Development and Prospective Strategy of Patient-Controlled Analgesia in China

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Abstract

Pain is always a focus of attention. Postoperative analgesia directly affects postoperative comfort and recovery quality. Patient-controlled analgesia (PCA) was developed by Shechzer in the early 1970s based on on-demand analgesia. In the year 1993, PCA was introduced in China. In 1994, Yuguang Huang introduced the Australian mechanical analgesic pump in Beijing. In the same year, Shouzhang She introduced the electronic analgesic pump in Guangzhou (British grasber-3100 and grasber-9300 electron pump). In 1997, China witnessed a boom in the use of PCA. In 2005, this technology was awarded the Second Prize for Scientific and Technological Progress by the Ministry of Education of the People's Republic of China for the contribution in postoperative analgesia promotion. According to a survey in 2016 and 2017, the incidences of moderate-to-severe pain (VAS score ≥ 4) on the first day and second postoperative day during rest were 10.6% and 3.8% respectively. Before the introduction of PCA, the incidences of moderate-to-severe pain during activity were 33.6% and 16.3% and the incidences with breakthrough pain were 41.4% and 18.8% respectively. In addition, the proportion of PCA administered by anesthesiologists was 32.6%, including PCIA (Patient-controlled intravenous analgesia): 73.53%, PCEA (Patient-controlled epidural analgesia): 18.03%. All of these indicated that the acute pain service (APS) infrastructure is relatively weak. With the emergence of new analgesics and the development of information technology, the quality of analgesia is strengthened and improved. Innovative PCA technology and improved management mode guided by patient-centered concept allow the combination of Internet and PCA to produce a human-machine-environment harmony. In order to achieve precision pain control and provide analgesic effects while ensuring patient safety, medical staff should adapt to the new concept and be actively involved in the multidisciplinary pain management team (PMDT). Nowadays, most hospital use governmental permitted wireless analgesic pump with patient controlled analgesia system solutions (PCASS) and has received positive feedback from both patient and medical staff. We should continue to improve the core technology and create a management platform for a good perioperative pain management of analgesia. The future of PCASS in China is to provide an efficient, fast and standardized cloud data management for medical staff and optimal pain relief for patients.

Keywords

Analgesic pump, Wireless, Patient-controlled, Intelligent management

Clinical anesthesia and analgesia has experienced 170 years of growth and development [1]. Pain has been recognized as the fifth vital sign, together with blood pressure, pulse, respiration, and body temperature [2]. According to the International Pain Conference held by the International Association for the Study of Pain (IASP) in 2002, pain is not just a symptom but a disease, therefore relieving pain is the basic right of the patient and the sacred duty of the health care personnel [3]. However, the precise quantification of opioid dosage and pain level measurement remain an urgent problem to be solved [4].

Patients seek out high quality treatment, while doctors ask for good curative results. Precision medicine is the solution for both needs. In 2001, the National Academy of Sciences (NAS) joined with the National Institutes of Health (NIH) and the National Science Board (NSB) to launch an initiative toward precision medicine, proposing a "tailored" treatment based on individual characteristics of each patient [5]. The concept of precision medicine can be used in anesthesiology to achieve precise anesthesia [6] and accurate analgesia [7]. The anesthesiology branch of the Chinese Medical Association put forward a "big five" development vision centered around the idea of bringing anesthesia to perioperative medicine: anesthesia should become the (i) Key discipline in medical safety, (ii) Take the leading role in promoting pain free care, (iii) Form the backbone of the future medicine development, (iv) Be the key medical discipline in scientific innovation, and (v) Serve as a popular social science. In order to achieve these five visions, the Chinese medical association anesthesiology branch/committee held an annual meeting in Zhengzhou in 2017, in which the Branch Director Professor Lize Xiong pointed out that "every anesthesiologist has the responsibility and obligation to embark on road of
bringing anesthesiology to perioperative medicine. It is only through this road, we can achieve the ultimate goal of optimal perioperative medicine development” [8].

Postoperative analgesia has a long history. Opioid morphine analgesia began in the early 19th century (1917). Before the 1970’s, in 1939, pethidine was used for intramuscular injections. After the 1980s (1983), a small dose of morphine was injected into the epidural cavity. After the 1990s (1996), patients were introduced to the idea of patient controlled analgesia (PCA), taking the initiative to regulate their own pain. The concept of PCA was put forward by Shechzer in the early 70’s of last century, based on on-demand analgesia and was put into practice. In the 1990’s, with a close combination of electronic technology and modern medicine, microcomputer assisted PCA developed rapidly. The standard PCA is a method for injecting quantitative analgesic drugs into the body through a computer-controlled micro-pump initiated by the patient pressing the start button when pain is perceived. Its advantage is that the patient can choose the timing of analgesic injection within the range that the doctor sets [9]. PCA is equipped with the following settings: loading dose, background dose, bolus dose, locking time, safety limit etc. PCA caters to the analgesic requirements of different patients at different times and with different pain intensity. With the patient’s own participation, enabled through settings built in (loading dose, continuous dose, PCA on the additional dose or shock dose, locking time, safety limit dose in unit time, etc.), PCA can be the most effective measure to tackle individual pain differences. In 1993, PCA was first introduced in China by Professor Ailun Luo and Yuguang Huang from Beijing Union Hospital and Shouzhang She from Guangzhou Medical College. In 1993, Yuguang Huang first reported the use of the foreign PCA mechanical pump for postoperative analgesia in the Guangxi Academic Conference. In 1994, Yuguang Huang introduced the Australian mechanical analgesic pump in Beijing. In the same year, Shouzhang she introduced the electronic analgesic pump in Guangzhou (British grasber-3100 and grasber-9300 electron pump). He conducted numerous clinical studies and organized chronic pain management workshops for three consecutive years. Professor Yuguang Huang, Martin Mok and Fulin Tang were invited to give lectures in Guangzhou for the benefit of promoting the knowledge on the different modes of PCA and the clinical application of different drug delivery routes. This has greatly improved the general knowledge of PCA analgesia. Furthermore, with new hospital policy recognizing PCA as a new technology and encouraging doctors to actively promote this concept, PCA and chronic pain treatment are in full progress. In 1995, during the Beijing International Anesthesia Academic Conference, Shouzhang She reported a widely praised lecture titled “Clinical Application of Epidural PCA”. From 1995 to 1997, we traveled to Singapore, Australia, the United Kingdom, the United States, Germany and Sweden for academic purposes, gaining confidence in applying PCA. In 1997, the electronic analgesic pump of Graseby was advertised on the back cover of the Chinese Journal of Anesthesiology, representing an upsurge of PCA in China, especially in Guangdong, Hunan, Jiangsu, Beijing and Shanghai. In 1996, the study of patient controlled epidural analgesia and the Acute Pain Service group (APS) received scientific and technological approval from the Guangdong government. In 1996, China’s first original study featuring epidural PCA application was published in the Chinese Journal of Pain Medicine [10]. In 1997, Shouzhang She delivered a special lecture at the National Anesthesia Annual Conference in Shenyang, entitled “The Future of PCA in China”. In 1998, a special report on the design and clinical application of the electronic PCA pump was presented in the Zhengzhou National Pain Conference and was well received. In 1999, a monograph authored by Professor Ailun Luo on patient controlled analgesia -PCA was published. From 2003 to 2004, Guangzhou First People’s Hospital won the Science and Technology Progress award in Guangdong and Guangzhou (second and third prize). Its main contribution was addressing three major problems in PCA applications, where it was first reported that patient controlled epidural analgesia is superior to patient controlled intravenous analgesia, and it was first to demonstrate the safety and efficacy of PCEA after combined lumbar anesthesia and epidural anesthesia. The study was also the first to show tremendous improvement in the analgesic effect from postoperative epidural continuous infusion with low concentration of anesthetic combined with epidural opioid [11-14]. From 2005 to 2007, three hospitals represented by Ailun Luo, Yuguang Huang, Shouzhang She and Shanglong Yao was awarded the second prize in the science and technology progress of the Ministry of Education and the third prize in Chinese medicine, for PCA postoperative analgesia and promotion. In the past, PCA achieved great progress in health care industries, especially in the development of the hospital and service to patients [15-19]. In 2003, the Graseby British Corporate Board decided not to produce electronic PCA pumps and voluntarily withdrew from the Chinese market, which was then replaced by the CADD electronic pump reduced by the American Smith company. In terms of the selection of analgesics, the drugs treated by PCA in the past were mainly opioid receptor agonists. PCIA mainly used morphine (10-20 mg/d) and fentanyl (0.3-0.5/d) [15]. The commonly used prescription for PCIA are morphine 20 mg with 0.9% normal saline 100 ml, which is set as: loading dose 5 ml, background dose 0.5-1.0 ml, bolus 1.0-2.0 ml, locking time 5-10 min, or fentanyl 1.0 g with 0.9% NS 100 ml, which is set as: loading dose 5 ml, background dose 0.5 ml, bolus 1.0 ml, locking time 5 min. PCEA is combined with morphine (0.3-0.5 mg/d) and low concentration ropivacaine (0.15%-0.25%) [11,13]. The common prescription
for PCEA is morphine 10 mg with 0.2% ropivacaine 100 ml, which is set as: loading dose 5 ml, background dose 0.5-1.0 ml, bolus 1.0-2.0 ml, locking time 20 min. PCIA can also be combined with haloperidol, and dexamethasone for analgesia. Adverse reactions should be mainly nausea, vomiting, and itching. And the incidence of respiratory depression is relatively low.

Nowadays, with the new concept of Enhanced Recovery after Surgery (ERAS), effective postoperative analgesia, being a key step and core element of ERAS, is getting increasing attention [20-22]. However, foreign clinical investigations still show that a significant number of postoperative pain has not been effectively alleviated [23]. In 2002, Dolin, et al. conducted an online retrospective analysis of 20,000 patients which show that the incidence of moderate to severe pain when resting was 29.7%, while incidence of moderate to severe pain on activity was 32.2%, and the incidence of severe pain was 10.9% [24]. Research by Gan (2013) and Bockel (2015) showed that 50% to 70% of patients still experienced moderate and severe pain after surgery [25-26]. In 2016, 12 Grade III A hospitals in Guangdong province joined a multi-center investigation led by Wenqi Huang on the analgesic conditions and the incidence of postoperative analgesia. According to the report which included 4370 patients, on the first and second day after surgery, the incidence of moderate to severe pain during resting (VAS score greater than 4) was 10.6% and 3.8%, respectively; while the incidence of pain during activity on the first and second day after surgery was 33.6% and 16.3% respectively. The incidence of moderate to severe pain during peak pain intensity on first and second day after surgery was 41.4% and 18.8% respectively [27]. In 2016, 1398 patients (32.6%) were managed by anesthesiologists in terms of postoperative pain, of which 1028 cases (73.53%) were PCA and 252 cases (18.03%) were PCEA. The results showed a decrease in 4.1% in terms of anesthesiologists participation when compared to a study conducted by Shouzhang She in 2010 involving 5245 patients in ac 12 Grade III A hospital in Guangdong province, results of which showed 36.7% patients were managed by an anesthesiologist. A survey conducted by Yuguang Huang in 2017 showed that in China prevalence of optimal analgesia remains low, the concept of multimodal analgesia is the direction of research. Furthermore, incomplete pain management can cause a longer length of hospital stay, increase the risk of readmission and increase the overall the cost of treatment. The perioperative acute pain evaluation and management guideline is helpful in improving the quality of analgesia [29-30]. Currently, in terms of the selection of analgesics, in addition to opioid receptor agonists, many hospitals use sufentanil instead of fentanyl, but also hydromorphone, oxycodone combined with local anesthetic nerve block or NSAIDs as a strategy of multi-modal pain management. Some hospitals have begun to adopt wireless intelligent patient-controlled analgesia (Ai-PCA) management system combined with analgesia to improve the quality of postoperative analgesia [31]. However, perioperative analgesia, nausea and vomiting are still difficult to overcome today. The hospital is extremely standardized in the management of morphine, fentanyl and other class drugs, and implements double-checking and special counter management. No abuse of opioid receptor agonist was reported [17,18]. At present, low-dose non-opioid agonist opioid receptor agonist-antagonist combined with adrenergic receptor agonist (dexmedetomidine) and other comprehensive measures of multimodal analgesia is the direction of research. The development of ERAS will be facilitated by the joint efforts of multiple disciplines [21].

In the future, advance in pain management would be an integral part of perioperative medicine. It’s unrealistic to talk about palliative care or painless treatment without comprehensive pain management skill. We still face many difficulties at the moment. Pain management is facing a bottleneck. How do we improve the analgesia effect and get anesthesiologists more involved with the rapidly developing minimally invasive surgery technique and ERAS concept? Where the future will lead us is unclear. To effectively relieve pain, both the analgesics and health care personnel need to be multimodal. Therefore, the clinician should maximize the analgesic effect and minimize unwanted side. The choice of analgesics and drug delivery route should be carefully selected. The goal of acute pain management in the future is to analyze both overseas and domestic trends of pain management, optimize perioperative analgesics and improve the analgesia effect, prevent incomplete analgesia, and
prevent acute pain from transforming into chronic pain. Postoperative patient controlled analgesia system solutions (PCASS) can improve the quality of analgesia in an ERAS setting [32-34]. In order to optimize analgesia and conduct precision medicine, we need to: (1) Strengthen basic research. The study by Manglik A of Stanford University focuses on a new drug, PZM21, through modified calculation of more than 3 million molecules of the G protein Gi receptor and the regulation of the beta-arrestin signaling pathway [35]. Kieffer BC comments that PZM21 not only reveals the different signaling pathways of mu opioid receptors, but also showed possibilities to develop new analgesic with less side effects through structure transformation based on existing opioids [36]; (2) Strengthen clinical research. Professor Bonica JJ once pointed out, “The most effective pain treatment will result from the best research”. New scientific data serves as evidence to back up our practice. Due to polymorphisms of individual genes, tolerance to pain, drug reaction and metabolic rate vary greatly between patients. Through the reasonable consideration of compatibility of drugs, we can strengthen the synergistic effect or additive effect of drugs and reduce adverse reactions. The precise compatibility of analgesic drugs should consider receptor sites and combine drugs acting through different mechanisms. Good analgesic selection and adding the technique of peripheral nerve block analgesia are essential. (3) Strengthen patient education about pain management. It benefit to inform the public that moderate to severe pain can be controlled and alleviation of pain can enhance rehabilitation. We should improve the APS management model and develop a dedicated team to provide highly efficient pain management service. (4) Promote PCA wireless intelligence. With government advocating Internet+, a specified postoperative wireless analgesic management system (WAMS) (intelligence, informatics, remote control and cloud data processing) was used for PCA. The aim is to optimize PCA analgesic dosing, drug delivery parameter setting and eventually improve the quality of analgesia through cloud information management. Precision medicine increases patient safety and comfort. At the same time, the medical staff works more efficiently. PCASS has the following advantages: (i) Wireless real-time monitoring of PCA operation and failure alarm; (ii) Wireless real-time monitoring of the patient, ensuring adequate analgesic effect and providing timely prevention of complications; (iii) Individualized regulation of PCA for drug delivery, such as in the new PCA model, with the self-controlled transdermal patch or the nasal administration; (iv) Providing necessary conditions for the standardization of effective pain management; (v) Enable information storage, big data, cloud analysis, etc. (5) With the standardization of PCASS, labor analgesia, and patients with chronic or cancer pain may benefit. The new PCA model, involving PCA+ breathing, HR, SpO2 and fetal heart monitoring combined with PCASS can be implemented in labor analgesia and greatly enhance safety and comfort. It is helpful to improve the quality of analgesia and improve the clinical effect in patients with the combination of self-controlled drug delivery device and nasal administration. (6) The current strategy of clinical medicine is shifting from the 4 p model to the 5 p mode: Predictive, Preventive, Pre-symptomatic, Personalized, Participatory. Pain medicine should also follow the 5 p mode [37]. PCASS serves as the internet for the anesthesia department, symbolizing the starting point of big data management. Created in the face of many difficulties faced by anesthesiology management, it is an important innovation and transforms the old routine. To date, most hospitals choose the government permitted wireless analgesia pump system (the machinery note quasi 20153540988) PCASS. It has made gratifying achievements and is popular among patients and medical staff.

Postoperative PCASS has a long way to go before achieving precision medicine and intellectual management [38]. Medical personnel should adapt to new concepts and be more actively involved in multiple disciplinary management teams for pain (PMDT). We should also improve the core technology and create management platforms through good perioperative pain management of analgesia (GPPM). With the goal of developing a continuous perioperative comprehensive optimization analgesic plan, we should strengthen scientific research, focus on the patient, and achieve a “full-time-professional-individualized” accurate analgesia effect. We should incorporate intelligent technology into APS analgesia management system and follow the 5P model in order for patients to benefit from “high quality-safety-comfort” medical service. Artificial intelligence will gradually replace manual labor and will be a great progress for our generation. We should aim far and race against time to implement postoperative PCASS optimization analgesic towards the direction of intelligence and precision.

References
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