Inhalational Inducing Agents

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Abstract

Inhalational Inducing Agents include gas like Nitrous Oxide and volatile liquids like Ether, Halogenated halothane, Enflurane, Sevoflurane, Isoflurane, Desflurane and Methoxyflurane. They have exterminated pain and anxiety control in Dentistry as well as in General Medicine for over a century. The following article outlines the detailed history, correspondence, distinction, and the clinical implementations of the few most prevailing inhalational agents used in Dentistry.

Keywords: *Inhalational anesthesia, Nitrous oxide, Isoflurane, Sevoflurane, Desflurane, Minimum alveolar concentration, solubility, cardiac output.*

Introduction

Inhalational Anesthetic agents are a chemical compound acquiring properties of a general anesthetic that are administered via Inhalation. They are delivered through a face mask, laryngeal mask airway or tracheal tube attached to an anesthetic vapouriser and an anesthetic delivery system. Dental and oral or Maxillofacial procedures have tended to perform office-based inhalation anesthesia along with the emergence of a more compact and transportable anesthesia apparatus. Inhalational Induction is comparatively slower. It depends on the inspired anesthetic agent, it's concentration in the blood, alveolar ventilation, the blood-gas partition coefficient, and cardiac output. if the blood-gas coefficient is less, then the anesthetic agent is more effective and the onset of anesthesia is faster. Anesthetic agents have to have a pleasant smell and a carrier gas like oxygen or oxygen with air is required for its use.[1]

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Inhalational Anesthesia is being considered equivalent to General Anesthesia. Even though there exist many drugs that can also be employed, whether through inhalation or intravenous to induce general anesthesia, Inhalational Inducing Agents are mostly used today in many of the hospitals and ambulatories. With continued progress of newer surgical approaches and easier obtainability of current short-acting drugs such as the addition of the intravenous agent Propofol, there is a sharp rise in the ambulatory services in the last Twenty Years. It also plays a significant role in children and needle-phobic patients[2].

Inhalational Anesthetic Agents must have these following characteristics: It must be possible to obtain a pure compound; It should be stable and not broken down by light or alkali; It should have low gas/blood coefficient; It should be a nonflammable and nonexplosive agent; It should not undergo metabolism and should be free of organ toxicity; It should have a pleasant smell; It should be readily reversible; There should be no adverse side effects if breathed in low concentration for a longer period; It should have minimal effect on the cardiovascular system; It should be practically potent, to allow use of an elevated concentration of oxygen; There should be no carcinogenic or teratogenic effect on the patient; It should own both analgesic and hypnotic property.[1,2]

History: All around History usefulness of herb

extracts to tonics and concoctions to sponges immersed with narcotics have been recorded to be used in surgical procedures. Explorations in the Eighteenth century made way for modern anesthesia. Diethyl ether, an inhalational anesthetic was the first publicly presented Anesthetic of the modern era. These agents have played an important role in Anesthesia history. Valerius Cordus was the one to synthesize Diethyl ether in 1540 and thus was seen to reduce pain. In the year 1772, Joseph Priestly synthesized Nitrous oxide and then sir Humphrey davy acclaimed its capability to reduce pain. The years 1920 to 1940 presented the introduction of Ethylene, Divinyl Ether, and Cyclopropane. But these drugs except for Nitrous Oxide were established to be nephrotoxic and combustible, making them unsuitable to be used in a clinical setup. Nitrous Oxide is known to be the most ancient anesthetic drug in clinical practice preceding Diethyl ether. Anesthesia was born on the 16th of October in the year 1846 known as Ether Day when there was a public Demonstration by Morton of Ether Anesthesia. Ether and Nitrous Oxide added with oxygen rendered anesthesia for a Century with fair competition in the 1930s to 1950s from Cyclopropane, Divinyl Ether, and Trichloroethylene.[3]

Modern Inhaled Anesthetics were introduced from the 1950s with agents that were partially or completely Halogenated which made them more stable and less noxious. Fluroxene was first synthesized with Halothane in the year 1951. The later one was then approved for clinical use in 1956. Similarly, Enflurane was popularised in 1972 and Isoflurane in the year 1980 and they did not pose threat for liver and kidney, unlike Methoxyflurane. Sevoflurane and Desflurane were manufactured in the year 1960s and 1970s but they were not economically accessible for clinical practice in the United States up until 1994. Xenon is a rare noble gas that was discovered by British Chemist sir William Ramsay in the year1898 and was first used as an anesthetic agent in 1951. Speedy Introduction with controlled nausea and vomiting facilitates for the drive of discoveries yet the 'modern' Agents continue to reform and rise upon those in the past. The most intriguing contrast over time is the potential to rapidly introduce new agents into the practice.[3]

Pharmacology: The Pharmacological characteristics of the recently used drugs sevoflurane, Isoflurane, and Desflurane are nearly equivalent to each other. They are noncombustible and remain as clear liquids at the normal room temperature. Their actions are as follows; They result in depression of the CNS and a decrease in the frequencies of the electroencephalogram and amplitude; they cause a surge in the cerebral blood flow which results in a rise in intracranial pressure; They also suppress the autoregulatory response to the cerebral blood flow; They produce a decline in Blood Pressure which is dose-dependent by reducing SVR except for sevoflurane; There is a prompt compensatory increase in the heart rate to maintain cardiac output despite peripheral vasodilatation and a decrease in peripheral vascular resistance.[3,4]

As compared to Sevoflurane and Desflurane, Isoflurane is the most potent vasodilator which was once known to give rise to coronary artery steal syndrome. studies and clinical trials have shown that Nitrous Oxide may cause a lenient increase in cardiac output followed by a sympathomimetic response with a higher concentration of the drug. The three volatile drugs namely sevoflurane, Isoflurane, and Desflurane create a surge in the respiratory rate which is dose-dependent and with a simultaneous decline in the Tidal Volume and a rise of arterial CO2. The breathing pattern in the case of volatile agents is swift but shallow. The reason behind the respiratory depression seen in cases of Inhalational Anesthesia is caused due to medullary depression of the ventilator drive of the central nervous system and also because of a cutback in the contraction of the muscles that are concerned in respiration. [3,4]

Overton and Meyer noticed a clear relationship among anesthetic efficacy and their solvability in olive oil, concluding that anesthetic drugs work unspecifically on the hydrophobic and lipid components of the cells. It has also been established in the last few decades that inhaled anesthetic agents depend on the action of protein receptors like ligand-gated ion channels. Inhalational Anesthetics decrease the supraspinal stimulation by declining the transposal of noxious afferent information that ascends from the spinal cord to the cortex of the cerebrum through the hypothalamus. It also reduces pain due to movement response by suppressing the spinal efferent neural activity. These agents affect the ion channels of neural tissue which can cause either presynaptic release of neurotransmitters and modify the post-synaptic response threshold to neurotransmitters or the two. They also have an inhibitory effect on the post-synaptic neuronal excitability by expanding the GABAa receptor facilitated inhibitory CL- current. [3,4]

Pharmacokinetics of Inhalational Anesthetic Agents: The Inhalation agents are titrable and their

pharmacology is unique; their uptake and release completely relies on the alveolar concentration of the anesthetic drug and its absorption by the pulmonary circulation through the alveoli. Their concentration relies mainly on 3 factors namely: Inspired concentration of the drug: the larger the inspired concentration, the more rapid is the rise in alveolar concentration to the inspired concentration and the fast induction of anesthesia. The second factor being the alveolar ventilation: alveolar ventilation is directly proportional to alveolar partial pressure as it steadily replaces the inhalational agent that is taken up by the pulmonary blood circulation. The last factor is functional residual capacity: A large functional residual capacity results in dilution of the inspired concentration of gas leading to an initial low alveolar partial pressure and slow advance of anesthesia. [4, 5]

The drug uptake from the lungs depends on the four factors namely:

Solubility: It is the blood-gas partition coefficient that illustrates the parallel affiliation of an anesthetic agent for two phases and how it distributes itself amongst both the phases when an equilibrium has been attained. It is the estimation of the solvability of an anesthetic agent amid the alveolar gas and pulmonary venous blood at equilibrium. An increase in the blood-gas partition coefficient results in higher uptake by the pulmonary circulation but a gradual and slower surge in alveolar partial pressure of the drug leading to a more late recovery from anesthesia. The values for brain: blood, fat: blood, and muscle: blood have an important influence and mainly for anesthetic procedures of longer duration for the drug is reallocated to the body compartments. The brain has a high perfusion rate and will achieve equilibrium quicker than fat or muscle. As the coefficient for blood: tissue is comparatively higher leading to most of the anesthetic being transported to the fat which perfuses it. The effect of anesthesia is increased for the fatty tissues having a higher affinity for them. The blood-gas partition coefficient for isoflurane, Sevoflurane and desflurane is 1.4,0.68 and 0.4 respectively at normal body temperature.[4,5]

Pulmonary alveolar blood flow: Pulmonary blood flow equals to cardiac output in case of a lack of a shunt. An increase in cardiac output leads to a higher intake of anesthetic agents from the lungs and further speedy distribution to the tissues along with the central nervous system. Thus low cardiac output results in decreased and a high alveolar pressure thus leading to faster induction of anesthesia. Increased delivery fastens the equilibrium of anesthetic partial pressure of tissues with that of arterial blood and leads to a decrease in the induction process.[4,5]

Difference between Alveolar to venous partial pressure and their tissue uptake: The contrast between the two is because of their uptake of inhalational agents by the tissue. Tissue consumption is reliant on the blood flow within tissues, the contrast between blood-partial pressure of tissue and blood-tissue solubility coefficient. An equal amount of anesthetic would be there both in the venous blood returning to the lungs as well as when it left the lungs in the absence of any uptake by the tissue. As the brain is highly perfused with blood, it equilibrates quickly unlike in the muscle tissue.[4,5]

Blood-gas solubility and how it presents in obese patients: Overweight patients contain a larger compartment for fat leading to prolonged time for equalization after induction and a sustained emergence time because of an increase in absorption and a slow release of anesthetic agents from the fat tissues. [4, 5]

Minimum Alveolar Concentration (MAC): It is defined as a measure of the efficacy of Inhaled anesthetics and is delineated as the minimum alveolar concentration at a constant state of an inhaled anesthetic at 1 atm of pressure that restricts deliberate movements in reaction to a surgical stimulus in fifty percent of the test population. It measures the somatic responses and can reflect the activity of an inhalational anesthetic drug on the spinal cord. The concentration required to repress the feedback to vocal and tactile stimulation and prevent consciousness is estimated by MAC-awake; where memory is being lost and MAC-BAR is the concentration required to hinder adrenergic reaction to surgical stimulation. Experiments have drawn an inference that MAC-awake is approximately 1/3rd of MAC for desflurane, isoflurane, and sevoflurane.[6]

Clinical Considerations of Nitrous Oxide, Isoflurane, Sevoflurane And Desflurane:

Nitrous Oxide: It is also known as 'laughing gas' and is a sweet-smelling, non-irritating, colorless gas, nonflammable, tasteless, inorganic gas that is not metabolized in the body and is the least hepatotoxic and teratogenic. Among all the prevailing inhalation inducing agents that are used in dentistry, Nitrous oxide is notably the commonly used drug in maximum dental procedures and surgeries and most commonly in

pediatric patients. It has to be often coadministered with oxygen or other volatile anesthetics because it cannot be utilized alone due to its high MAC value of 104%. The gas is stored as a liquid in the cylinders at a pressure of 760psi. It is known to be a powerful anesthetic but has a weak analgesic property; it does not produce adequate muscle relaxation. It does not depress the respiration and there is rapid elimination mostly through the lungs, and in small amounts through the skin, sweat glands, urine and intestinal gas. It can concentrate the halogenated anesthetics in the alveoli when they are simultaneously administered because of its fast uptake from the alveolar gas known as the 'second gas effect'.[7]

It does not affect the cardiovascular system and the cerebral blood flow. Nitrous oxide can have a very deadly effect on gas-filled spaces, it can diffuse up to 20 times quicker into closed spaces than it can be removed leading to the expansion of pneumothorax, bowel gas, or air embolism. Functions of nitrous oxide sedation are they reduce fear, anxiety, and fatigue. They increase pain reaction threshold, tolerance for longer appointments, and aid in the treatment of special patients. They also control non-compliant or uncontrolled behavior and pain by replacing local anesthesia. The drawbacks of using this agent are they need supplementation to be administered, they can cause hypoxia and inhibit vit B12 metabolism and methionine synthetase which is necessary for myelin formation and DNA synthesis. Prolonged exposure to this drug can cause bone marrow depression leading to megaloblastic anemia.[7]

Isoflurane: It is an isomer of enflurane and a halogenated ether derivative which is a colorless, volatile liquid, has a pungent odor, and is stable. The induction dose is 1.5-3% and the maintenance dose is 1-2%, by special vaporizer. Effects of this drug are; It causes dose-dependent depression of ventilation; It is a muscle relaxant and also causes relaxation of uterine muscles; It is a myocardial depressant and also causes coronary vasodilatation; the administration of this drug causes an increase in cerebral blood flow and a reduction in the cerebral metabolism.[7]

The advantages of this drug are there its fast induction and recovery with minimal risk of hepatic or renal toxicity. There is less nausea and vomiting. It does not induce cardiac arrhythmias, there is reduced myocardial depression and no myocardial sensitization to adrenaline. It is a very stable molecule and undergoes little metabolism. The disadvantages are they have a pungent odor, irritating vapor thus not commonly used for induction. They cause coronary vasodilatation and respiratory depression.

Desflurane: It has an extremely low blood-gas coefficient of 0.42. Due to its low fat-blood solubility, it has a very fast emergence from the anesthesia. It has the potency to induce tachycardia along with stimulation of the sympathetic nervous system with fast variations in inhaled concentration that might compromise a cardiovascular patient. It is not suitable to be used as an anesthetic agent as it possesses a fetid odor and which can be very agonizing to the pulmonary tissues and respiratory tract. It has a MAC of 6%, the least potent but the most expensive of the volatile agent. It causes dysphoria in pediatric patients.[8]

Sevoflurane: It is a new drug and the most commonly used volatile anesthetic agent used in ambulatory and office-based anesthesia. It is stable, nonflammable has a pleasant smell, and a MAC value of 2%. It is the most commonly used agent because it causes less irritation, unlike the other gases. It is metabolized by the liver releasing fluoride ions thus can be nephrotoxic. It may cause respiratory depression, muscle relaxation, is a myocardial depressant, and can cause a rise in cerebral blood flow and a decline in cerebral metabolism.[8]

The advantages of this drug are it has a rapid onset and offset of effect, nonirritant, sweet odor, rapid induction and recovery, suitable for pediatric patients and does not lead to the production of carbon monoxide with dry soda lime. The drawbacks of this agent include; it is less potent than the corresponding halogenated agents; children might experience postoperative agitation; only 5% of the drug is metabolized resulting in an elevation of fluoride levels and associated risk of renal toxicity.[8]

Conclusions

Inhalational anesthesia is the most commonly used agent in hospitals and ambulatory surgery operating rooms as it provides multiple delivery method and allows the anesthesiologist to choose from a varied and appropriate anesthetics for a given patient in a dental setup.

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