SEE Summaries of Emerging Evidence

SEE Question

A healthy 24-year-old woman is scheduled to undergo a diagnostic hysteroscopy with general anesthesia. You choose a first-generation laryngeal mask airway (LMA) for airway management. According to a recent study, risk of which of the following would MOST likely be reduced if you use a lower cuff pressure (20 cm H_2O) compared to a higher cuff pressure (60 cm H_2O)?

☐ (A) Postoperative nausea and vomiting ☐ (B) Sore throat ☐ (C) Gastric insufflation

LMAs have gained widespread support for use in airway management during general anesthesia since their introduction into clinical practice in the late 1980s. Forming a proper seal with the cuff of the LMA and the surrounding periglottic tissue is crucial for generating and maintaining adequate alveolar ventilation. If an inadequate seal is formed in the oral cavity, air may leak from the oral cavity, but if an inadequate seal is formed near the distal tip of the LMA, this may result in propagation of air toward the distal esophagus and stomach. With gastric insufflation of air, the risk of pulmonary aspiration of gastric contents increases. Previous studies have shown that increasing cuff volume in an LMA and decreasing leakage of air through the oral cavity are associated with an increased rate of gastric insufflation. However, the question remains whether the actual cuff pressure (not volume) of a first-generation LMA has any impact on the occurrence of gastric insufflation of air.

A recent randomized controlled crossover study was conducted in a single center to evaluate the effect on gastric insufflation with a lower (20 cm H_2O) versus higher (60 cm H_2O) cuff pressure in first-generation LMAs. A cuff pressure of 20 cm H_2O has been described as the minimum necessary to achieve an adequate seal, while a cuff pressure of 60 cm H_2O is the upper limit recommended by the manufacturer. A total of 164 women scheduled for minor gynecological surgery were randomized to one of two intervention groups. One group started with the lower cuff pressure of 20 cm H_2O followed by the higher cuff pressure of

60 cm H_2O, while the second group followed the reverse order of cuff pressures. At each cuff pressure, the ventilation method consisted of eight breaths with pressure-controlled ventilation followed by 20 seconds of continuous positive airway pressure (CPAP) with corresponding peak pressures of 15, 20, 25, and 30 cm H_2O. A positive end-expiratory pressure of 5 cm H_2O was also maintained during the entire procedure. Ventilation sequences were terminated by the occurrence of any of the following: presence of gastric insufflation, tidal volume exceeding 18 mL/kg, end-tidal CO_2 falling below 4 kPa (30 mm Hg), or the sequence being completed. After finishing all sequences and measurements, the patients were ventilated for the remainder of the procedure with the same cuff pressure that had been assigned for the initial phase.

The anesthesia plan for all patients began with preoxygenation to an end-tidal expiratory oxygen fraction of at least 0.8. Remifentanil and propofol were used for induction of anesthesia with a controlled infusion. Depth of anesthesia for the procedure was observed with a bispectral index monitor and titrated to a value between 40 and 60. No manual face mask ventilation was performed prior to insertion of the LMA. A size 4 first-generation LMA was inserted by the same experienced provider throughout the study. A pressure gauge was used for continuous monitoring to first inflate to the desired pressure and then to re-evaluate and adjust as needed to maintain that pressure. If the LMA did not meet criteria for successful placement, two additional attempts were allowed before the patient would be excluded from analysis. A fiberoptic scope was also used to assess the LMA's position around the periglottic tissue.

Continuous real-time gastric ultrasound measurement was performed by two experienced providers who were blinded to the patients' intervention group allocations. A standard sagittal plane through the aorta and superior mesenteric vein in the supine position was used to assess for qualitative and quantitative signs of gastric insufflation at the gastric antrum. When gastric insufflation was detected by ultrasound, the ventilatory sequence was halted. All patients were scanned prior to induction, and any patient with a cross-sectional area of 3.6 cm^2 or greater at the gastric antrum was excluded from the study given the increased aspiration risk. A total of 20 patients were excluded for this reason. Patients underwent structured interviews one hour after surgery and again one week later to assess possible airway complications, including sore throat, dysphonia, breathing complaints, cough, dysphagia, postoperative nausea and vomiting (PONV), fever, and other severe illnesses.

The results of this study showed that an LMA cuff pressure of 20 cm H_2O was more effective in avoiding gastric insufflation than a cuff pressure of 60 cm H_2O during increasing peak airway pressures. For 59 patients (36%), gastric insufflation occurred at higher peak airway pressures for a cuff pressure of 20 cm H_2O compared to 60 cm H_2O. For 16 patients (10%), gastric insufflation occurred more commonly at 20 cm H_2O compared to 60 cm H_2O. Among the remaining 89 patients (54%), cuff pressure did not have any impact on the peak airway pressure that produced gastric insufflation. Overall, a cuff pressure of 20 cm H_2O decreased the relative risk of gastric insufflation by 30% compared to a cuff pressure of 60 cm H_2O.

The results of the study also showed that gastric insufflation occurred more often during the CPAP phase of ventilation compared to the pressure-controlled breaths for both groups, with evidence of

gastric insufflation present in 35% of the low-pressure group and 48% of the high-pressure group with a peak airway pressure of 20 cm H_2O or less. No difference was found in the severity or frequency of sore throat, dysphonia, breathing complaints, cough, dysphagia, PONV, fever, or other severe illnesses between groups one hour or one week after surgery.

In summary, the use of 60 cm H_2O in first-generation LMA cuffs was associated with an increased rate of gastric insufflation compared to 20 cm H_2O. Prolonged positive airway pressure also resulted in an increased rate of gastric insufflation compared to regular pressure-controlled ventilation. Interestingly, there was evidence of gastric insufflation even with CPAP peak airway pressures of 20 cm H_2O or less in almost half of the patients. ■

Bibliography:

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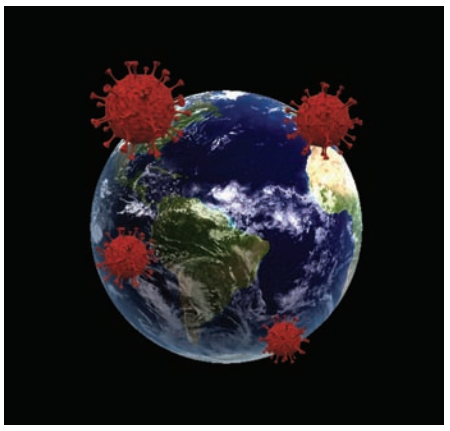
2. Keller C, Pühringer F, Brimacombe JR. Influence of cuff volume on oropharyngeal leak pressure and fibreoptic position with the laryngeal mask airway. *Br J Anaesth.* 1998;81(2):186-7. doi:10.1093/bja/81.2.186

Answer: C

Trends & Technology

Trends

Merck agrees to sublicense deal to supply underserved countries with COVID-19 treatment



Merck has agreed to supply its COVID-19 pill, molnupiravir, to over 100 low- and middle-income countries through a sublicensing deal with Medicines Patent Pool (MPP).

The contract with MPP, a United Nations-backed public health organization, is just one of several recent agreements Merck has signed with generics manufacturers to license its COVID-19 oral medication. This is MPP's first time licensing a COVID-19 treatment, but in the past it has distributed HIV, hepatitis C, and tuberculosis therapies.

MPP executives said they hope this collaboration with Merck will inspire other COVID-19 therapy makers to share their treatments with non-wealthy nations in serious need of more tools to fight the pandemic. Merck, Ridgeback Biotherapeutics, and Emory University – the co-creators of molnupiravir – will not receive royalties on the treatment under their agreement with MPP until the World Health Organization no longer classifies COVID-19 as an international public health concern.

The MOVe-OUT study of molnupiravir showed a 50% reduction of death risk in high-risk, nonhospitalized adults with mild to moderate COVID-19 when given molnupiravir.

Source: **asamonitor.pub/3q7yYdA**

Axcella Therapeutics tests new "long COVID" drug

Axcella Therapeutics is testing its investigational therapy for nonalcoholic steatohepatitis (NASH) in patients with "long COVID" who still experience symptoms such as muscle fatigue and weakness.

A phase 2a trial led by Axcella and the University of Oxford was scheduled for the end of 2021. Axcella was founded by the same incubator as Moderna/Flagship Pioneering.

Researchers are comparing the efficacy of Axcella's new drug against placebo in approximately 40 patients in the U.K. A 2b study was also begun in 2021. The investigation treatment, which is called AXA1125, is a dry powder drug that gets mixed into four to six ounces of water and is intended to treat the most common symptoms of "long COVID."

The 2a trial will include a six-minute walk test to determine levels of fatigue as well as safety and tolerability of the oral drug in study participants. After trials are complete, Axcella will seek accelerated FDA approval.

Source: **asamonitor.pub/3GMU9b8**

Technology

Scientists explore potential new chronic pain therapies from shelved cancer drugs

In search of a novel way to treat chronic pain, scientists from Duke University and the University of California at Irvine worked together to identify existing compounds that treat pain by targeting the genetic switches responsible for chronic pain. Armed with the knowledge that several cancer therapies can influence gene regulation, the researchers screened over 1,000 drugs from the National Cancer Institute's libraries, looking for old compounds with the ability to enhance the body's expression of the KCC2 gene, which silences pain signals.

As reported in *Nature Communications*, an experimental cancer drug named kenpaullone successfully treated mouse models of pain, including nerve injury and bone cancer (*Nat Commun* October 2021). Four drugs, including kenpaullone, emerged as the top candidates for the scientists' study.

Rather than cover up chronic pain, such as some over-the-counter analgesics and opioids do, potentially causing uncomfortable side effects or addiction in patients, these shelved cancer drugs could hold the key to restoring KCC2 functioning, researchers said. They are also exploring their use as therapies for neurologic disorders, including spinal cord injury and epilepsy.

Scientists discover potential source of negative emotional aspects of pain

The results of a study published in *Nature Neuroscience* in October 2021 identify a previously unknown neuronal circuitry in the brains of rodents that may be a key driver in the regulation of pain-induced anhedonia (*Nat Neurosci* October 2021). Anhedonia is a decreased motivation to complete reward-driven actions.

In the study, scientists measured rats' dopamine neuronal activity as they pressed a lever with their front paw to receive a sugar tablet as a reward. To simulate a pain condition, some rats' paws were injected with saline to produce local inflammation. After 48 hours, rats with inflamed paws pressed the lever to receive the sugar tablet less, showing that their motivation to receive a reward had decreased. This showed their dopamine neurons were less active. But when scientists restored the rats' dopamine neurons using a process called chemogenetics, the negative effect of pain was reversed and the test subject's motivation to press the lever for a reward increased again, even though their paws were still inflamed.

Scientists say this discovery could help them one day influence mental health to achieve behavioral changes as a treatment for patients with conditions such as depression. The study was funded by the National Institute on Drug Abuse, which is part of the National Institutes of Health.

FDA expands indication for SPRINT Peripheral Nerve Stimulation System

Source: SPR Therapeutics, Inc.

The FDA has granted clearance of an expanded indication for the SPRINT Peripheral Nerve Stimulation (PNS) System. The SPRINT PNS System, made by SPR Therapeutics, was previously limited for use only on the back and extremities. Now, based on safety data collected from over 5,500 patients, the device can also be used on the regions of the head, neck, and the front of the torso.

The SPRINT PNS System uses an implanted lead to deliver continuous pulse therapy for 60 days. Patients can customize their stimulation levels using a remote control. Before the FDA's expanded indication grant, the SPRINT PNS System was used by almost 7,000 patients.

This device is designed to relieve acute and chronic pain without surgery, permanent implants, or opioids. ■