SEDATION FOR ENDOSCOPY: WHAT DOES THE FUTURE HOLD?

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Recent developments in procedural sedation continue to gravitate in the arena of propofol-mediated sedation: who has the right to its administration and the payment for it? The macroeconomics of the sedation practice is also being scrutinized from a payer perspective. With drug shortages and curriculum development, this area remains a touchstone for future policy changes and hopefully, the breaching of black box fortresses with evidence-based salvos.

Pharmacoeconomics of Sedation

Clearly, anesthesia services for endoscopic procedures have undergone impressive growth over the past 10 years. It should be emphasized that there is no data showing that anesthesia assisted sedation improves patient safety. The development of the "employee model" wherein anesthesia providers are given a salary and the remaining profit is shunted to the ambulatory endoscopy center corporation has been repeatedly assailed by the American Society for Anesthesiologists. A recent case brought by the attention of the Office of the Inspector General chief counsel to the Inspector General stated that "on your request for an advisory opinion and supplemental submissions, we conclude that the proposal arrangements could potentially generate prohibited remuneration under the anti-kickback statue..." This could represent the tipping point for the viability of the "employee model" and could result in a reversion back to the consultant-based anesthesia model or perhaps a bundling of anesthesia and endoscopy costs which would result in a loss of revenue for gastroenterologists utilizing this model of anesthesia services.

Khiani et al. utilized the Surveillance Epidemiology End Results Medicare database to examine the use of anesthesiologist assisted sedation for screening colonoscopy from 2001 to 2006. The frequency of anesthesiologist involvement increased from 11% in 2001 to 23.6% in 2006. The use of anesthesia services displayed geographic variation. Anesthesia assisted colonoscopy was only noted in 1% of patients in San Francisco whereas it was 57.8% in New Jersey. It was estimated that the addition of anesthesia services increase the cost burden for colonoscopy by 20%. There was also variation in the degree of anesthesiologist involvement based on ethnicity and the degree of co-morbidities present. African-American patients were significantly less likely to undergo colonoscopy with anesthesiologist involvement (adjusted OR: 0.76; 95% CI: 0.61-0.94). Assuming a 100% penetrance of anesthesia services, the cost burden would jump to a staggering $120 million. Liu et al. conducted a retrospective analysis of a 5% representative sample of Medicare fee for service patients (1.1 million adults) in a sample of 5.5 million commercially insured patients between 2003 and 2009. The proportion of procedures utilizing anesthesiology services increased from 14% in 2003 to more than 30% in 2009. Again, geographic variation in practice was found with anesthesia services utilized in only 13% of the patients in the West as compared to over 59% in the Northeast. The growth doubled in Medicare patients but quadrupled in commercially insured patients. At a national level, annual spending for gastroenterology anesthesia services more than tripled, increasing from 0.3 billion in 2003 to 1.3 billion in 2009. Hassan et al. conducted a cost effectiveness analysis comparing endoscopist-directed propofol to anesthesia assisted sedation for patients undergoing screening for colorectal cancer. Assuming a 50% penetrance of propofol mediated sedation colorectal cancer screening, an adoption of endoscopist directed propofol sedation (EDP) would result in a $3.2 billion savings over a 10-year period. The incremental cost effectiveness of anesthesia-assisted sedation when compared to EDP would be a prohibitive $1.5 million per life year saved. In order for anesthesiologist assisted sedation to become the dominant strategy, the mortality of EDP would need to increase by 18-fold or the cost of anesthesia-assisted sedation would need to decrease by 17-fold.

Computer-assisted Personalized Sedation (CAPS): The "Black Box" Opens

Aside from gastroenterologist directed propofol administration with its hurdles surrounding the black box labeling, the only other potentially viable avenue for the non-anesthesiologist administration of propofol lies with CAPS, the computer-aided propofol delivery platform which is currently in front of the FDA. A randomized trial pitting the CAPS platform against a combination of an opioid and benzodiazepine for ambulatory upper endoscopy and colonoscopy has been published. The study used the primary endpoint of area under the curve for hypoxemia (AUC). This is a function of the incidence, depth and duration of hypoxemia. The study found that the AUC was significantly less for patients undergoing colonoscopy with CAPS than for standard sedation. There was no statistical significance for the primary outcome with respect to subjects undergoing upper endoscopy. CAPS exhibited a higher level of clinician and patient satisfaction as well as faster recovery profile. The initial submission to the FDA was met with an eventual "not approvable" letter. However in November 2011, a petition by the company led to an "approvable" letter. On May 3, 2013, the U.S. Food and Drug Administration granted

a PMA approval of the SEDASYS® system. It is expected to be available on a limited basis beginning in 2014. Indications are for the performance of EGD and colonoscopy in adults (> 18) in whom minimal to moderate sedation is targeted. The system will only be used in healthcare systems where an anesthesia professional is immediately available for assistance or consultation as needed. Training of physician-nurse teams involves a combination of a web-based curriculum coupled with hands-on simulation and airway management techniques under the supervision of an anesthesiologist-led instruction team. It is expected that post-approval studies will be undertaken.

It should be pointed out, however, that the subjects in the pivotal trial were highly selected and did not include those with a BMI greater than 35. Additionally, ASA physical classification III as well as patients about age 70 will require further study. It should be noted that the SEDASYS® exhibited a similar depth of sedation that was seen with traditional moderate sedation. This means that it will not be of use in patients who require prolonged levels of deeper sedation.

Propofol Outcomes

A retrospective cohort study compared subjects undergoing colonoscopy with either moderate sedation with GI-directed midazolam/fentanyl or monitored anesthesia care with anesthesiologist-directed propofol. The primary endpoint was the pathologically proven adenoma detection rate (ADR). There was no difference in the detection rate between the anesthesiologist-propofol group and the gastroenterologist-midazolam/fentanyl group (28.1% vs. 27.1%, P = 0.53). When adjusted for ethnicity, gender, age group, or colonoscopy indications, the odds ratio for adenoma detection was no different for the propofol group when to the reference standard fentanyl/midazolam group (OR 1.09;95% CI: 0.93-1.28). A criticism of this study was the fact that the ASA physical classification was not provided and could be a potential source of confounding. A retrospective review of the Clinical Outcomes Research Initiative database showed that more large (> 9 mm) polyps and masses were detected during average risk screening colonoscopy exams using deep sedation with propofol than with moderate conscious sedation (OR 1.25;95% CI:1.10-1.43). It is important to point out that this was not based on histology and hence, a formal ADR could not be calculated. In fact, on univariate analysis, only a 1% detection difference was seen between the two sedation regimens. Though this was found to be statistically significant, the clinical impact of this difference is dubious at best as the number needed to treat was 141 and the additional burden to the U.S. health system would be $1.3 billion.

Clearly, a goal of sedation would be to have full psychometric recovery (PMR) following the procedure. Horiuchi et al. utilized GI-directed propofol sedation targeted to moderate sedation. Subjects received a loading dose of propofol which was stratified by age. Intermittent propofol was also used. Forty-eight patients received propofol for elective colonoscopy with a median dose of 90 mg and a median procedure time of 13 minutes. In order to monitor PMR, the authors utilized a driving simulator coupled with a number connection test. Blood concentrations of propofol were also obtained. One hour following the procedure all of the components of the driving simulator, namely accelerating reaction time breaking reaction time and tracking error rate, were at baseline values. Interestingly, the number connection test exhibited a significantly increased median value one hour after colonoscopy, but well within the standardized limits for the test. Does this mean that we are free to turn our patients loose to walk, drive and fly after one hour? Probably not, but a more rapid recovery may lead to decreased costs associated with the recovery process by minimizing time lost from work by both the patient and the accompanying driver.

Drug Shortages

Drug shortages have unfortunately found their way into the fabric of our medical practice in the United States. It appears that the main culprit for the shortages is economic. The manufacturers do not make enough profit, and they may not continue to manufacture generic drugs. Contamination or inadequate amounts of raw materials probably account for less than 10% of the shortages. Growing use of "grey market" sources of medication raises the issues of safety and quality control. Other contributing factors for drug shortages include: raw/bulk material unavailability, restricted drug distribution/allocation, and inventory practices. Drug shortages including fentanyl and midazolam and propofol have also created challenges for procedural sedation. For example, one manufacturer ceased the production and distribution of a 5 mg/mL in 1 mL dose of midazolam. Additionally, another manufacturer temporarily halted its production and distribution of this same dosage platform for maintenance requalification of their manufacturing equipment. A survey conducted by the ASGE included 428 member practices. The survey found that 42% of survey respondents were experiencing drug shortages on a weekly basis. 34% of the respondents indicated that their practice is experiencing significant shortages on a weekly basis. Almost 40% of respondents noted having less than one week of fentanyl supplied. This shortage was equal across inpatient and outpatient practice settings. 54% of practitioners in the office endoscopy setting described having one week or less of a midazolam drug supply. This shortage has also affected the availability of propofol. 19.8% of the respondents in the hospital or hospital outpatient category

noted this significant shortage. This has led to the resurgent use of diazepam, benadryl, morphine, and meperidine. As of this writing, the FDA drug shortage watch list indicated a potential shortage of fentanyl, midazolam due to manufacturing delays and increased demand.

In summary, the science and practice of procedural sedation remain separated by policy and pharmacoeconomics. Clearly, the most cost effective and highest quality sedation strategy needs to be the ultimate winner. The most likely scenario will be a combination of cost bundling of gastroenterologist and anesthesia services, and a resurgence of gastroenterologist-directed moderate sedation. In the former scenario, restrictions on patient candidacy will be implemented as there is no data to show that anesthesia-directed sedation has made a palpable difference in terms of colonoscopy outcomes (adenoma detection rate, cecal intubation rate, population-based screening rates and comparative safety with respect to conventional moderate sedation regimens). Patients with adverse physiologic profiles and/or requirements for procedures requiring prolonged deep sedation will continue to receive anesthesiologist-directed sedation. The recent FDA approval of computer-assisted personalized sedation has added a new wrinkle to the landscape. Its impact on patient safety and procedural outcomes appears excellent, but this is based upon a single albeit large multicenter trial. More experience will be necessary to determine whether this platform becomes a mainstream option.

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