Dr. BobbieJean Sweitzer: Hello, I’m BobbieJean Sweitzer, Professor of Anesthesiology at Northwestern University and an Associate Editor for ANESTHESIOLOGY and you are listening to an ANESTHESIOLOGY podcast designed for physicians and scientists interested in the research that appears in our journal.

Today we are speaking with the author of a publication that appears in the August 2019 issue of the journal. With us is Dr. Leonard U. Edokpolo. Dr. Edokpolo is the lead author of an article titled “Discharge Readiness after Propofol with or without Dexmedetomidine for Colonoscopy: A Randomized Controlled Trial.”

Dr. Edokpolo completed this study when he was a resident in anesthesia at State University of New York Downstate Medical Center in Brooklyn, New York. But currently he is a Clinical Anesthesiologist in the Fairfield County Division of Integrated Anesthesia Associates in Connecticut. Welcome, Dr. Edokpolo.

Dr. BobbieJean Sweitzer: Great. So, maybe you can start by telling us what your hypothesis was for this study?

Dr. Leonard Edokpolo: Yes, we hypothesized that adding a low dose of dexmedetomidine to propofol for anesthesia in the ambulatory colonoscopy setting would lower the propofol requirement while improving the intra-procedural hemodynamic state and not increase time to discharge readiness.

Dr. BobbieJean Sweitzer: You said without increasing the time to discharge? I see.

Dr. Leonard Edokpolo: Exactly.

Dr. BobbieJean Sweitzer: So, you weren’t necessarily looking for an improvement, you just didn’t want it to have any downside, the dexmedetomidine?

Dr. Leonard Edokpolo: Yes.

Dr. BobbieJean Sweitzer: So, can you tell us about the details of this study a little more? What types of procedures were these patients having and did you conduct a single-center study?

Dr. Leonard Edokpolo: Yes. This was a single-center prospective randomized study at the State University of New York, SUNY Downstate Medical Center, like you mentioned. Patients were adults having colonoscopy procedures in the outpatient setting. The recruits were limited to ASA physical status I, II and II patients.

Study subjects were randomized to receive either propofol alone for their colonoscopy procedure or to receive propofol combined with a low dose of dexmedetomidine, 0.3 μg/kg.

Dr. BobbieJean Sweitzer: And did you monitor the depth of the sedation objectively with a BIS monitor or a formalized sedation assessment?

Dr. Leonard Edokpolo: Yes. We did assess and monitor the depth of anesthesia objectively using the Bispectral Index monitor, commonly known as the BIS monitor. Specifically we used the BIS/VISTA device by Aspect Medical Systems.

Dr. BobbieJean Sweitzer: And what kind of level of BIS were you targeting?

Dr. Leonard Edokpolo: We were targeting a level of approximately 60 for the duration of the procedure. We found that that BIS target value provided an adequate depth of anesthesia for the procedure.

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Dr. BobbieJean Sweitzer: And what kind of level of BIS were you targeting?

Dr. Leonard Edokpolo: We were targeting a level of approximately 60 on the BIS device because data has shown that that seemed to correlate a level of anesthesia that bordered between MAC and general anesthesia.

Dr. BobbieJean Sweitzer: Did you control for the doses of propofol and dexmedetomidine or were you targeting just the BIS level? And how were the drugs administered?

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Dr. Leonard Edokpolo: The doses of both propofol and dexmedetomidine were standardized. Immediately after the standard monitors and the BIS monitor had been applied, dexmedetomidine was given as a single bolus dose of 0.3 μg/kg IV push, then propofol 1 mg/kg was given in divided doses to allow initial passage of the endoscope.

Additional doses of propofol were given at the discretion of the anesthesiologist to maintain the BIS value of approximately 60. This was to standardize the level of anesthesia in our study.

And partly, the anesthesiologist was instructed not to view the BIS monitor until after the first dose of propofol had been administered and the endoscope had been introduced. This ensured that the anesthesiologist was not provided with information regarding which study on the patient was randomized.

Dr. BobbieJean Sweitzer: And no premed, no benzodiazepines?

Dr. Leonard Edokpolo: No, absolutely not.

Dr. BobbieJean Sweitzer: So, tell us again what happened if the providers thought the patients needed additional drugs? How would they handle that?

Dr. Leonard Edokpolo: The clinical anesthesiologist was allowed the flexibility to administer additional doses of propofol at their clinical discretion. However, such doses were administered with a goal to target a BIS value of approximately 60 for the duration of the procedure. We found that that BIS target value provided an adequate depth of anesthesia for the procedure.

Dr. BobbieJean Sweitzer: Were the providers in the PACU personnel blinded to the administered drugs?

Dr. Leonard Edokpolo: Absolutely, yes. One of the main strengths of this study is that virtually everyone involved in the data collection process was blinded to the administered drug, including the PACU personnel, the research investigators, as well as the clinical anesthesiologists. Only the pharmacist dispensing the medication syringes knew the group assignment of the numbered syringe.

Dr. BobbieJean Sweitzer: That’s impressive. Do you think it was obvious to providers which patients received dexmedetomidine, though, versus the placebo?

Dr. Leonard Edokpolo: No, I don’t believe it was all just for providers to accurately guess which patients receive dexmedetomidine versus which patients received propofol. We certainly found that several providers tended to guess that the patient was to receive dexmedetomidine if they administered less propofol than they expected for the procedure. However, the accuracy of their guess could not be confirmed since the assignments remained blinded until the total number of subjects had been recruited for the study.

Dr. BobbieJean Sweitzer: So, how did you determine readiness for discharge?

Dr. Leonard Edokpolo: Readiness for discharge was assessed objectively every 10 minutes in the post-anesthesia care unit using the modified post-anesthetic discharge scoring system, commonly abbreviated as the MPADSS scale.

Dr. BobbieJean Sweitzer: So, can you remind me and our listeners what exactly you assess with that and how it is administered?

Dr. Leonard Edokpolo: The Modified Aldrete Scoring System is used clinically to assess the physical status of patients recovering from the immediate effects of anesthetics in Phase I recovery. This is done by objectively scoring the patient on five clinical signs: 1) activity level, 2) respiration, 3) circulation, 4) consciousness, and 5) oxygen saturation.

Each sign is given either a score of 0, 1 or 2 with the lowest possible score of 0 and the highest possible score of 10; a total score greater than or equal to 9 means that the patient is ready to be discharged from Phase I recovery to Phase II recovery. It is important to note that this scoring system alone does not mean that the patient is ready to be discharged home.
In addition to vital signs, the Modified Post Anesthetic Discharge Scoring System—that's the MPADSS scale—includes assessment of home readiness such as the patient's ability to ambulate, the presence of nausea and vomiting, pain control and control of surgical bleeding.

Similar to the Modified Aldrete Scoring System, a score greater than or equal to 9 on the MPADSS scale means the patient is ready to be discharged home.

**Dr. BobbieJean Sweitzer:** And what did you find? Was there a difference in readiness for discharge times between the two groups?

**Dr. Leonard Edokpolo:** We found that both immediate recovery from the effects of anesthetics as well as home readiness were significantly delayed in the group of patients who received the combined regimen of propofol with a low dose of dexmedetomidine compared to the group that received propofol only such that at 30 minutes after the procedure end time, only 51% of subjects in the combined propofol-dexmedetomidine group were ready for discharge to home while up to 88% of the subjects who received only propofol were ready for discharge to home 30 minutes after the procedure end time.

**Dr. BobbieJean Sweitzer:** So, there was this kind of surprisingly big difference between the groups of 30 minutes. But how long did this difference last? Did you assess the patients then at a regular interval and at what point did you see an improvement, I guess, in that dexmedetomidine group?

**Dr. Leonard Edokpolo:** Yes. Every 10 minutes from the end of the procedure, the patient was being regularly assessed. We found that the difference between the groups diminished significantly by 40 minutes from the procedure end time such that an aggregate of 82% of subjects receiving the combined regimen of propofol-dexmedetomidine and 96% of subjects receiving propofol only were ready to go home after 40 minutes.

**Dr. BobbieJean Sweitzer:** So, what were the reasons for patients not being ready for discharge, because you mentioned all those different assessment pieces? And was it the same reason in both groups or was the reason different?

**Dr. Leonard Edokpolo:** In both groups the delay in discharge was primarily due to an inability to ambulate. Of those who failed to meet criteria at 30 minutes, we found that 88% in the combined group were too drowsy to ambulate safely at that timepoint whereas all six subjects that were not ready for discharge at 30 minutes in the propofol-only group were also too drowsy to ambulate.

**Dr. BobbieJean Sweitzer:** Which is kind of interesting because we don't think of dexmedetomidine as being that potent of a sedative and it's relatively short-acting.

**Dr. Leonard Edokpolo:** Yes. We believe that there must be an additive-seating effect and that it certainly does endure longer than propofol alone. But it's probably an additive effect.

**Dr. BobbieJean Sweitzer:** Did you objectively assess for adverse effects? And if so, what did you look for?

**Dr. Leonard Edokpolo:** We objectively assessed three adverse effects. These include: 1) incidence of apnea requiring positive-pressure ventilation; 2) episodes of sustained bradycardia defined as a heart rate less than 50 beats per minute sustained for five minutes or more; and, 3) the largest decrease in the mean arterial pressure, or MAP, from the baseline to the lowest value observed during the procedure.

**Dr. BobbieJean Sweitzer:** So, did these adverse effects occur in both groups or in one group or another? And was there a difference in between the two groups?

**Dr. Leonard Edokpolo:** So, for apnea there were no episodes of apnea requiring positive-pressure ventilation in either group; however, a sustained bradycardia occurred in 3 of 51 subjects receiving the combined drug compared with 1 of 50 subjects receiving only propofol. This sustained bradycardia, however, was neither clinically nor statistically significant because of the three subjects with bradycardia in the combined propofol-dexmedetomidine group, one of them had a baseline heart rate of 46. Thus, only two new cases of sustained bradycardia occurred in the combined propofol-dexmedetomidine group compared to one new case in the propofol-only group.

For blood pressure during the procedure, subjects receiving the combined propofol with dexmedetomidine did experience a larger decrease in blood pressure from the preoperative baseline value. There was a median decrease in MAP of about 30% in the combined propofol-dexmedetomidine group compared to a median decrease of about 21% in the propofol-only group. The median MAP remained greater than 70 mmHg in both groups.

**Dr. BobbieJean Sweitzer:** So, it sounds like it wasn't really a clinically significant decrease in blood pressure. Would you agree?

**Dr. Leonard Edokpolo:** I totally agree. While it was statistically significant, the clinical implications are likely less relevant because there was a recent publication in ANESTHESIOLOGY of a retrospective cohort in 2017 that pretty much demonstrated that to maintain a MAP of 60 or higher seemed to be equally good as the classic 20% rule of keeping the blood pressure within 20% of preoperative baseline.

**Dr. BobbieJean Sweitzer:** I think it was a MAP of 65 wasn't that…?

**Dr. Leonard Edokpolo:** Sixty-five, exactly.

**Dr. BobbieJean Sweitzer:** Yes. I think it was out of Cleveland Clinic, Dr. (Salman) I believe we actually maybe interviewed him on one of our podcasts about that study. Thank you for mentioning that.

**So, did you assess the satisfaction of the patients?**

**Dr. Leonard Edokpolo:** No. So, that's one of the factors we wish we had assessed. We did not assess that factor because we felt like a lot of findings of this study did support the use of propofol alone for colonoscopy procedures from a recovery standpoint. But we felt that there were things that may have been beneficial with the propofol-dexmedetomidine group that we did not assess like patient satisfaction, patient body movement because several studies have reported that pretty much there was less patient body movement that affected the procedure when (sounds like: Precedex) was used as an adjunct.

**Dr. BobbieJean Sweitzer:** Yes, which leads me to ask this follow-up question. Did you assess the satisfaction at the procedure level?

**Dr. Leonard Edokpolo:** Similarly, that's another one of those factors that we though may have favored the propofol-dexmedetomidine group if we had assessed it, but we did not.

**Dr. BobbieJean Sweitzer:** So, are there similar studies in the literature looking at dexmedetomidine alone or dexmedetomidine combined with propofol or other drugs for similar cases? So, I guess I want you to just kind of put from perspective your study against what maybe we already know or don't know.

**Dr. Leonard Edokpolo:** Yes. So, from our study standpoint, we're not aware of other studies that use validated discharge criteria to assess recovery after colonoscopy with propofol and adjunctive low dose of dexmedetomidine. However, several studies have assessed the effects of dexmedetomidine used either alone or in combination with other anesthetic agents for a wide range of procedures.

Perhaps one of the most widely known publications was the 2005 study in ANESTHESIOLOGY by Jalowiecki and Associates. They essentially validated the sole use of dexmedetomidine for conscious sedation during outpatient colonoscopy in a randomized trial. Comparing sedation relied on meperidine (inaudible) midazolam or sedation with fentanyl only. That study was terminated early due to significant adverse effects in the group receiving only dexmedetomidine.

Although that study highlights the clinical limitations of using high doses of dexmedetomidine for sedation, numerous studies since then have demonstrated that dexmedetomidine has several benefits when used as an adjunct with other anesthetic agents for a wide range of procedures ranging from MRI sedation to open-heart surgery.

And more recently a randomized trial in the Journal of ANESTHESIOLOGY, clinical pharmacology evaluated effects of adjunctive
dexmedetomidine with propofol and fentanyl for brain surgery in about 49 subjects, they drew similar conclusions that the adjunctive use of dexmedetomidine decreased opioid utilization, decreased hypnotic utilization; however, there was no additional advantage in terms of recovery from anesthesia.

**Dr. BobbieJean Sweitzer**: And I assume that the cost of dexmedetomidine would make it unfavorable if you tried to make the argument that you were just going use less propofol or less volatile agents or something like that. Is that true?

**Dr. Leonard Edokpolo**: I totally agree, especially for a procedure like colonoscopy where the average, at least in our study, duration of the procedure was about 20 minutes. So, the amount of propofol you’re going to use in 19 or 20 minutes, I’m not sure that you’re going to get the price advantage if you added the dexmedetomidine.

**Dr. BobbieJean Sweitzer**: So, do you think we need any further studies of dexmedetomidine and maybe specifically for procedural sedation? Or do you think your study added to what we already know should be the definitive answer here?

**Dr. Leonard Edokpolo**: I think my study and a lot of studies seem to definitively answer a lot of the questions around dexmedetomidine. Granted, we did only use one dose of dexmedetomidine. Perhaps it’s worth looking at a lower dose of dexmedetomidine as an adjunct and seeing if we lose some of these delay in recovery.

However, our dose was pretty low at 0.3 μg/kg. Going much lower than that, I guess, starts to raise a question of whether you need it at all.

**Dr. BobbieJean Sweitzer**: Right. Especially for, as you mentioned, these relatively short procedures like this: having to (sounds like: draw up) another drug, having to have another drug and then wasting what you didn’t use.

**Dr. Leonard Edokpolo**: Exactly.

**Dr. BobbieJean Sweitzer**: Well, thank you so much. I do hope today’s discussion will interest many of our listeners and lead you to read this important article to learn more. We appreciate Dr. Edokpolo for discussing his work with us today and I wish you well as you continue your efforts to enhance the practice of anesthesiology and strive to improve the care of our patients.

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