

Significance of Vagovagal Reflex During Anesthesia

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Abstract

The vagovagal reflex, mediated by the vagus nerve, is a vital mechanism in maintaining homeostasis during anesthesia. This complex reflex involves intricate neural pathways that regulate heart rate, blood pressure, gastrointestinal motility, and respiratory function. Certain anesthetic agents can trigger vagal activation, leading to reflex responses that pose potential complications, including bradycardia, hypotension, bronchospasm and gastrointestinal disturbances. Taking into account factors such as patient age, medical conditions and medication use, a tailored approach can be developed. Proactive and vigilant monitoring of vital signs is essential in detecting and addressing any vagal reflex-mediated changes promptly. Adjusting anesthetic depth, administering intravenous fluids, utilizing pharmacological interventions and employing positive pressure ventilation techniques are effective strategies to counteract vagal reflex responses. Ongoing research efforts aim to further understand the vagovagal reflex and develop improved strategies for its management during anesthesia.

Keywords: anesthesia, bradycardia, homeostasis, vagovagal reflex

Key points

- Vagovagal reflex, involving the vagus nerve, is a negative feedback loop that helps maintain cardiovascular and gastrointestinal homeostasis.
- Activation of the reflex during anesthesia can lead to complications such as bradycardia, hypotension, bronchoconstriction, and gastrointestinal disturbances.

The vagovagal reflex, a complex neurophysiological phenomenon involving the vagus nerve, plays a significant role in the field of anesthesia.¹ It is a feedback loop involving the vagus nerve (cranial nerve X), characterized by afferent and efferent pathways, that regulates various physiological functions in the body, including heart rate, blood pressure, gastrointestinal motility, and respiratory function during surgical procedures.² Recognizing the significance of the vagovagal reflex during anesthesia is essential for optimizing patient safety.¹ By employing proactive monitoring, tailoring

anesthetic management, and staying abreast of current research, anesthesiologists and healthcare providers can mitigate the risks associated with vagal reflex-mediated complications, thereby ensuring optimal anesthesia outcomes.

The vagus nerve is the longest and most complex cranial nerve, extending from the brainstem to various organs within the thorax and abdomen. It consists of both sensory and motor fibers. The sensory fibers transmit information from the peripheral organs back to various nuclei within the brainstem, including the nucleus tractus solitarius (NTS). The NTS receives and integrates sensory information and relays it to other brain regions involved in autonomic control and homeostatic regulation, while the motor fibers carry signals from the brain to the muscles and glands.³

The vagus nerve has multiple branches and connections throughout the body, allowing it to exert widespread control over various organs.⁴ These connections include:

1. Cardiac branches that innervate the heart and contain both sensory and motor fibers. The sensory fibers provide information on cardiac function and transmit signals related to heart rate, blood pressure, and oxygen levels back to the brain. The motor fibers regulate heart rate and contractility by modulating the activity of the sinoatrial (SA) node, atrioventricular (AV) node, and myocardium.⁵

2. Pulmonary branches that innervate the lungs and provide sensory innervation to the bronchi and pulmonary vasculature. They relay sensory information regarding lung inflation, bronchial smooth muscle tone, and blood

oxygen levels to the brain.⁶

3. Gastrointestinal branches that play a significant role in the regulation of the gastrointestinal tract, including the esophagus, stomach, small intestine, and colon. The sensory fibers transmit information regarding distension, acidity, and chemical composition of gastrointestinal function to the brain. The motor fibers contribute to peristalsis and regulate secretory functions of the digestive system.⁷

The vagovagal reflex, also known as the Bezold-Jarisch reflex, is a negative neural feedback loop that helps maintain cardiovascular and gastrointestinal homeostasis.⁸ It acts to counteract potentially deleterious situations, such as cardiac overload, hypovolemia, or excessive sympathetic activity. The reflex is triggered when sensory receptors located within the thoracic and abdominal organs detect specific stimuli.⁸ Cardiac stretch receptors in the atria or ventricles detect increased wall tension or decreased filling. Sensory signals are transmitted via the vagus nerve to the brainstem, where the NTS sends inhibitory signals to the cardiovascular centers in the medulla, leading to parasympathetic activation. This results in the release of acetylcholine acts on muscarinic receptors, onto the SA node, slowing down the heart rate, which helps decrease cardiac workload and allows the heart to fill adequately. Simultaneously, parasympathetic activity decreases sympathetic outflow, leading to vasodilation and a subsequent decrease in blood pressure.⁵

Distension of the gastrointestinal tract, changes in its chemical composition, or the presence of food, send signals to the NTS,

resulting in contraction and increased motility of smooth muscle cells. This helps propel food through the digestive system and facilitates proper digestion and absorption.⁷ Changes in lung inflation, respiratory muscle stretch, or carbon dioxide levels send signals to the NTS, resulting in bronchoconstriction, mucus secretion, and increased smooth muscle tone in the airways. These responses help regulate airflow, maintain optimal gas exchange, and protect the lungs from potential irritants or harmful substances.⁶ However, it is important to note that while the vagovagal reflex generally maintains physiological balance, its dysregulation or overactivation can lead to complications. Excessive vagal stimulation can result in bradycardia, hypotension, bronchoconstriction, or gastrointestinal disturbances.

Impact on anesthesia

Mechanical ventilation, certain anesthetic agents used during anesthesia, surgical manipulation, and painful stimuli during surgery can activate the vagovagal reflex.⁹ Noxious stimulation or tissue injury can trigger sensory receptors in the surgical area, transmitting signals via the vagus nerve to the brainstem.¹⁰ The reflex responses, such as bradycardia and hypotension, can impair cardiac output and tissue perfusion, while bronchospasm can cause airway obstruction and compromise oxygenation.¹¹ Gastrointestinal disturbances can lead to the regurgitation or aspiration of stomach contents.¹²

Preoperative management

Preoperative management is a crucial component of patient care, especially in

identifying individuals at higher risk for vagovagal reflex-related complications. It is important to recognize that some patients may be more susceptible to vagal responses, and thorough patient selection and preoperative assessment are essential in identifying this vulnerability. In pediatric patients, the reflex may be more pronounced due to their developing autonomic nervous system.¹³ Conversely, geriatric patients may exhibit altered responses to anesthesia due to reduced baroreceptor sensitivity, decreased cardiac reserve, and altered medication metabolism.¹⁴ Anesthesiologists should pay close attention to the patient's medications, as certain drugs like beta-blockers or calcium channel blockers can affect cardiovascular function and impact the patient's response to vagal stimulation.

Patients with preexisting arrhythmias or conduction abnormalities, coronary artery disease, or heart failure may have impaired autonomic regulation, while those with respiratory conditions like asthma or chronic obstructive pulmonary disease may experience increased bronchial tone and airway hyper-reactivity, making them more susceptible to vagal stimulation.¹⁵ Gastrointestinal disorders, such as gastroesophageal reflux disease or gastroparesis, can also heighten vagal responses.¹⁶ Preemptive measures, such as minimizing fasting times prior to surgery and administering gastric-emptying medications such as metoclopramide, may also help reduce the incidence of gastrointestinal disturbances.¹⁷ Given the varying sensitivity of patients to the vagovagal reflex during anesthesia, premedication with anticholinergic drugs like atropine or glycopyrrolate can be

employed to suppress vagal reactions, decrease secretions, and restore heart rate to a safe range.¹⁸ A comprehensive overview of anesthesia techniques should be discussed in detail. This discussion should encompass their indications, advantages, and disadvantages to ensure an informed decision regarding the most appropriate technique for each patient.¹⁸

Intraoperative management

During the intraoperative period, continuous assessment of the patient's response to anesthesia is vital to optimize management and reduce the risk of complications. Anesthesiologists and healthcare providers must closely monitor vital signs and be prepared to respond promptly to ensure patient safety and achieve optimal anesthesia outcomes. Close monitoring of vital signs, including heart rate, blood pressure, oxygen saturation, and end-tidal carbon dioxide levels, is essential for early detection and timely intervention. Real-time information about heart rate and rhythm can be obtained through continuous electrocardiogram monitoring, enabling the prompt identification of bradycardia or arrhythmias. Non-invasive blood pressure monitoring or arterial line placement allows for monitoring blood pressure trends and early detection of hypotension. Pulse oximetry provides continuous monitoring of oxygen saturation, alerting healthcare providers to any decrease in oxygen levels. End-tidal carbon dioxide monitoring helps assess ventilation status and can indicate the presence of bronchospasm or airway obstruction.¹⁹

Tailoring the anesthetic management to the patient's specific needs is crucial. This includes selecting the appropriate anesthetics,

such as induction agents, inhalational agents, muscle relaxants, opioids, and local anesthetics, while considering their effects on the vagovagal reflex. Dosages or concentrations may need to be adjusted accordingly.¹⁸ Volatile anesthetics, such as sevoflurane, isoflurane, and desflurane, can directly stimulate sensory receptors in the cardiovascular system, particularly the atrial stretch receptors and SA node, resulting in bradycardia, vasodilation, decrease in systemic vascular resistance and subsequent hypotension.²⁰ Opioids, such as morphine or fentanyl, can directly activate sensory receptors or indirectly affect the reflex through central mechanisms via opioid receptors in the brain, resulting in bradycardia, hypotension, and gastrointestinal disturbances such as nausea, vomiting, or increased bowel movements.²¹

Certain medications can influence the vagovagal reflex and its response to anesthesia. For example, reversal agents that enhance parasympathetic activity, such as cholinesterase inhibitors or direct cholinergic agonists, can potentiate vagal effects and increase the risk of complications.²² Conversely, medications with anticholinergic properties, such as anticholinergic drugs or certain antihistamines, can attenuate vagal stimulation and mitigate reflex responses. Anesthesiologists can adjust the depth of anesthesia to modulate the vagovagal reflex. Lightening the depth of anesthesia can reduce vagal stimulation and minimize reflex responses. This can be achieved by decreasing the dosage or concentration of volatile anesthetic agents or adjusting the infusion rate of intravenous anesthetics. Monitoring the depth of anesthesia using various parameters, such as bispectral index

or end-tidal concentration of volatile agents, helps guide the adjustment of anesthetic depth. Anesthesiologists aim to maintain an optimal balance between sufficient depth to ensure patient comfort and safety, and avoiding excessive depth that could potentiate reflex responses.

Regarding excessive vagal stimulation, it can result in bradycardia or even sinus arrest, especially in patients with pre-existing cardiovascular disease. Bradycardia can decrease cardiac output, impair tissue perfusion, and reduce oxygen delivery to vital organs. In some cases, this excessive vagal stimulation can also trigger other cardiac arrhythmias, such as AV nodal blocks or ventricular arrhythmias, further compromising cardiac function and patient safety.⁵ Interventions for excessive vagal stimulation may include administering anticholinergic medications, such as atropine or glycopyrrolate, to counteract the vagal effects and increase heart rate. These medications block the action of acetylcholine at muscarinic receptors, preventing excessive vagal stimulation. By inhibiting parasympathetic activity, anticholinergics can increase heart rate and counteract bradycardia.¹⁹ In severe cases, external pacing may be necessary to restore a normal heart rate.²³ Anticholinergic medications are typically administered intravenously, and their dosage is titrated based on the patient's response and the desired heart rate.

Excessive vagal stimulation can cause vagal-induced vasodilation, leading to a decrease in blood pressure. Hypotension resulting from this can impair tissue perfusion and compromise oxygen delivery to vital organs, increasing the risk of organ dysfunction and ischemia. Inadequate tissue perfusion can have detrimental effects on

various organs, including the heart, brain, kidneys, and gastrointestinal tract. It can result in myocardial ischemia, stroke, renal dysfunction, or impaired wound healing.^{5,9} Interventions for hypotension caused by excessive vagal stimulation may involve administering intravenous fluids, such as crystalloids or colloids, to expand blood volume and restore blood pressure. The choice and rate of fluid administration depend on the patient's fluid status, the severity of hypotension, and the surgical procedure. Monitoring blood pressure and adjusting fluid administration based on the patient's response are essential to avoid fluid overload or exacerbation of other conditions. Additionally, vasoactive medications, such as vasopressors, can be administered to restore blood pressure within a safe range.²⁴

On the other hand, increased gastrointestinal motility and tone resulting from excessive vagal stimulation can lead to complications such as increased bowel movements, impaired surgical field visualization, regurgitation, or aspiration of stomach contents into the upper airway, subsequently inhaled into the lungs.²⁵ Aspiration can cause severe respiratory complications, including aspiration pneumonia, bronchospasm, or even acute respiratory distress syndrome. These complications can result in respiratory failure, hypoxemia, compromised lung function, and potential damage to lung tissue.

Interventions for managing gastrointestinal complications due to excessive vagal stimulation may include administering bronchodilators, such as beta-agonists (e.g., albuterol) or anticholinergic medications (e.g., ipratropium), to relax airway smooth muscles and alleviate airway obstruction.²⁶ Antiemetic medications, such as ondansetron or

metoclopramide, can be administered to manage nausea and vomiting. In severe cases, advanced airway management techniques, such as mask ventilation, bag-mask ventilation, intubation, or mechanical ventilation, may be necessary to improve airway patency and oxygenation. Monitoring patient-reported symptoms, assessing the presence of nausea or vomiting, and observing bowel movements are essential for managing these complications effectively.

Postoperative management

Immediate postoperative care for patients with intraoperative vagovagal reflex involves:

Pain control: Monitor the patient's pain level using appropriate pain assessment tools. Administer analgesic medications as prescribed, considering the patient's individual needs and potential interactions with other medications.

Oxygenation and airway management: Monitor oxygen saturation levels using pulse oximetry and ensure adequate oxygenation. Maintain a patent airway and assess for any signs of airway obstruction or respiratory distress. Importantly, administer supplemental oxygen as needed, and implement appropriate airway management techniques if airway compromise is present or anticipated.

Potential complications: Monitor for signs of bradycardia, hypotension, or other cardiac arrhythmias resulting from excessive vagal stimulation. Address complications promptly by administering anticholinergic medications, fluid therapy, or vasoactive medications, as indicated. Moreover, monitor for gastrointestinal complications such as increased bowel movements, regurgitation, or aspiration, and take appropriate measures to prevent and manage them.

Transfer criteria and considerations:

Assess the patient's stability and recovery status to determine the appropriateness of transferring to the ward or intensive care unit. Consider factors such as the patient's vital signs, level of consciousness, pain control, oxygenation, and airway stability. Additionally, evaluate the need for ongoing monitoring, specialized care, or interventions that may warrant transfer to the intensive care unit. Notably, collaborate with the surgical team, and nursing staff to make the transfer decision based on the patient's condition and available resources.

Ongoing research in the field of vagovagal reflex during anesthesia aims to understand its mechanisms and develop improved management strategies. The goal is to enhance patient safety, optimize anesthesia outcomes, and reduce complications. The research focuses on several key areas including investigating the pathways and regulation of the vagovagal reflex to identify targets for intervention and develop targeted management strategies.²⁷ Identifying predictive factors and developing tools to assess the risk of complications related to the vagovagal reflex.

Conclusion

The vagovagal reflex holds great significance during anesthesia due to its profound impact on maintaining homeostasis and influencing patient outcomes. It can lead to various complications, including bradycardia, hypotension, bronchospasm, and gastrointestinal disturbances. Prompt recognition and intervention are essential to prevent inadequate tissue perfusion, arrhythmias, and aspiration. Anesthesiologists

employ a range of strategies to mitigate risks associated with complications and ultimately improving patient care during the perioperative period. Ongoing research endeavors further enhance our understanding of the vagovagal reflex.

References

1. Jang YE, Do SH, Song IA. Vasovagal cardiac arrest during spinal anesthesia for cesarean section-a case report. *Korean J Anesthesiol*. 2013;64:77-81.
2. Powley TL. Brain-gut communication: vagovagal reflexes interconnect the two “brains”. *Am J Physiol Gastrointest Liver Physiol*. 2021;321: G576-87.
3. Ahmed U, Chang YC, Zafeiropoulos S, Nassrallah Z, Miller L, Zanos S. Strategies for precision vagus neuromodulation. *Bioelectron Med*. 2022;8:9.
4. Prescott SL, Liberles SD. Internal senses of the vagus nerve. *Neuron*. 2022;110:579-99.
5. Capilupi MJ, Kerath SM, Becker LB. Vagus nerve stimulation and the cardiovascular system. *Cold Spring Harb Perspect Med*. 2020;10:a034173.
6. Weijs TJ, Ruurda JP, Luyer MD, Nieuwenhuijzen GA, Van HR, Bleys RL. Topography and extent of pulmonary vagus nerve supply with respect to transthoracic oesophagectomy. *J Anat*. 2015;227:431-9.
7. Tao J, Campbell JN, Tsai LT, Wu C, Liberles SD, Lowell BB. Highly selective brain-to-gut communication via genetically defined vagus neurons. *Neuron*. 2021;109:2106-15.
8. Campagna JA, Carter C. Clinical relevance of the Bezold-Jarisch reflex. *Anesthesiology*. 2003; 98:1250-60.
9. Kumar A, Goyal A, Rehman F, Hariharan U. Vagal stimulation causing intra-operative cardiac arrest, a major dilemma whether to proceed or to defer surgery: a case report. *Explor Res Hypothesis Med*. 2023;8:77-80.
10. Kollarik M, Ru F, Brozmanova M. Vagal afferent nerves with the properties of nociceptors. *Auton Neurosci*. 2010;153:12-20.
11. Garcia D, Kehar M, Khan ES, Mendonca R, Girshin M. Multiple episodes of severe bronchospasm during general anesthesia: a case report. *Cureus*. 2022;14:e21521.
12. Hunt EB, Sullivan A, Galvin J, MacSharry J, Murphy DM. Gastric aspiration and its role in airway inflammation. *Open Respir Med J*. 2018;12:1-10.
13. Mulkey SB, du Plessis AJ. Autonomic nervous system development and its impact on neuropsychiatric outcome. *Pediatr Res*. 2019;85:120-6.
14. Mahender A, Chavan SS, Saroa R, Chauhan M. Recent advances in geriatric anaesthesia. *Indian J Anaesth*. 2023;67:152-8.
15. Arnold AC, Ng J, Lei L, Raj SR. Autonomic dysfunction in cardiology: pathophysiology, investigation, and management. *Can J Cardiol*. 2017;33:1524-34.
16. Lu KH, Cao J, Oleson S, et al. Vagus nerve stimulation promotes gastric emptying by increasing pyloric opening measured with magnetic resonance imaging. *Neurogastroenterol Motil*. 2018;30:e13380.
17. Sayyadi S, Raoufi M, Dolatabadi AA, Rostami M, Memary E. Ultrasonographic assessment of metoclopramide administration effectiveness in accelerating gastric emptying before urgent surgery in patients with insufficient NPO time. *Anesth Pain Med*. 2020;10:e107331.
18. Dabbous AS, Baissari MC, Nehme PW, Ezzo JJ, Abu Leila AM. Perioperative reflex bradycardia and cardiac arrest. *Middle East J Anaesthesiol*. 2014;22:353-60.
19. Haahr-Raunkjaer C, Molgaard J, Elvekjaer M, et al. Continuous monitoring of vital sign abnormalities; association to clinical complications in 500 postoperative patients. *Acta Anaesthesiol Scand*. 2022;66:552-62.
20. Eis S, Kramer J. Anesthesia inhalation agents and their cardiovascular effects. 2022 Jun 4. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2023.
21. Pathan H, Williams J. Basic opioid pharmacology:

- an update. *Br J Pain*. 2012;6:11-6.
22. Yun Y, Cao D, Zhang X, et al. Glycopyrrolate versus atropine for preventing bradycardia induced by neostigmine injection after general anesthesia surgery: a randomized open, parallel-controlled multicenter clinical trial. *Am J Transl Res*. 2021;13:12996-13002.
23. Doukky R, Bargout R, Kelly RF, Calvin JE. Using transcutaneous cardiac pacing to best advantage: how to ensure successful capture and avoid complications. *J Crit Illn*. 2003; 18:219-25.
24. Valverde A. Fluid resuscitation for refractory hypotension. *Front Vet Sci*. 2021;8:621696.
25. Travagli RA, Anselmi L. Vagal neurocircuitry and its influence on gastric motility. *Nat Rev Gastroenterol Hepatol*. 2016;13:389-401.
26. Scullion JE. The development of anticholinergics in the management of COPD. *Int J Chron Obstruct Pulmon Dis*. 2007;2:33-40.
27. Chapleau MW, Sabharwal R. Methods of assessing vagus nerve activity and reflexes. *Heart Fail Rev*. 2011;16:109-27.