

## Opioid Epidemic: *Cellular & Molecular Anesthesia* as a Key Solution

Opioids are one of the most important arsenals armamentarium of physicians for fighting against pain. During the decades, opioids have been used in a wide range of indications; both for treatment of acute and chronic pain; as natural and synthetic compounds and in a variety of delivery forms from intravenous infusion to intrathecal adjuvants of local anesthetics or as transdermal patches (1-7).

However, opioids as we know are not harm free drugs with a number of side effects attributable to them. There are very strong concerns regarding the risk of opioid dependence. Currently, in the United States, more than millions of people worldwide are involved with opioid abuse, often as the aftermath of acute or chronic pain management. The US CDC (Centers for Disease Control and Prevention) has announced that the US has reached an epidemic level regarding opioid abuse; leading to increased frequency of opioid abuse and opioid related death (2, 6-8). Currently, the following topics are quoted as the main reasons leading to this devastating epidemic:

- Irrational practice in opioid prescription
- Ascensional trend in opioid prescription and misuse
- Increasing trend of illegal or illicit opioid misuse
- Illicit opioid overdose-related deaths
- Ease of access to opioids as highly addictive agents

All stakeholders; including medical care providers, researchers in the field of medicine, surveillance bodies and most importantly, policy makers including high rank decision makers are seriously concerned with the recent increased trend of opioid use in the US (4, 5, 9, 10). The issue is that on one side, we have to help patients suffering pain especially acute perioperative pain and on the other hand, we are faced with an increasing trend of opioid abuse partially due to opioid dependence after acute pain relief using opioids (4, 5, 8-11).

How can we get rid of this epidemic while we impose no more harm to the patients suffering acute or chronic pain? As we know, getting rid of this problem need a well-designed strategic planning; this is well beyond the scope of this editorial. However, one of the

main steps in this strategy is to create alternative pathways to bypass opioid use in acute and chronic pain control. The role of emerging drugs is a real promise. Acute and chronic pain control without opioid use is now an attainable objective in the current era of cellular and molecular medicine (12-15).

In this volume of JCMS, a number of studies are published that directly aim the goals of the above strategic planning in harm reduction, through introducing novel analgesic methods; these studies replace opioids with novel non-opioid drugs in controlling pain totally or partially (16-20). Taheri et al, Moshari et al and Aghadavoudi et al deal with acute pain management using opioid sparing methods; with a partial or total replacement of opioids with non-opioids (16-18). On the other hand, Taherian et al, represent their study demonstrating cellular and molecular mechanisms of pain alleviating properties of Malva neglecta on Expression of Inflammatory Biomarkers in patients with chronic crippling pain (19) while Alipour et al present an integrated basic/clinical review dealing with the future novelty windows for pain control based on biologic mechanisms especially considering the role of gut microbiota (20). Of course, there are a number of pioneering ideas and qualified studies published in the previous issues of JCMS and other journals that could effectively lead us to new promising pathways in opioid-free pain control approaches (3, 12-15, 21-25).

There is no doubt that we are in an opioid misuse epidemic status; whether in the US or other countries; but if we want to resolve this miserable multilateral complication, there is no doubt that *Cellular and Molecular aspects of Anesthesia* has a key role in resolving the problem; through creating an opioid free pain management era (8).

## References

1. Webster LR. Risk Factors for Opioid-Use Disorder and Overdose. *Anesth Analg.* 2017;125(5):1741-8.
2. Soelberg CD, Brown RE, Jr., Du Vivier D, Meyer JE, Ramachandran BK. The US Opioid Crisis: Current Federal and State Legal Issues. *Anesth Analg.* 2017;125(5):1675-81.
3. Nicol AL, Hurley RW, Benzon HT. Alternatives to Opioids in the Pharmacologic Management of Chronic Pain Syndromes: A Narrative Review of Randomized, Controlled, and Blinded Clinical Trials. *Anesth*

- Analg. 2017;125(5):1682-703.
4. Johnson RL, Williams BA. No Surprise-For Long-term Opioid Avoidance, Do We Reap What We Sow? *Anesth Analg.* 2017;125(3):721-3.
  5. Hah JM, Bateman BT, Ratliff J, Curtin C, Sun E. Chronic Opioid Use After Surgery: Implications for Perioperative Management in the Face of the Opioid Epidemic. *Anesth Analg.* 2017;125(5):1733-40.
  6. Brown RE, Jr., Sloan PA. The Opioid Crisis in the United States: Chronic Pain Physicians Are the Answer, Not the Cause. *Anesth Analg.* 2017;125(5):1432-4.
  7. Ballantyne JC. Opioids for the Treatment of Chronic Pain: Mistakes Made, Lessons Learned, and Future Directions. *Anesth Analg.* 2017;125(5):1769-78.
  8. Kamdar NV, Hoftman N, Rahman S, Cannesson M. Opioid-Free Analgesia in the Era of Enhanced Recovery After Surgery and the Surgical Home: Implications for Postoperative Outcomes and Population Health. *Anesth Analg.* 2017;125(4):1089-91.
  9. Dunn LK, Durieux ME, Nemergut EC, Naik BI. Surgery-Induced Opioid Dependence: Adding Fuel to the Fire? *Anesth Analg.* 2017;125(5):1806-8.
  10. Dosenovic S, Jelcic Kadic A, Miljanovic M, Biocic M, Boric K, Cavar M, et al. Interventions for Neuropathic Pain: An Overview of Systematic Reviews. *Anesth Analg.* 2017;125(2):643-52.
  11. Brandal D, Keller MS, Lee C, Grogan T, Fujimoto Y, Gricourt Y, et al. Impact of Enhanced Recovery After Surgery and Opioid-Free Anesthesia on Opioid Prescriptions at Discharge From the Hospital: A Historical-Prospective Study. *Anesth Analg.* 2017;125(5):1784-92.
  12. Lu Z, Xu J, Xu M, Rossi GC, Majumdar S, Pasternak GW, et al. Truncated mu-Opioid Receptors With 6 Transmembrane Domains Are Essential for Opioid Analgesia. *Anesth Analg.* 2017.
  13. Lin YC, Wan L, Jamison RN. Using Integrative Medicine in Pain Management: An Evaluation of Current Evidence. *Anesth Analg.* 2017;125(6):2081-93.
  14. Kumar K, Kirksey MA, Duong S, Wu CL. A Review of Opioid-Sparing Modalities in Perioperative Pain Management: Methods to Decrease Opioid Use Postoperatively. *Anesth Analg.* 2017;125(5):1749-60.
  15. Knezevic NN, Yekkirala A, Yaksh TL. Basic/Translational Development of Forthcoming Opioid- and Nonopioid-Targeted Pain Therapeutics. *Anesth Analg.* 2017;125(5):1714-32.
  16. Taheri M MA, Manafi Rasi A, Adili Y. . Comparing the Use of Memantine with Dextromethorphan and Placebo to Reduce Pain before Orthopedic Surgery. . *J Cell Mol Anesth.* 2017;2(4):157-64.
  17. Moshari MR MB, Vosoughian M, Dahi-Taleghani M, Ghasemi M, Seyed-Alshohadaei SM. Comparing the efficacy and safety of Dexmedetomidine-Lidocaine and Propofol-Fentanyl-Midazolam combinations during endoscopic retrograde Cholangiopancreatography. . *J Cell Mol Anesth.* 2017;2(4):171-9.
  18. Aghadavoudi O SA, Nowrouzi Z. Comparison of adding neostigmine and fentanyl to bupivacaine in caudal analgesia in pediatric inguinal herniorrhaphy. . *J Cell Mol Anesth.* 2017;2(4):165-70.
  19. Taherian R TM, Maghsoudi H, Haj-alahyari S. . The Effect of Aqueous Extract of Malva neglecta on Expression of Inflammatory Biomarkers Involved in Pain in Synoviocytes and THP-1 Cells as a Model of Monocyte/Macrophage and Human Cartilage Cells in Osteoarthritis. . *J Cell Mol Anesth.* 2017;2(4):149-56.
  20. Alipoor E SM, Dabbagh A. . Acute post-operative pain and gut microbiota: is there any (clinical) relationship? *J Cell Mol Anesth.* 2017;2(4):189-93.
  21. Rajaei S, Dabbagh A. The molecular mechanisms of Vitamin D effects on alleviating premenstrual syndrome pain. *J Cell Mol Anesth.* 2017;2(1):30-6.
  22. Talebi Z DA. Perioperative Pain: Molecular Mechanisms and Future Perspectives. *J Cell Mol Anesth.* 2017;2(3):134-41.
  23. Dabbagh A. Microglial Cells: the Bridge Between the Immune System and Pain in the Central Nervous System. *J Cell Mol Anesth.* 2016;1(4):135-6.
  24. Dabbagh A, Elyassi H. Cellular and Molecular Anesthesia: from Bench to Bedside. *J Cell Mol Anesth.* 2016;1(1):1-2.
  25. Bagheri B, Razavi, S., Gohari, A., Salarian, S., Dabbagh, A. Toll-Like Receptor 4 in Ventilator-Induced Lung Injuries: Mechanism of Disease. *J Cell Mol Anesth.* 2016;1(1):34-9.
  - Chronic Pain Physicians Are the Answer, Not the Cause. *Anesth Analg.* 2017;125(5):1432-4.
  7. Ballantyne JC. Opioids for the Treatment of Chronic Pain: Mistakes Made, Lessons Learned, and Future Directions. *Anesth Analg.* 2017;125(5):1769-78.
  8. Kamdar NV, Hoftman N, Rahman S, Cannesson M. Opioid-Free Analgesia in the Era of Enhanced Recovery After Surgery and the Surgical Home: Implications for Postoperative Outcomes and Population Health. *Anesth Analg.* 2017;125(4):1089-91.
  9. Dunn LK, Durieux ME, Nemergut EC, Naik BI. Surgery-Induced Opioid Dependence: Adding Fuel to the Fire? *Anesth Analg.* 2017;125(5):1806-8.
  10. Dosenovic S, Jelcic Kadic A, Miljanovic M, Biocic M, Boric K, Cavar M, et al. Interventions for Neuropathic Pain: An Overview of Systematic Reviews. *Anesth Analg.* 2017;125(2):643-52.
  11. Brandal D, Keller MS, Lee C, Grogan T, Fujimoto Y, Gricourt Y, et al. Impact of Enhanced Recovery After Surgery and Opioid-Free Anesthesia on Opioid Prescriptions at Discharge From the Hospital: A Historical-Prospective Study. *Anesth Analg.* 2017;125(5):1784-92.
  12. Lu Z, Xu J, Xu M, Rossi GC, Majumdar S, Pasternak GW, et al. Truncated mu-Opioid Receptors With 6 Transmembrane Domains Are Essential for Opioid Analgesia. *Anesth Analg.* 2017.
  13. Lin YC, Wan L, Jamison RN. Using Integrative Medicine in Pain Management: An Evaluation of Current Evidence. *Anesth Analg.* 2017;125(6):2081-93.
  14. Kumar K, Kirksey MA, Duong S, Wu CL. A Review of Opioid-Sparing Modalities in Perioperative Pain Management: Methods to Decrease Opioid Use Postoperatively. *Anesth Analg.* 2017;125(5):1749-60.
  15. Knezevic NN, Yekkirala A, Yaksh TL. Basic/Translational Development of Forthcoming Opioid- and Nonopioid-Targeted Pain Therapeutics. *Anesth Analg.* 2017;125(5):1714-32.
  16. Taheri M MA, Manafi Rasi A, Adili Y. . Comparing the Use of Memantine with Dextromethorphan and Placebo to Reduce Pain before Orthopedic Surgery. . *J Cell Mol Anesth.* 2017;2(4):157-64.
  17. Moshari MR MB, Vosoughian M, Dahi-Taleghani M, Ghasemi M, Seyed-Alshohadaei SM. Comparing the efficacy and safety of Dexmedetomidine-Lidocaine and Propofol-Fentanyl-Midazolam combinations during endoscopic retrograde Cholangiopancreatography. . *J Cell Mol Anesth.* 2017;2(4):171-9.
  18. Aghadavoudi O SA, Nowrouzi Z. Comparison of adding neostigmine and fentanyl to bupivacaine in caudal analgesia in pediatric inguinal herniorrhaphy. . *J Cell Mol Anesth.* 2017;2(4):165-70.
  19. Taherian R TM, Maghsoudi H, Haj-alahyari S. . The Effect of Aqueous Extract of Malva neglecta on Expression of Inflammatory Biomarkers Involved in Pain in Synoviocytes and THP-1 Cells as a Model of Monocyte/Macrophage and Human Cartilage Cells in Osteoarthritis. . *J Cell Mol Anesth.* 2017;2(4):149-56.
  20. Alipoor E SM, Dabbagh A. . Acute post-operative pain and gut microbiota: is there any (clinical) relationship? *J Cell Mol Anesth.* 2017;2(4):189-93.
  21. Rajaei S, Dabbagh A. The molecular mechanisms of Vitamin D effects on alleviating premenstrual syndrome pain. *J Cell Mol Anesth.* 2017;2(1):30-6.
  22. Talebi Z DA. Perioperative Pain: Molecular Mechanisms and Future Perspectives. *J Cell Mol Anesth.* 2017;2(3):134-41.
  23. Dabbagh A. Microglial Cells: the Bridge Between the Immune System and Pain in the Central Nervous System. *J Cell Mol Anesth.* 2016;1(4):135-6.
  24. Dabbagh A, Elyassi H. Cellular and Molecular Anesthesia: from Bench to Bedside. *J Cell Mol Anesth.* 2016;1(1):1-2.
  25. Bagheri B, Razavi, S., Gohari, A., Salarian, S., Dabbagh, A. Toll-Like Receptor 4 in Ventilator-Induced Lung Injuries: Mechanism of Disease. *J Cell Mol Anesth.* 2016;1(1):34-9.

**Ali Dabbagh, MD**

**Professor, Editor in Chief, JCMA**

**Anesthesiology Research Center,**

**Shahid Beheshti University of Medical Sciences, Tehran, Iran**