biosafety, pharmacokinetics, and bioavailability. Despite the significant progress in anesthesia and operating rooms following the advent of smart drug delivery, the use of these systems is associated with limitations. It should be noted that careful examination of drug effects, optimal dosage, possible side effects, and drug toxicity is very important for the use of smart drug delivery systems in clinical studies. We see a clear horizon for smart drug delivery as an efficient, low-risk, and safe treatment in clinical cases, which can play a valuable role in future pain control procedures.

Footnotes

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