Conscious sedation and electroporation: A new perspective

ABSTRACT
Tumor-specific electroporation (TSE) is a technique involving the application of high voltage pulsed electric impulses to the tumor lesions. We performed TSE in four patients with different indications and airway scenarios. We kept all four patients under conscious sedation using trans-nasal humidified rapid-insufflation ventilatory exchange (THRIVE) and dexmedetomidine infusion. This case series reflects those various untoward effects of general anesthesia that can be avoided by oxygenating the patient with THRIVE and dexmedetomidine infusion, which provide analgesia, sedation, and amnesia.

Key words: Dexmedetomidine, electroporation, THRIVE

Introduction
Tumor-specific electroporation (TSE) is a new technique where high voltage pulsed electric impulses are applied to the tumor lesions. It is also known as dynamic-electro enhanced chemotherapy, an evolution in oncology. The electric field creates open pores in the tumor cells, thus increasing the permeability of the cell membrane. Electrochemotherapy using chemotherapy and electroporation generates adequately sized open pores through which anticancer drugs could enter tumor cells and produce a therapeutic effect. Thus, electrochemotherapy is a proven drug delivery technology. There is no definite anesthetic management strategy for patients undergoing TSE in the present scenario. As per the limited literature available for anesthetic concerns, general anesthesia is considered a standard technique for electroporation. We have conducted around 21 cases of TSE under sedation using dexmedetomidine primarily with or without using fentanyl, depending upon the scenario. With this, we present a case series of four patients with different indications and airway scenarios undergoing TSE. Through these case series, we will be highlighting various anesthetic implications of TSE and measures to be taken to prevent or minimize complications.

Case Series
TSE is being done in our institution by using a dynamic pulse train of eight 1000-400 V, 100 micro-seconds duration pulses applied at 5 kHz. It successfully treats tumors above 3 cm in diameter or 1 cm in depth. After taking written and informed consent from all the patients, TSE is performed in four patients. We oxygenated all four patients using trans-nasal humidified rapid-insufflation ventilatory exchange (THRIVE) with 100% inspired oxygen concentration with a flow rate of 40 L/min throughout the procedure. We preferred giving conscious sedation by using dexmedetomidine at a loading dose of 1 µg/kg for 10 min,

Access this article online

Website: www.saudija.org

DOI: 10.4103/sja.sja_95_22

How to cite this article: Sethi P, Vyas R, Kaur M, Bhatia P. Conscious sedation and electroporation: A new perspective. Saudi J Anaesth 2022;16;475-7.

Priyanka Sethi, Raksha Vyas, Manbir Kaur, Pradeep Bhatia
Department of Anesthesia and Critical Care, All India Institute of Medical Sciences (AIIMS), Jodhpur, Rajasthan, India

Address for correspondence: Dr. Manbir Kaur, Department of Anesthesia and Critical Care, All India Institute of Medical Sciences (AIIMS), Jodhpur - 342005, Rajasthan, India.
E-mail: doctor.manbir@gmail.com

Submitted: 31-Jan-2022, Revised: 01-Feb-2022, Accepted: 02-Feb-2022, Published: 03-Sep-2022
followed by an infusion of 0.5 mcg/kg/min for the remaining surgery. Bi-spectral index (BIS) was maintained in the range of 60-70. Post-procedure THRIVE, dexmedetomidine infusion was stopped for all our patient, and we altogether avoided general anesthesia and muscle relaxant. As a result of this, we will be discussing the different scenarios of these four patients.

Case 1
A 66-year-old female with a known case of breast carcinoma, presented for TSE of unilateral skin nodule. She was known case of hypertension for 10 years on regular antihypertensive treatment. All standard American Standards of Anesthesiologists (ASA) monitors were attached along with BIS monitoring. We conducted this case on THRIVE and dexmedetomidine infusion (as mentioned above). Analgesia was topped up with inj. fentanyl in the titrated dose of 0.5–1 mcg/kg.

Case 2
A 44-year-old male with a known case of left gingivobuccal sulcus squamous cell carcinoma. He had undergone hemi-mandibulectomy for the same. Now, he was planned for TSE of metastatic skin over the left cheek. The patient had undergone three cycles of radiotherapy post-surgery. Post-radiotherapy, he developed skin lesions. The patient had a difficult airway with a mouth opening of two finger mouth opening and decreased neck mobility on examination. The case was conducted similarly using THRIVE and dexmedetomidine infusion. As there was a complex airway scenario, we managed the oxygenation and analgesia requirement adequately, thus avoiding any adverse event associated with general anesthesia.

Case 3
A 78-year-old male patient, with a known case of carcinoma esophagus status, was operated on for robotic esophagectomy 5 months ago. The patient is now posted for a left metastatic nodule over the chest wall. The patient had a history of atrial fibrillation postoperatively after the first surgery, for which the patient was observed in the intensive care unit. On examination, the patient was edentulous, blood investigations were within the standard limit, and an electrocardiogram showed T-inversions in V2-V4. 2D Echocardiography was normal. In this case, also we used THRIVE and dexmedetomidine infusion.

Case 4
A 60-year-old male patient with left gingiva-buccal carcinoma was posted for TSE of three skin nodules. He underwent a hemi-mandibulectomy with a pectoralis major myocutaneous flap 4 months back. The patient had a difficult airway with a 1.5 finger mouth opening and a complete neck restriction on examination. The case was conducted similarly as mentioned above. All our patients were comfortable postoperatively.

Discussion
Electroporation can be reversible, irreversible, or ablation type, depending on the magnitude of applied voltage. TSE is a new procedure conducted on patients with primary or secondary skin tumors when surgery is not feasible and fails chemotherapy or radiotherapy. TSE has an additional advantage of non-thermal effect on cells, thus fewer chances of damage to surrounding structures, including blood vessels or any vital structure, unlike radio-frequency ablation. The electric pulse field generated by TSE is a risk factor for cardiac arrhythmias, cardiovascular abnormalities, abnormal cerebral activity, post-procedural pain, and muscle spasm. This case series reflects those various untoward effects of general anesthesia that can be avoided by oxygenating the patient with THRIVE and dexmedetomidine infusion, which provide analgesia, sedation, and amnesia. Top-up drugs like paracetamol, ketamine, or fentanyl can be used in titrated justified doses. In all four cases, no adverse events were noted. All ASA monitors were attached and observed throughout the procedure and post-anesthesia care unit. All parameters were within the normal limit. Patients were followed up for 2 days and had no complaints post-procedure.

There is no definite anesthetic management plan for electroporation. Few case reports and small trials are being done. This case series depicts that general anesthesia can be prevented by using THRIVE and dexmedetomidine infusion. Complications associated with TSE are hypertension, arrhythmia, seizures, muscle spasm, and pain. No significant complications were noted among the cases studied. TSE’s advantage over irreversible electroporation is that it allows the cell to come to its original state by re-arrangement at the cellular level. TSE delivers minimal voltage to generate porosity and increase the cytotoxicity of chemotherapy agents in the lesion.

Conclusion
We conclude that conscious sedation is a possible option for conducting TSE. General anesthesia can be avoided in such high-risk patients with multiple co-morbidities. Under proper monitoring, it can be performed under dexmedetomidine infusion with judicious use of THRIVE and anesthetic drugs. This seems to be a much safer option for this subgroup of patients. A parallel communication between the anesthesiologist and the surgeon is the need for
an hour to prepare the anesthetic plan and avoid potential complications during the procedure. There is a good scope of further research in this field.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Glossary: TSE = Tumor-specific electroporation; THRIVE = Trans-nasal Humidified Rapid-Insufflation Ventilatory Exchange; ASA = American Standards of Anesthesiologists; BIS = bi-spectral index; PMMC = pectoralis major myo-cutaneous.

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