Preventive Dorzolamide-Timolol for Rising Intraocular Pressure During Steep Trendelenburg Position Surgery

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The study purpose was to evaluate preventive use of dorzolamide-timolol ophthalmic solution (Cosopt) during laparoscopic surgery with the patient in steep Trendelenburg (ST) position. Periorbital swelling, venous congestion, and elevated intraocular pressure (IOP) may produce low ocular perfusion. Prompt IOP reduction is important because 30- to 40-minute episodes of acute IOP elevations can result in retinal ganglion cell dysfunction. Dorzolamide-timolol ophthalmic drops reduce IOP and may ameliorate this effect. A double-blind randomized experimental study was conducted to test the effect of dorzolamide-timolol on IOP elevation during laparoscopic surgeries in ST position. Patients were randomly assigned to receive dorzolamide-timolol treatment or balanced salt solution following anesthesia induction. The IOP levels were measured at baseline and 30-minutes intervals throughout surgery. The generalized estimating equations model was used to analyze treatment and time effects and treatment by time interactions. Ninety patients were recruited, with 46 receiving dorzolamide-timolol treatment and 44 receiving balanced salt solution. Statistical analysis revealed significant treatment and time effects and treatment-time interactions on IOP. Patients’ IOP was significantly lower in the treatment group than controls (P < .05 to P < .001). Treatment effects were medium to strong. Prophylactic therapy with dorzolamide-timolol significantly reduced IOP of surgical patients during ST positioning.

Keywords: Chemosis, intraocular pressure, ischemic optic neuropathy, ocular perfusion pressure, postoperative visual loss.
> 50 mm Hg). Peak IOP was a principal determinant of functional loss in these studies. Rhee et al. demonstrated that trabecular meshwork-dysregulated, pressure-dependant outflow caused increased periorbital swelling and venous congestion, leading to a low flow state in the eye.

Johnstone and Grant studied this phenomenon and concur that with increased IOP, there is dysregulation of the orbital aqueous outflow. They showed that dependent orthostatis increased this effect and resulted in a collapse and occlusion of the lumen of the Schlemm canal. These pressure-responsive aqueous outflow changes caused reflux of blood into the anterior chamber, reversing flow. Increased IOP and impaired orbital outflow can compress the pial vessels in the posterior segment. Therefore, ocular perfusion is impaired through a progressive series of changes. Regional ischemia and death of optic nerve cells both in the anterior and posterior segments can be explained, potentially resulting in POVL. When patients have prolonged laparoscopic surgery in ST position, the physiologic result is analogous to acute glaucoma.

The purpose of this study was to evaluate preventive use of dorzolamide-timolol (Cosopt) as a measure to limit IOP increase during lower abdominal laparoscopic procedures using ST position. This fixed combination of topical dorzolamide hydrochloride and timolol maleate is widely used by ophthalmologists to control elevated IOP. Dorzolamide hydrochloride is a carbonic anhydrase II inhibitor, and timolol maleate is a topical β-adrenergic receptor blocking agent. Dorzolamide-timolol reduces IOP by decreasing the production of aqueous humor and a direct action on β₂-adrenergic receptors in the ciliary processes. In a previous study, dorzolamide-timolol was administered intraoperatively to 63 of 194 subjects at 3 separate institutions when their IOP reached 40 mm Hg. A nontreatment group did not receive medication because their IOP remained below 35 mm Hg. Interventional dorzolamide-timolol decreased IOP and maintained near-normal pressures while the subjects were in the ST position for 3-hour durations.

The hypothesis of this current study is that preventive treatment with dorzolamide-timolol would maintain near-normal IOP during laparoscopic surgery with ST positioning, while reducing orbital edema and preventing orbital outflow dysregulation.

Materials and Methods
• Study Design. A randomized, double-blind, experimental design was used to test the effect of preventive use of dorzolamide-timolol vs balanced salt solution (BSS) on maintaining IOP levels during a laparoscopic procedure in ST position. Subjects were randomly assigned to 2 groups: the dorzolamide-timolol treatment group and the control group (BSS). One drop of topical dorzolamide-timolol (containing 20 mg of dorzolamide and 5 mg of timolol) or BSS was administered topically to both eyes immediately following induction of anesthesia. Patients in both groups received standard anesthesia care throughout the surgery. This included dorzolamide-timolol administration when IOP reached 40 mm Hg during surgery as a standard treatment for all ST-positioned procedures at our institutions. We measured each subject's IOP at 30-minute intervals throughout the surgery after an anesthetized baseline measurement in the supine position. A final postprocedure measurement in the supine position was obtained after termination of laparoscopy.

• Setting and Samples. All patients planned for prolonged ST procedures at the medical center were eligible for the study. They were recruited from a population scheduled for robotic-assisted laparoscopic prostate and gynecologic procedures projected to require the ST position for at least 120 minutes. Full institutional review board approvals were obtained from the regional medical center for the July 2012 to July 2014 timeframe. With no exclusions, informed consent was obtained from each participant before surgery. The sample size estimate was calculated in the Power Analysis and Sample Size (PASS) software package (version 8.0.6, NCSS Statistical Software). Based on our previous findings of a medium to strong effect size (d = 0.60) of dorzolamide-timolol intervention compared with the standard care on IOP reduction during ST position, 45 subjects were needed in each group with α = .05 and power .80.

• Instruments and Measures.
• Demographics. Age, sex, height, weight, body mass index (BMI), and ASA physical status (classes 1-5) were documented, along with surgical procedure, medically indicated tests, fluid maintenance, and vital signs.

• Intraocular Pressure. An applanation tonometer was used for IOP monitoring (Reichert Tono-Pen XL, Reichert Technologies). This applanation tonometer is accepted as the most reliable IOP monitor in both awake and anesthetized patients. This device was determined to be the most accurate instrument for IOP measurement in a comparison study with other minimally invasive applanation devices.

• Mean Arterial Pressure. The MAP was measured by an arterial catheter or noninvasive blood pressure cuff (NIBP). For direct arterial measurement, MAP was measured after calibrating the transducer at heart level (midaxillary line) when the patients were supine. For measurements in ST position, mean direct arterial pressures were measured with the transducer zeroed to the level of carotid artery. In each case, the MAP was determined as the direct mean carotid level or NIBP determinations. The OPP was calculated as the difference between MAP and IOP in all positions.

• Procedures.
• Training. Five anesthesia providers who served as research assistants were credentialed to monitor IOP
with the patient under anesthesia in ST position during laparoscopic urologic and gynecologic procedures. Credentialled individuals took a video course, and the technique was demonstrated with volunteers. Calibration of the applanation tonometer was performed as outlined in the Reichert Tono-Pen XL manual (black button tapped twice and inverted upside down when “UP” is visualized in the chamber; “GOOD” is visualized when calibrated). This maneuver took place before each patient’s data collection. The principal investigator (BLM) then observed each of the 5 research assistants’ technique and measurements with 10 subjects to determine interrater reliability (IRR). The principal investigator’s rating and the calibrated reading displayed in the applanation tonometer’s window were the determinants of the correct measure. Trochim’s12 IRR correlation method was used for 60 observations and established a 98% IRR value.

• Preoperative Procedures. A sterile cover was used on the head of the tonometer for each patient in preparation for IOP monitoring. Four vials of solution were contained in our case; 2 were marked A and B (explained in the section “Tonometry Measurement”), the third was BSS, and the fourth was dorzolamide-timolol. Physiologic anesthesia monitors included a 5-lead electrocardiogram (ECG), NIBP and digital pulse oximetry. Inspired and exhaled gases were monitored by side-stream infrared gas analysis (Dräger/Fabius GS).

• Intraoperative Procedures. Anesthesia protocol was standardized for all patients. Midazolam, 1 to 2 mg, was given in the preoperative holding room. Anesthesia induction consisted of administration of fentanyl (1-2 μg/kg), propofol (2-3 mg/kg), and rocuronium (0.07 mg/kg) or vecuronium (0.01 mg-0.015/kg) to facilitate endotracheal intubation. Additional muscle relaxant use was left to the anesthesiologist’s discretion. Abdominal insufflation pressure was maintained at 14 to 15 mm Hg throughout the procedures. General anesthesia was maintained with a volatile inhalation agent (sevoflurane or desflurane) in 100% oxygen. Supplemental fentanyl was administered as needed. Bispectral index monitoring was used to assess the depth of anesthesia. Minute ventilation was adjusted with volume- or pressure-controlled ventilation to keep end-tidal carbon dioxide in the range of 30 to 39 mm Hg during the intraoperative period. Peak airway pressures were maintained at less than 40 cm H₂O and positive end-expiratory pressure ranged from 0 to 5 cm H₂O.

• Tonometry Measurement. Baseline IOP was determined by applanation tonometry after induction of anesthesia with the patient in the supine position. A sterile cover was placed on the head of the tonometer, and sterile BSS eyedrops were applied before each measurement to prevent dryness. The applanation tonometer was placed above the pupil of each eye, and the black button was pressed once. Following 3 beeps a mean value is displayed in the window, combining measures of 3 readings. One drop of either vial A or vial B (dorzolamide-timolol or BSS) was administered in each eye following induction of anesthesia. Vial A or vial B was the only marking on the vials, and anesthesia research assistants were blinded as to which solution was administered. The BSS eyedrops were applied before each reading, and ocular tonometry was repeated every 30 minutes during the surgery while the patient was in ST position. The patient’s eyes were taped to prevent drying between measurements. Protective foam was placed over the patient’s face to prevent injury. If the IOP measurement surpassed 40 mm Hg in either group, the surgeon was made aware of the elevated IOP and 1 drop of dorzolamide-timolol was then administered to each eye as a protective measure. If IOP continued to rise in this subset of patients, a timeout occurred and all anesthesia, surgery and operating room personnel were involved in determining the additional surgical time needed. A reverse ST positioning took place for a 10-minute interval at that time if the surgeon was not nearing completion of the procedure. A return to ST then took place and tonometry monitoring continued, but these participants were removed from the study thereafter because escalating trends of IOP were affected by the interventions. There was no variation in the anesthetic treatment.

A protractor at the bedside determined the degree of ST, which ranged from 32 to 40 degrees. Fluid administration was limited to 200 mL/h unless blood loss, hemococoncentration noted by laboratory findings, metabolic acidemia, or hypotension was noted.13 Arterial or venous blood was drawn to assess acid-base status at periodic intervals during the procedures if blood loss or respiratory status warranted. When the patient was returned to the supine position, a final IOP measurement was obtained before emergence from anesthesia. The MAP was obtained for determination of OPP at the time of IOP reading.

• Statistical Analysis. The IBM SPSS Statistics software version 20 was used for data analysis. Descriptive statistics including means, standard deviations, and frequencies were used to describe the demographic data and IOP, MAP, and OPP patterns over time. To address the treatment effect (dorzolamide-timolol vs control) on repeated measures of outcomes (IOP, MAP, or OPP) throughout the surgery, the generalized estimating equations (GEE) model was used to analyze treatment and time effects and treatment by time interactions. In all GEE models, the baseline values were used as covariates. An a priori level of significance was set at \( P < .05 \).

Results
A total of 90 patients, 42 (47%) men and 48 women (53%), were recruited for the study. Forty-six patients were randomly assigned to the dorzolamide-timolol treatment group and 44 patients were assigned to the control
There were no significant differences in demographic characteristics between the 2 groups (Table 1).

- **Intraocular Pressure.** There was no difference in the baseline IOP levels between the 2 groups. The GEE analysis revealed significant treatment effect (Wald $\chi^2(1) = 21.85$, $P < .001$) and time effect (Wald $\chi^2(6) = 284.74$, $P < .001$) and treatment by time interactions (Wald $\chi^2(6) = 22.81$, $P < .01$). Throughout the surgery, patients’ IOP levels were significantly lower in the dorzolamide-timolol group than in the control group at 60-minute, 90-minute, 120-minute, 150-minute, and 180-minute points ($P < .05$ to $P < .001$; Table 2, Figure 1). In the final flat position, no significant differences in IOP were found between the 2 groups. The effect size of the dorzolamide-timolol treatment on IOP reduction compared with the control during the ST position was medium to large ($\text{Cohen } d = 0.57$ to 0.92).

- **Mean Arterial and Ocular Perfusion Pressures.** There was a significant time effect on MAP values (Wald $\chi^2(6) = 47.74$, $P < .001$) throughout the surgery, but there were no treatment effect and interaction of treatment by time on MAP values (Table 3). The OPP values were significantly affected by the treatment (Wald $\chi^2(1) = 4.93$, $P < .05$) and time (Wald $\chi^2(6) = 113.37$, $P < .001$) and the interaction of treatment by time (Wald $\chi^2(6) = 12.81$, $P < .05$). At 120 and 180 minutes, OPP values were calculated to be higher in the treatment group than in the control group ($P < .05$, respectively), but no differences were found at other data points (Table 4).

**Discussion**

To the best of our knowledge, the present double-blind randomized experimental study is the first to examine prophylactic therapy with Cosopt eyedrops on reducing IOP of patients who undergo laparoscopic surgery in ST position. The results suggest that throughout the surgery, the IOP was significantly lower in the treatment group compared with the control group and that treatment effects were medium to strong across different time points. The current findings are consistent with our previous study in which dorzolamide-timolol was used as a perioperative intervention when IOP approached 40 mm Hg and was shown to be beneficial; in the prior study, dorzolamide-timolol reduced the IOP by a mean of 26%, providing a statistically significant decrease at all time points. That study was conducted at 3 different institutions, with results and conclusions being the same at all sites and providing a strong basis for conducting the present research. The highest risk population included patients with a BMI greater than 35 kg/m² and age above 62 years. In addition, diabetes, vascular disease, and history of glaucoma were cited as increasing the risk of elevated IOP regardless of surgical position. Patients with glaucoma are asked to take their medications before laparoscopic surgery in ST position and their IOP is routinely monitored at our institution.

Gilbert reviewed the literature and concluded that any interruption to blood flow autoregulation can lead to POVL. The IOP must remain within normal ranges to maintain optimum anatomical conditions for refraction and thus vision. Harris et al. studied human autoregulation and found that retinal blood flow in response to increased IOP varied markedly. An IOP of 47 mm Hg, in one subject, reduced flow to one-third of normal, suggesting that human autoregulation may fail if IOP approaches within 40 to 45 mm Hg of the

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**Table 1.** Demographic Characteristics, and Health and Surgical Procedure Status

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Dorzolamide-timolol group</th>
<th>Control group</th>
<th>Total sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, No. (%)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td><strong>M</strong></td>
<td>19 (45.23)</td>
<td>23 (54.76)</td>
<td>42 (46.67)</td>
</tr>
<tr>
<td><strong>F</strong></td>
<td>27 (56.25)</td>
<td>21 (43.75)</td>
<td>48 (53.33)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>56.98 (9.52)</td>
<td>57.43 (10.68)</td>
<td>57.20 (10.04)</td>
</tr>
<tr>
<td>BMI</td>
<td>30.85 (9.13)</td>
<td>29.88 (6.72)</td>
<td>30.37 (8.00)</td>
</tr>
<tr>
<td>CO2 (L/min)</td>
<td>34.49 (3.49)</td>
<td>34.74 (3.79)</td>
<td>34.61 (3.62)</td>
</tr>
<tr>
<td>PIP (cm H2O)</td>
<td>32.42 (5.14)</td>
<td>32.71 (5.10)</td>
<td>32.56 (5.08)</td>
</tr>
<tr>
<td>EBL (mL)</td>
<td>145.65 (113.09)</td>
<td>156.25 (80.24)</td>
<td>150.58 (98.19)</td>
</tr>
<tr>
<td>Fluids (mL)</td>
<td>2,600.00 (678.97)</td>
<td>2,381.48 (452.38)</td>
<td>2,488.68 (579.76)</td>
</tr>
<tr>
<td>ASA class</td>
<td>40.85 (2.30)</td>
<td>40.85 (0.60)</td>
<td>40.85 (2.22)</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>39.04 (3.92)</td>
<td>39.04 (3.92)</td>
<td>39.04 (3.92)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; CO2, carbon dioxide; EBL = estimated blood loss; fluids, fluid maintenance; PIP, peak inspiratory pressure.

Data are shown as mean and standard deviation except for gender, which is number and percentage. There were no significant differences in demographic characteristics between the 2 groups.
MAP (a critical threshold). The authors suggest that response to an autoregulatory plateau may vary with age, individual anatomy, atherosclerosis, and/or arterial hypotension. Indeed, preexisting pathophysiology, drug therapy, and existing disease entities, such as glaucoma, will disrupt an individual’s response mechanism as seen in the studies by Evans et al.\(^1\) In their research, 20 patients with open-angle glaucoma were placed in the ST position, and results were compared with those of 20 healthy subjects in ST position; the results showed that all 20 patients with glaucoma exhibited faulty autoregulation of central retinal artery blood flow measured by Doppler flow imaging. Such variation in patient history may explain why ophthalmic compartment syndrome, unlike intracranial or tissue compartment syndrome, is not uniformly observed at or below a range of OPPs. A compartment syndrome occurs when increased pressure in a closed tissue compartment crosses a critical perfusion threshold beyond which blood flow to tissues in the compartment is compromised.

Studies performed by Molloy\(^1\) and Awad et al\(^2\) noted a marked increase in IOP on ST positioning during surgery.

### Table 2. Intraocular Pressure (IOP) Measures During Surgery

<table>
<thead>
<tr>
<th>Time point (patient position)(^{\text{a}})</th>
<th>Group</th>
<th>n</th>
<th>IOP (mm Hg)</th>
<th>P Value(^{\text{b}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial (flat)</td>
<td>Control</td>
<td>44</td>
<td>12.00</td>
<td>&gt; .05</td>
</tr>
<tr>
<td></td>
<td>Dorzolamide-timolol</td>
<td>46</td>
<td>12.61</td>
<td>5.32</td>
</tr>
<tr>
<td>30 min (ST)</td>
<td>Control</td>
<td>44</td>
<td>22.90</td>
<td>&gt; .05</td>
</tr>
<tr>
<td></td>
<td>Dorzolamide-timolol</td>
<td>46</td>
<td>19.83</td>
<td>5.50</td>
</tr>
<tr>
<td>60 min (ST)</td>
<td>Control</td>
<td>44</td>
<td>27.41</td>
<td>&lt; .05</td>
</tr>
<tr>
<td></td>
<td>Dorzolamide-timolol</td>
<td>46</td>
<td>23.15</td>
<td>5.48</td>
</tr>
<tr>
<td>90 min (ST)</td>
<td>Control</td>
<td>44</td>
<td>28.30</td>
<td>&lt; .01</td>
</tr>
<tr>
<td></td>
<td>Dorzolamide-timolol</td>
<td>46</td>
<td>22.89</td>
<td>5.14</td>
</tr>
<tr>
<td>120 min (ST)</td>
<td>Control</td>
<td>43</td>
<td>30.88</td>
<td>&lt; .001</td>
</tr>
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<td></td>
<td>Dorzolamide-timolol</td>
<td>45</td>
<td>24.11</td>
<td>5.93</td>
</tr>
<tr>
<td>150 min (ST)</td>
<td>Control</td>
<td>24</td>
<td>31.21</td>
<td>&lt; .001</td>
</tr>
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<td>Dorzolamide-timolol</td>
<td>31</td>
<td>25.00</td>
<td>7.90</td>
</tr>
<tr>
<td>180 min (ST)</td>
<td>Control</td>
<td>8</td>
<td>35.00</td>
<td>&lt; .01</td>
</tr>
<tr>
<td></td>
<td>Dorzolamide-timolol</td>
<td>16</td>
<td>26.06</td>
<td>8.06</td>
</tr>
<tr>
<td>Final (flat)</td>
<td>Control</td>
<td>44</td>
<td>18.30</td>
<td>&gt; .05</td>
</tr>
<tr>
<td></td>
<td>Dorzolamide-timolol</td>
<td>46</td>
<td>16.91</td>
<td>6.19</td>
</tr>
</tbody>
</table>

\(^{\text{a}}\)Intraocular pressures were measured at baseline supine position (initial, flat), during every 30-minute interval throughout the surgery in steep Trendelenburg (ST) position, and at a final postprocedure in the supine position (final, flat).

\(^{\text{b}}\)Treatment by time interaction effects in the generalized estimating equations model. Boldface indicates statistically significant.

**Figure 1.** Profile Plot: Preventive Dorzolamide-Timolol (Cosopt) versus Control Group at Surgical Time Points

Abbreviation: IOP, intraocular pressure.
### Table 3. Mean Arterial Blood Pressure (MAP) Measures During Surgery

Mean arterial pressures were measured at baseline supine position (initial, flat), during every 30-minute interval throughout the surgery in steep Trendelenburg (ST) position, and at a final postprocedure in the supine position (final, flat).

<table>
<thead>
<tr>
<th>Time point (patient position)</th>
<th>Group</th>
<th>n</th>
<th>MAP (mm Hg)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Initial (flat)</td>
<td>Control</td>
<td>44</td>
<td>89.02</td>
<td>15.10</td>
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<td></td>
<td>Dorzolamide-timolol</td>
<td>46</td>
<td>86.20</td>
<td>14.83</td>
</tr>
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<td>30 min (ST)</td>
<td>Control</td>
<td>44</td>
<td>96.05</td>
<td>13.19</td>
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<td></td>
<td>Dorzolamide-timolol</td>
<td>46</td>
<td>93.15</td>
<td>13.29</td>
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<td>60 min (ST)</td>
<td>Control</td>
<td>44</td>
<td>94.74</td>
<td>10.26</td>
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<td>Dorzolamide-timolol</td>
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<td>91.70</td>
<td>12.42</td>
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<td>89.70</td>
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<td>Dorzolamide-timolol</td>
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<td>43</td>
<td>89.45</td>
<td>12.04</td>
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<td>Dorzolamide-timolol</td>
<td>45</td>
<td>87.69</td>
<td>12.00</td>
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<td>150 min (ST)</td>
<td>Control</td>
<td>25</td>
<td>87.00</td>
<td>10.46</td>
</tr>
<tr>
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<td>Dorzolamide-timolol</td>
<td>30</td>
<td>87.53</td>
<td>10.46</td>
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<td>180 min (ST)</td>
<td>Control</td>
<td>8</td>
<td>83.75</td>
<td>8.70</td>
</tr>
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<td>Dorzolamide-timolol</td>
<td>16</td>
<td>89.44</td>
<td>11.45</td>
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<td>Control</td>
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<td>85.55</td>
<td>11.62</td>
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<td>Dorzolamide-timolol</td>
<td>46</td>
<td>86.59</td>
<td>11.48</td>
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### Table 4. Ophthalmic Perfusion Pressure (OPP) Measures During Surgery

Ocular perfusion pressures were measured at baseline supine position (initial, flat), during every 30-minute interval throughout the surgery in steep Trendelenburg (ST) position, and at a final postprocedure in the supine position (final, flat).

<table>
<thead>
<tr>
<th>Time point (patient position)</th>
<th>Group</th>
<th>n</th>
<th>MAP (mm Hg)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
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<td>Control</td>
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<td>77.16</td>
<td>15.51</td>
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<td>74.09</td>
<td>14.05</td>
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<td>73.98</td>
<td>14.13</td>
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<td>68.20</td>
<td>12.34</td>
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<td>68.63</td>
<td>11.72</td>
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<td>64.93</td>
<td>12.03</td>
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<td>58.69</td>
<td>12.93</td>
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<td>Dorzolamide-timolol</td>
<td>45</td>
<td>64.42</td>
<td>10.70</td>
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<td>150 min (ST)</td>
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<td>56.40</td>
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<td>62.20</td>
<td>9.96</td>
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<td>8</td>
<td>49.75</td>
<td>11.35</td>
</tr>
<tr>
<td></td>
<td>Dorzolamide-timolol</td>
<td>16</td>
<td>63.13</td>
<td>9.87</td>
</tr>
<tr>
<td>Final (ST)</td>
<td>Control</td>
<td>44</td>
<td>66.42</td>
<td>11.31</td>
</tr>
<tr>
<td></td>
<td>Dorzolamide-timolol</td>
<td>46</td>
<td>68.41</td>
<td>11.36</td>
</tr>
</tbody>
</table>
robotic procedures in higher risk populations. Recent recommendations from the Anesthesia Patient Safety Foundation (APSF) propose that preoperative consent include informing such patients of their risk of visual impairment and that this information be given by both surgical and anesthesia providers. The APSF held a POVL multidisciplinary conference in 2013 with anesthesia, surgery, and ophthalmology researchers and clinicians. A consensus recommendation was to elevate the head of ST position procedures at intervals to relieve venous congestion and to stage long prone procedures.21

Because most anesthesia providers rarely measure IOP, a visual observation scale was developed by Molloy/Bridgeport Anesthesia Associates for patients undergoing laparoscopic procedures in ST position. This measurement scale correlates ocular signs to IOP levels.22 Eyelid edema warns the practitioner that IOP is rising. In the study by Molloy,22 there was a correlation of eyelid edema with 2.5 times the baseline IOP. Conjunctival edema, known as chemosis, proved a valuable predictor of IOP above 40 mm Hg (area under the curve of the receiver operator curve, 0.79 ± SD 0.718), the critical threshold at which point ophthalmologists suggest intervention. Chemosis correlated with IOP 3.4 times the baseline via a logistic regression analysis. In most cases this approaches an IOP of 40 mm Hg since the normal IOP is 10 to 15 mm Hg. Because chemosis has reliably predicted IOP elevation above 35 mm Hg, we recommend treatment whenever chemosis is observed (Figure 2). With the preventive dorzolamide-timolol therapy, visual signs of periorbital edema and chemosis together with IOP decreased.

- **Alternative Interventions.** Porciatti and Nagaraju23 cited a benefit in reverse Trendelenburg positioning (head-up tilt) and illustrated both a decrease in IOP and an improvement in retinal ganglion cell function with this intervention. Linder et al24 also proposed that elevation of the head above the level of the heart may reverse the effects of the gravity-induced, orthostatic venous pressure gradient, resulting in a decreased IOP. A trial of flat supine rest stop was investigated by Molloy and Watson25 at the 60-minute point of ST positioning. This intervention requires undocking and redocking the robot for only 7 to 10 minutes during robotic cases, removing instrumentation, then replacing and returning to ST position. The IOP decreased toward normal when tonometry was measured within 30 minutes of the flat supine intervention. By the second hour the mean IOP for the supine intervention group was 18.4 mm Hg, whereas it was 31.6 mm Hg in the control group. The findings support the contention that a flat supine interval minimizes the impact on IOP and OPP of lengthy laparoscopic surgery in ST position. The beneficial effect was demonstrable after an additional 2 hours’ return to the ST position. Johnstone and Grant2 also found that outflow improved on inversion. They showed that the orthostatic pressure change unloaded the trabecular meshwork drainage system and reopened the lumen of the Schlemm canal.

Surgeons may be resistant to modifying position once surgery is under way. Therefore, preventive measures that directly limit escalating IOP without disruption of surgery should be considered.

- **Practice Implications.** Both preventive and intervention dorzolamide-timolol may be employed to control IOP during laparoscopic procedures involving ST position. Shamesh et al26 identified the benefits of a second daily dose. Subsequent dosing lowers IOP 25.9%. As a result, we employ preventive dorzolamide-timolol in the high-risk population (diabetes, vascular disease, glaucoma history, high BMI, and age above 62 years). Also, when patients present with a history of glaucoma or high IOP, their scheduled therapy is administered before they enter the operating room, as a preventive measure. A subsequent dorzolamide-timolol intervention should be considered if IOP levels approach 40 mm Hg or if chemosis is observed.

Pinkney and colleagues27 reviewed the relationship of patient positioning and IOP across all surgical specialties. They concluded that the rise in IOP was time dependent and, consequently, that patients were very likely to be at risk of POVL events as the duration of surgery increased. Both prone and ST position cases were included. Cases of POVL reported to the American Society of Anesthesiologists registry occurred after a mean surgical time of 5.5 hours.1 We recommend a time-out at the 4-hour surgical time point to discuss projected surgical completion. A supine intervention is introduced at that time if ST or prone position is needed for an additional hour or more.

**Conclusion**

Dorzolamide-timolol (Cosopt) drops significantly reduce elevated IOP and periorbital edema of patients who

---

**Figure 2. Chemosis Effects After 2.5 hours of Steep Trendelenburg Position**

Chemosis correlated to 3.4 times baseline intraocular pressure (> 35-40 mm Hg).
undergo lengthy laparoscopic robotic surgery in the ST position. Preventive and interventional treatment at any time during the ST procedure arrested the trend in escalating IOP. Practitioners should monitor signs of periorbital edema if not IOP, and an institutional protocol may help limit the potential for ischemic optic neuropathy and POVL when procedures in prolonged ST or prone position are indicated. Preventive dorzolamide-timolol may provide practitioners with an alternative to frequent repositioning during these prolonged surgical procedures.

REFERENCES


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Pseudocholinesterase abnormalities are a genetic cause of aberrant metabolism of the depolarizing muscle relaxant succinylcholine. This article examines a case where succinylcholine was chosen to facilitate intubation due to its ultra short duration and the request of the surgeon to monitor motor evoked potentials. Following succinylcholine administration the neurophysiologist was unable to obtain motor evoked potentials. This case study highlights the intraoperative and postoperative management of an elderly patient with an unknown pseudocholinesterase deficiency.

Keywords: Anesthesia, dibucaine number, motor evoked potentials, pseudocholinesterase deficiency.

Cholinesterase is a broad term used to describe a family of enzymes that hydrolyze choline esters. Two subtypes of cholinesterase exist: acetylcholinesterase and pseudocholinesterase (PChE). Some individuals demonstrate genetic variations in PChE that can cause prolonged apnea and paralysis when exposed to the depolarizing muscle relaxant succinylcholine due to aberrant metabolism of the drug. Sixty-five inherited variants have been identified that may cause slight to marked post-succinylcholine paralysis. Monitoring intraoperative motor evoked potentials requires the absence of paralysis. This frequently leads the anesthesia provider to select succinylcholine to facilitate intubation due to its ultra short duration. In the presence of an unknown pseudocholinesterase deficiency, the duration of paralysis after succinylcholine administration may be significantly increased, resulting in the inability to monitor evoked potentials. This case report is an addition to the available literature describing the impact an unknown pseudocholinesterase deficiency can have on the anesthetic plan.

Case Summary
An 81-year-old man (182 cm, 88 kg) presented to the surgical suite for C3-C6 anterior discectomy and fusion. The patient had a past medical history significant for hypertension, sleep apnea, chronic obstructive pulmonary disorder (COPD), and lung cancer status post chemo and radiation. Past surgical history included an appendectomy, cholecystectomy, surgically repaired abdominal aortic aneurysm (AAA), and left upper lobectomy. The preoperative evaluation completed by the anesthesiologist indicated that the patient complained of fear due to the inability to move during a previous anesthetic. During the interview with the student registered nurse anesthetist, the patient could not recall what surgery this had occurred but stated it was not experienced during his last procedure. The patient had no allergies and was unaware of any surgical or anesthetic complications among his closest blood relatives. The student registered nurse anesthetist’s subjective preoperative airway assessment did not indicate a potential difficult airway. The patient’s electronic record from the previous aneurysm repair revealed an uncomplicated intubation facilitated by succinylcholine. When reviewing the record for the lobectomy it was noted that rocuronium had been given to assist with intubation.

The patient was transported into the OR. Standard anesthesia monitors were applied and preoxygenation occurred with 10 L per minute of oxygen. General anesthesia was induced at 0754 with lidocaine, 100 mg; propofol, 150 mg; and fentanyl, 250 μg. Intubation was facilitated with 100 mg, succinylcholine.

In this case the surgeon requested that nervous system function be monitored utilizing motor evoked potentials (MEPs). When MEP monitoring is indicated, anesthesia providers typically avoid nondepolarizing neuromuscular blockers and volatile anesthetics due to profound depression of motor evoked response amplitude. For this reason succinylcholine was chosen to assist with tracheal intubation and total intravenous anesthesia was planned. The anesthetist intubated the patient without difficulty and endotracheal tube placement was confirmed by the presence of end-tidal carbon dioxide (ETCO₂), chest rise, and bilateral breath sounds. Total intravenous anesthesia (TIVA) was initiated utilizing a propofol drip started at100 μg/kg/min and a remifentanil drip started at 0.25 μg/kg/min. These infusions were titrated based on hemodynamic parameters and surgical stimulation to maintain an adequate plane of anesthesia.

The patient was prepped and an arterial line was placed for hemodynamic monitoring. Incision was made at 0856.
The neurophysiologist attempted to establish the patient’s baseline MEPs. At 0901 the neurophysiologist made the surgeon, CRNA, and student registered nurse anesthetist aware that motor evoked potentials were unable to be elicited. After informing with the anesthesia team that succinylcholine had been administered the neurophysiologist began to troubleshoot the monitoring equipment.

The student registered nurse anesthetist checked a train of four (TOF) response using the nerve stimulator to evaluate the patient’s recovery from neuromuscular blockade. The lack of response led to a presumptive diagnosis of pseudocholinesterase deficiency. The battery and electrodes of the nerve stimulator were checked and confirmed to be in working order. The surgeon and anesthesiologist were made aware of the lack of response. The surgeon stated the case could be safely continued without the motor evoked potentials and requested that MEPs periodically be followed to detect the return of muscle responsiveness.

Early in the case the patient experienced hypotension and a phenylephrine infusion was initiated and titrated to maintain a mean arterial pressure of 70 or greater. Otherwise, the case remained uneventful. Approximately 3 hours into the case, at 1202, the neurophysiologist notified the team that the MEPs had returned to the patients’ presurgery baseline. The student registered nurse anesthetist rechecked the TOF response and noted 4 strong equal twitches. MEPs were then monitored continuously throughout the remainder of the surgery.

The case was completed at 13:04. Five hours and 10 minutes had elapsed since the succinylcholine had been administered. After discussion among the anesthesia team, propofol and remifentanil were discontinued in anticipation of emergence. Approximately 20 minutes later, despite measurable MEPs and a complete return of the TOF, the patient remained weak. The patient was able to blink eyes in response to questions but could not lift arms, legs, or head off the bed. When asked to take a maximal inhalation, tidal volume was noted to be less than 100 mL. The cause of the prolonged paralysis was explained to the patient to decrease anxiety. Fentanyl, 100 μg and a propofol drip at 50 μg/kg/min were initiated for patient comfort and sedation. The patient was taken to the post anesthesia care unit (PACU) intubated. The anesthesiologist continued the care of the patient in PACU. According to the extubation note written by the anesthesiologist, the patient was weaned to a t-piece and the endotracheal tube was removed at 14:46. This was approximately 7 hours after the succinylcholine administration. The patient was taken from the PACU to the intensive care unit for continued airway monitoring and subsequently discharged to a rehabilitation facility 5 days later.

Discussion
Prolongation of succinylcholine can be caused by either a decreased quantity or quality of pseudocholinesterase. Diminished quantities may be seen in the presence of malignancies, pregnancy, liver disease, collagen vascular disease, malnutrition, and hypothyroidism. In this case, the dibucaine inhibition test was drawn and sent for analysis to determine if the patient had an atypical variant of PChE. The normal result of the dibucaine inhibition test is 80. This means that 80% of the PChE activity was inhibited by the local anesthetic dibucaine. These individuals are labeled homozygous normal and would be briefly paralyzed by succinylcholine. Those with a dibucaine number of 20 would be homozygous atypical and can be expected to have a marked response to succinylcholine with paralysis typically exceeding 1 hour. A dibucaine inhibition test result of 60 would be defined as heterozygous and generally only produce a slight prolongation of succinylcholine. Postoperatively, it was noted that the patient’s dibucaine inhibition test result was 27. This indicates an atypical PChE variant with the genetic label of homozygote atypical. The incidence of a patient homozygous for pseudocholinesterase mutations is one in 2,500 patients. Studies have shown that patients with pseudocholinesterase deficiency have a normal response to remifentanil, leading the author to believe it is unlikely that the remifentanil contributed to the prolonged recovery of the patient. Remifentanil is a synthetic opioid with swift onset and short duration. It allows predictable titration of anesthesia with rapid recovery of consciousness and respiration independent of the duration of infusion. The context-sensitive half-life is 3-4 minutes. Remifentanil is metabolized by nonspecific esterases in tissues and blood and is not mediated by pseudocholinesterase.

An indication that this patient may have had a pseudocholinesterase deficiency came from the preoperative interview when the patient stated that he was unable to move during a prior anesthetic. Past surgical records for the aortic aneurysm repair did include the administration of succinylcholine followed by rocuronium. TOF response had not been charted between the two, however 6 hours later a four-twitch response to TOF was documented prior to reversal. The patient was taken to PACU intubated and the reason indicated on the anesthesia discharge summary was pulmonary edema. The lobectomy had occurred after the AAA repair and succinylcholine had not been administered. This explains why the patient had indicated he could not recall having an anesthetic complication with his most recent surgery.

The author acknowledges that a baseline TOF should have been elicited prior to the administration of succinylcholine. An early discovery could have alerted the surgeon to the inability to elicit intraoperative MEPs prior to skin incision. Multiple case reports describe the importance of monitoring neuromuscular blockade when administering succinylcholine.
When faced with a patient experiencing a prolonged duration of paralysis, in addition to safety, a primary goal is comfort of the patient. The patient was found to be awake and able to blink eyes in response to questioning. The patient was reassured, sedated, and ventilated until it was decided by the anesthesiologist that the patient satisfactorily met the extubation criteria. The patient was educated regarding his atypical enzyme and given a letter regarding his pseudocholinesterase deficiency for future anesthesia experiences.

**Conclusion**

In summary, this was a unique case of unanticipated prolonged paralysis observed in an elderly patient during a surgery where motor evoked potentials were being monitored. The inability to elicit a TOF response led the student registered nurse anesthetist to an early presumptive diagnosis of pseudocholinesterase deficiency. In this patient population education regarding the cause of the paralysis is important to decrease anxiety and avoid the future use of depolarizing muscle relaxants by other healthcare providers.

**REFERENCES**


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AANA Journal Course
Update for Nurse Anesthetists

Tranexamic Acid in Anesthetic Management of Surgical Procedures

Jessica Mayeux, MSN, CRNA
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Blood loss during surgical procedures poses a grave risk to the patient, but transfusion is costly and associated with adverse outcomes. Antifibrinolytics, however, offer an economical and effective means of decreasing blood loss associated with surgical procedures. Tranexamic acid (TXA) is an antifibrinolytic that blocks lysine-binding sites of fibrinogen and fibrin, preventing the breakdown of existing clots. This journal course reviews extensive research demonstrating that antifibrinolytics such as TXA decrease blood loss and in some studies reduce allogeneic transfusion requirements. In addition, this journal course addresses concerns that use of antifibrinolytics increases embolic events, reviews research that demonstrates TXA does not increase the incidence of vascular occlusive events, and describes methods of TXA use in cardiac and orthopedic surgical procedures, neurosurgery, and obstetrics. The Certified Registered Nurse Anesthetist should consider the possibility, on a case-by-case basis, of using TXA in surgical procedures to reduce blood loss with minimal adverse effects.

Keywords: Antifibrinolytic, coagulant, surgery, surgical blood loss, tranexamic acid.

Objectives
At the completion of this course, the reader should be able to:
1. Describe the physiologic process in which tranexamic acid inhibits fibrinolysis.
2. Identify contraindications to the administration of tranexamic acid.
3. Describe administration guidelines of tranexamic acid.
4. Identify surgeries in which tranexamic acid could provide benefit to the patient.
5. Discuss adverse effects associated with administration of tranexamic acid.

Introduction
Higher perioperative blood loss is associated with surgical procedures such as cardiac, orthopedic, and trauma procedures. One of the most common treatments of massive blood loss is blood transfusion, but there are many complications and risks associated with this practice. With advancements in surgical techniques, autologous blood donations, cell scavenge, and antifibrinolytic drugs, healthcare providers have been able to decrease the number of blood transfusions and thus the associated complications. Decreasing perioperative bleeding through the prophylactic use of antifibrinolytic agents, such as aprotinin, tranexamic acid (TXA), and ε-aminocaproic acid (EACA), has become increasingly popular. This journal course will examine the properties of TXA and use of this medication in the operating room.

Historical Background
Presently, the only labeled indications for TXA by the US Food and Drug Administration (FDA) are for short-term use in patients with hemophilia undergoing tooth extractions and to treat menorrhagia. However, since the 1960s, TXA commonly has been prescribed off-label to minimize blood loss for various high blood loss surgeries such as cardiac and orthopedic surgical procedures. Recently, TXA also has been used in trauma surgery to decrease blood loss. Despite the success of TXA as an antifibrinolytic—and its widespread use in countries such
as the United Kingdom and Japan—it was not as popular in the United States until the early 2000s, when aprotinin, an antifibrinolytic, was removed from the market.

In 2008, TXA was proposed to be included in the World Health Organization (WHO) Model List of Essential Medicines for reducing perioperative blood loss in adults undergoing cardiac surgical procedures requiring cardiopulmonary bypass (CPB); in 2011, that proposal was approved. The Model List of Essential Medicines helps countries plan for effective healthcare delivery by identifying the potential impact and importance of medications. Following inclusion of TXA in the Model List of Essential Medicines for cardiac procedures, in 2013 it was included for use in adult trauma patients with ongoing substantial hemorrhage, or at risk of severe hemorrhage within 8 hours of injury.3

Use of Tranexamic Acid to Decrease Allogeneic Blood Requirements

Providing universal access to safe blood products is a major objective of global health agencies, such as the WHO. However, considering the limited supply and cost of blood products and the risk of adverse outcomes associated with blood transfusion, interventions such as TXA administration that could reduce transfusion requirements are highly desirable. A systematic literature review suggests that administration of blood products is associated with increased morbidity and mortality, and urges reevaluation of transfusion practices among healthcare providers.4

Allogeneic blood transfusion is a multibillion-dollar industry with increasing costs and decreasing supply.5 In 2009 alone, the costs the American Red Cross incurred to provide whole blood and its components were estimated to be $2.217 billion.5 The most recent estimated cost of 1 U of red blood cells is $210.74, and the charge to the patient receiving the transfusion is $343.63.6 In comparison, 1 g of TXA supplied in a 10-mL vial is estimated to cost between $45 and $55.7 There is growing evidence to support the use of drugs such as TXA in the reduction of perioperative blood loss; this could reduce the frequency of blood transfusion requirements, ultimately allowing for improved allocation of resources and decreased costs to patients.5

Coagulation and Fibrinolysis

Hemostasis is the complex process of maintaining vascular integrity, limiting blood loss, and keeping blood in a fluid state. It is a delicate balance between vascular, platelet, and plasma factors that create a fibrin clot and the regulatory mechanisms of the fibrinolytic system that dissolve a fibrin clot.8 Hemostasis begins with the formation of a platelet plug, followed by the creation of a fibrin network that binds to and strengthens the platelet plug.8

Figure 1. Coagulation Cascade and Fibrinolysis

Abbreviations: Ca++, calcium ion; tPA, tissue plasminogen activator; uPA, urokinase.
The coagulation cascade and fibrinolytic system are activated simultaneously in normal circumstances, which allows repair of the vascular injury while preventing thrombosis and ischemia. Figure 1 depicts the different components of hemostasis: platelet-mediated hemostasis, plasma-mediated hemostasis, and fibrinolysis.

Just as important as forming a blood clot through coagulation is the process of removing the blood clot by fibrinolysis. The coordinated events of coagulation and fibrinolysis must occur together to allow appropriate blood flow without blood loss. The fibrinolytic system consists of plasminogen, which becomes converted into plasmin by tissue plasminogen activator (tPA) and urokinase. In the initial stages of coagulation, plasminogen becomes trapped in the clot while waiting to be activated into plasmin. Plasminogen activators tPA and urokinase are released slowly by the surrounding damaged endothelial cells. Within a few days of the clot being formed and the blood vessel stabilized, tPA reaches plasminogen and converts it into plasmin.

Once activated, lysine-binding sites on plasmin are responsible for binding with fibrin, cell surface receptors, and other proteins that help mediate fibrinolysis, such as α2-antiplasmin. One of the primary regulatory proteins of the fibrinolytic system, α2-antiplasmin is responsible for inactivating tPA and urokinase. Plasmin proteolyzes fibrin into soluble fibrin degradation products and dimer, which are then removed by the circulatory system. Figure 2 presents a schematic diagram of fibrinolysis.

Inhibition of fibrinolysis can occur at 2 points, by either inhibiting binding of the plasminogen activators or preventing the binding of plasmin to the fibrin mesh by blocking the lysine-binding sites. Tranexamic acid acts to prevent fibrinolysis by blocking the lysine-binding sites in a similar mechanism to α2-antiplasmin.

**Pharmacology of Tranexamic Acid**

Tranexamic acid is a synthetic antifibrinolytic amino acid that competitively blocks the lysine-binding sites of both plasminogen and plasmin, therefore inhibiting each enzyme’s action. Plasmin usually assists with dissolving blood clots, but when TXA saturates the lysine-binding sites of plasminogen and plasmin, plasminogen can still be converted to plasmin, but plasmin can no longer bind to fibrin. Without the presence of plasmin, there is no degradation of fibrin, and thus bleeding is reduced.

Potency comparisons have varied significantly according to tests used, but TXA has approximately 8 times the antifibrinolytic activity of EACA. Tranexamic acid is minimally protein bound and cleared by the kidneys. In patients with normal renal function, TXA’s half-life is 2 to 3 hours. Lower dosing strategies should be considered for patients with kidney disease because of TXA being cleared by the kidneys. Impaired renal function does not constitute a contraindication, but to avoid accumulation, it should be given over longer intervals and adjusted to patient weight. The most recent suggestions regarding renal dosing have been given by Nuttall et al (Table 1).

Side effects and adverse reactions of TXA are rare and appear limited; mild side effects include nausea, vomiting, and diarrhea. Absolute contraindications include active intravascular clotting disorders (Table 2). Use of TXA in conjunction with other procoagulant drugs could also increase the likelihood of thrombotic complications. The most recent 2011 Cochrane Review on antifibrinolitics indicated that TXA does not increase or decrease the risk of thrombotic events such as myocardial infarction, stroke, or renal dysfunction (Table 3). The low incidence of these adverse events and lack of evidence showing a positive correlation or association with TXA administration compared with placebo suggest its safety for use in the perioperative period.

In addition to undesirable procoagulant effects, a potential adverse effect of TXA is retinal change. In an animal model, doses approximately 7 times greater than the maximum dose for humans were associated with retinal changes. For diagnosis of TXA toxicity using an ophthalmic examination, it would require a patient to have functioning color vision before surgery. Therefore, patients with acquired defective color vision (color blindness) should not receive TXA. Despite no human testing having been done, it is still recommended to screen patients for acquired defective color vision.

Although TXA has a low incidence of side effects, its safety has recently been challenged. The large retrospective study of Sharma et al associated a cumulative high
dose of TXA (80 mg/kg) with an increased incidence of postoperative seizures in cardiac surgical patients. Controversy remains regarding this association because of the selection bias that confounds retrospective studies. Researchers theorize that seizures due to TXA may be secondary to neuronal γ-aminobutyric acid (GABA) inhibition or the crossing of TXA into cerebrospinal fluid.\(^{23}\)

There are only a few reported studies on the pharmacokinetics of intravenous TXA; therefore, determining the minimum effective dose that inhibits fibrinolytic activity has been challenging. Furthermore, those studies have investigated TXA plasma concentrations in healthy volunteers, and have not proven relevancy in more hemodynamically fragile older patient populations.\(^{24}\) Dosing schedules thus far have been empirical and hypothesized, and dosages cited in studies may vary over a 10-fold range (loading dose, 10-150 mg/kg).\(^{20}\) The discrepancy of dosing and efficacy among studies has created confusion about the optimal duration of TXA treatment and techniques to maintain therapeutic TXA concentrations.\(^{20}\) Comparatively, there is a higher ratio of cardiac studies concerning the dosing of TXA vs TXA dosing in orthopedic or trauma surgeries. Without definitive guidelines, anesthesia providers must proceed with caution when choosing a dosing regimen for their patient. A summary of dosing strategies for specific procedures can be seen in Table 1.

### Use in Cardiac Surgery

Close to 1.25 million adults worldwide undergo cardiac surgery each year.\(^{25}\) Surgical blood loss and the need for blood transfusions pose serious complications for many

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**Table 1. Recommended Dosing Strategies for Tranexamic Acid**

<table>
<thead>
<tr>
<th>Procedure (unlabeled use)</th>
<th>Dosing regimen(^a)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective cesarean delivery</td>
<td>10 min before incision: 1 g over 5 min</td>
<td>Gungorduk, 2013(^{14})</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>At delivery of anterior aspect of shoulder: 1 g over 5 min</td>
<td>Gungorduk, 2013(^{14})</td>
</tr>
<tr>
<td>Hip fracture surgery</td>
<td>15 mg/kg; repeat dose 3 h later</td>
<td>Zufferey, 2010(^{15})</td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td>30 mg/kg over 30 min, followed by 16 mg/kg/h until sternal closure; add 2 mg/kg to CPB circuit</td>
<td>Fergusson, 2008(^{16})</td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td>10 mg/kg over 20 min, followed by 2 mg/kg/h continued for 2 h after transfer to ICU; add 50 mg for a 2.5-L CPB circuit</td>
<td>Nuttall, 2008(^{13})</td>
</tr>
<tr>
<td>Spinal surgery</td>
<td>10 mg/kg, followed by 1 mg/kg/h until wound closure</td>
<td>Wong, 2008(^{17})</td>
</tr>
<tr>
<td>Total hip arthroplasty</td>
<td>15 min before skin incision: 10-15 mg/kg (or 1 g) over 5-10 min; followed by either of the following: 1. 10 mg/kg (or 1 g), 3 h after surgery 2. 1 mg/kg/h for 10 h</td>
<td>Oremus, 2014(^{18})</td>
</tr>
<tr>
<td>Total knee arthroplasty</td>
<td>First dose (10 mg/kg) immediately before tourniquet was deflated; repeat dose 3 h later</td>
<td>Camarasa, 2006(^{19})</td>
</tr>
<tr>
<td>Trauma</td>
<td>1 g over 10 min, followed by 1 g over 8 h; begin treatment within 8 h of injury</td>
<td>CRASH-2 Trial Collaborators, 2010(^{2})</td>
</tr>
<tr>
<td>Renal dosing, cardiac surgery</td>
<td>Same loading dose. Reduce maintenance infusion based on serum creatinine level as follows: 1. 1.6-3.3 mg/dL 1.5 mg/kg/h (25% reduction) 2. 3.3-6.6 mg/dL 1 mg/kg/h (50% reduction) 3. &gt; 6.6 mg/dL 0.5 mg/kg/h (75% reduction)</td>
<td>Nuttall, 2008(^{13})</td>
</tr>
</tbody>
</table>

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**Table 2. Contraindications to Tranexamic Acid\(^{12}\)**

<table>
<thead>
<tr>
<th>Absolute contraindication</th>
<th>Relative contraindication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquired defective color vision</td>
<td>History of vascular occlusive events</td>
</tr>
<tr>
<td>Hypersensitivity to TXA</td>
<td>Concomitantly with another procoagulant</td>
</tr>
<tr>
<td>Active intravascular clotting</td>
<td>Concomitantly with hormonal contraception</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td></td>
</tr>
</tbody>
</table>

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**Abbreviations:** CPB, cardiopulmonary bypass; ICU, intensive care unit.

\(^{a}\)Tranexamic acid should be administered intravenously immediately before skin incision unless specified otherwise. Tranexamic acid may be mixed with any crystalloid solution, and loading doses of varying amounts diluted in 50 to 250 mL administered over 5 to 30 minutes. With rapid administration, one may see orthostatic reaction; therefore, the recommended maximum rate of injection should be 100 mg/min.
cardiac surgical patients and have shown a strong association with in-hospital mortality. These risks have led to the use of antifibrinolytics such as TXA in the cardiac surgical patient to minimize blood loss. Although its use in cardiac surgery remains off-label, TXA shows promise in decreasing complications associated with blood loss.

Over the last 20 years, several meta-analyses have assessed the efficacy and safety of TXA using endpoints such as blood loss, frequency of blood transfusions, occurrence of adverse events, in-hospital mortality rate, and reoperation due to rebleeding. Unfortunately, the measurement of these endpoints has differed substantially among studies, making it difficult for researchers to decipher statistically significant results. To make analysis even harder, some studies have grouped the lysine analogs TXA and EACA together when comparing them with aprotinin, instead of assessing each independently. Overall, meta-analyses of randomized clinical trials agree that TXA is effective at decreasing complications associated with blood loss.

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.60</td>
<td>0.33 to 1.10</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.79</td>
<td>0.41 to 1.52</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.23</td>
<td>0.49 to 3.07</td>
</tr>
<tr>
<td>Deep venous thrombosis</td>
<td>0.71</td>
<td>0.35 to 1.43</td>
</tr>
<tr>
<td>Renal failure</td>
<td>0.89</td>
<td>0.33 to 2.37</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0.67</td>
<td>0.23 to 1.99</td>
</tr>
</tbody>
</table>

Table 3. Adverse Events Associated With Tranexamic Acid Administration during the Perioperative Period

Abbreviations: CI, confidence interval; RR, risk ratio.

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary embolism</td>
<td>0.67</td>
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<td>0.23 to 1.99</td>
</tr>
</tbody>
</table>

Use in Orthopedic Surgery
Orthopedic surgery can be associated with substantial intraoperative and postoperative blood loss and may require blood transfusion to replace blood loss. Although the pneumatic tourniquet is one strategy commonly used to address blood loss intraoperatively, recent meta-analyses have found that the use of a tourniquet does not decrease total blood loss or the transfusion rate in the perioperative period, and there are several adverse complications associated with its use, including increased risk of thromboembolic events.

However, TXA does effectively reduce postoperative blood loss. A Cochrane Review compares TXA with placebo in orthopedic surgery, including total knee and total hip arthroplasties. It finds that the use of TXA in orthopedic surgery reduced intraoperative blood loss by 116 mL per patient, and postoperative blood loss by 229 mL per patient.
mL per patient. Overall, the review concludes that the use of TXA in orthopedic surgery significantly reduces the total amount of blood lost during the perioperative period. This conclusion is based on the results of 20 trials that compared TXA with placebo in orthopedic surgery, including 1,201 patients, of which 605 received TXA and 596 received a placebo.

Many meta-analyses and studies have been conducted attempting to discern the best practice for administering TXA in orthopedic surgery; however, the best drug dosage, dosing regimen, or method of delivery of TXA for total knee or total hip arthroplasty has yet to be definitively determined. Studies either choose to give an upfront bolus of medication before inflation of tourniquet or skin incision, with no medication to follow, another bolus to follow, or a continuous infusion to follow. In a subgroup analysis of the meta-analysis by Huang et al, it was determined that regardless of the dosing scheme or amount delivered, there continued to be a positive effect and reduction of blood loss from TXA administration. A systematic review of the literature by Alshryda et al concluded that not only did TXA reduce blood loss, but it also reduced blood transfusion requirements during total knee arthroplasties. A meta-analysis evaluating the use of TXA for total hip arthroplasty also determined that TXA reduces intraoperative blood loss by a mean of 104 mL and reduces allogeneic blood transfusions. These meta-analyses support continued investigation and improved heterogeneity in further studies to obtain clear data on proper TXA administration.

A major concern with the use of TXA in orthopedic procedures is the risk of thrombosis. Administration of TXA has been slow to become popular in orthopedic populations because of this perceived risk. In their systematic review of the literature, Huang et al observed no increase in thromboembolic events in patients who received TXA compared with placebo. Other meta-analyses, performed by Alshryda et al and Sukeik et al, confirmed that there was no increased risk of adverse events or complications among study groups when TXA was used for total knee or total hip arthroplasty.

Although there remains controversy over optimal timing, dosage and method of administration of TXA in orthopedic surgery, there is overwhelming evidence to suggest that providing TXA in these procedures reduces blood loss in total knee and total hip arthroplasty. A survey of the literature reveals that TXA does not increase likelihood of adverse effects, such as deep-vein thrombosis or pulmonary embolism as previously believed. Continued research is necessary to fully determine best practice for TXA administration in orthopedic procedures.

Use in Neurosurgery
In spine surgery, higher blood loss occurs because of surgical techniques using spinal instrumentation since bony surfaces are not conducive to traditional hemostatic maneuvers used during soft-tissue surgery. Other potential causes of blood loss during spinal surgery include surgery duration and the number of vertebral levels decompressed. Formation of an epidural hematoma in close proximity to the spinal canal can lead to severe neurologic damage due to spinal cord or cauda equina compression.

A meta-analysis published in 2013 suggests TXA significantly decreases blood loss and frequency of blood transfusion, without increasing the risk of deep-vein thrombosis in spine surgery. However, a limitation of the publication is the small number of studies that were included in the meta-analysis. In 2008, Wong et al assessed the efficacy of TXA in adults undergoing elective spinal reconstructive surgery and found that calculated perioperative blood loss was significantly less in the TXA group vs the placebo group. The incidence of transfusion of blood products or the hospital length of stay did not differ significantly between the 2 groups.

Topical use of TXA in lumbar spine fixation surgery has the potential to reduce postoperative blood loss. Krohn et al compared 30 patients who received either TXA in irrigation solution during wound closure (n = 16) or saline irrigation solution alone (n = 14). The TXA group had significantly reduced postoperative blood loss compared with the placebo group.

Substantial perioperative blood loss is associated with surgical correction of scoliosis in the pediatric population and often requires administration of blood products. Sethna et al studied efficacy of TXA in children and adolescents undergoing elective spinal fusion, evaluating whether TXA administration would decrease blood loss or transfusion requirements. The TXA group had a statistically significant reduction in blood loss, by 41%, compared with the placebo.

Further research comparing dosing regimens, (eg, single bolus vs bolus and continuous infusion) is important to determine a safe and effective treatment for patients undergoing neurosurgery. At this time, there is a discrepancy between study dosing strategies, as well as insufficient numbers of studied patients to be able to determine best practice. Although current evidence strongly suggests TXA reduces blood loss in neurosurgery, additional research is necessary to establish best practice.

Use in Trauma Surgery
Trauma is the sixth leading cause of death worldwide, with hemorrhaging as the secondary cause. Trauma patients experience many coagulopathies, including hyperfibrinolysis leading to hemorrhage, and it is believed that trauma and surgery have similar hemostatic responses after severe vascular injury. Tranexamic acid may oppose hyperfibrinolysis and reduce mortality due to bleeding in trauma patients. Recently, TXA has been incorporated...
into several resuscitation and massive transfusion protocols across the United States.

The Clinical Randomization of an Antifibrinolytic in Significant Haemorrhage-2 (CRASH-2) study was the first to assess the effects of TXA administration in trauma patients with or at risk of major hemorrhaging. This study specifically looked at the influence of TXA on death rate, vascular occlusive events, and frequency of blood transfusions in more than 10,000 patients randomly assigned to receive TXA. Both all-cause mortality and risk of death due to bleeding were significantly reduced with TXA administration. Vascular occlusive events and blood product administration did not vary significantly between placebo and TXA groups. The absence of an increased risk of thrombotic events with TXA administration reemphasizes its safety profile. The power of the study may be reduced because diagnosis of traumatic hemorrhage is difficult and the study included patients in the trial who may not have been actually hemorrhaging. As of now, no other studies have been published comparing TXA with placebo in trauma patients.

Early administration of TXA is crucial to decrease blood loss. Therefore, the CRASH-2 study dosed TXA as a bolus of 1 g over 10 minutes and then an infusion of 1 g over 8 hours. The study investigators also believed that stopping TXA administration within 8 hours would decrease the risk of death due to thrombotic events and coagulopathies associated with trauma in the later hours after injury. In the event of an emergency, it may be difficult to determine a patient’s weight, so fixed dosing was the best solution.2

Use in Obstetric and Gynecologic Procedures

The use of TXA in obstetric-gynecologic procedures is controversial; however, multiple studies are under investigation to determine the safety and efficacy of TXA in the obstetric population. In 2013, global accounts of maternal mortality included 289,000 women who died from complications during pregnancy or childbirth, 99% of which occurred in developing countries.43 Because severe bleeding accounts for 27% of all maternal deaths worldwide, the use of TXA could prove beneficial in reducing blood loss and saving lives.

Tranexamic acid crosses the placenta, producing cord blood concentrations similar to maternal plasma concentrations.44 The FDA has categorized TXA as a Category B drug, because there have been no adequate, well-controlled studies in pregnant women; however, the administration of TXA in animal reproduction studies has failed to demonstrate risk to the fetus.12 Tranexamic acid is present in mothers’ breast milk at low concentrations, approximately 1% of the maternal serum concentration.44

The WHO recommends the use of TXA for postpartum hemorrhage in the event that the administration of oxytocin and second-line treatment options are ineffective, or if the bleeding is also due to trauma.43 A Cochrane Review published in 2010, concludes, from the results of 2 randomized control trials, that there was decreased postpartum blood loss after vaginal and cesarean births when TXA was used.46 However, the reviewers recommend that further investigations are necessary to illustrate the safety and efficacy of TXA in preventing postpartum hemorrhage.46

The use of TXA has been studied for populations undergoing elective cesarean delivery or vaginal delivery.44,47 Each study demonstrated decreased mean estimated blood loss in the TXA group compared with the placebo group. There was no significant difference between the 2 study groups for requiring blood transfusion or hospital length of stay for those undergoing cesarean delivery or having vaginal delivery. However, significantly more women in the placebo group required additional uterotonic agents and had lower hemoglobin and hematocrit levels the day after delivery in the study assessing use of TXA for vaginal delivery.14

A large, international, randomized, double-blind study, World Maternal Antifibrinolytic Trial (WOMAN), is currently under way to determine the efficacy of TXA compared with a placebo in 15,000 women with postpartum hemorrhage.48 It aims to determine the effect of early administration of TXA following vaginal or cesarean delivery assessing mortality, hysterectomy, surgical intervention, and blood transfusion.48 Studies to date have not been powered sufficiently to demonstrate risk of adverse vascular events related to TXA administration, but the WOMAN Trial will have sufficient power to determine the risk of TXA.46 Recruitment is ongoing, with hospitals from Africa, Asia, Latin America, and Europe currently collaborating.

Conclusion

Currently, TXA is being used in a wide range of surgical procedures without increased risk of thrombosis or other adverse effects.20 The results of several large clinical trials and many small trials support its use to decrease bleeding and reduce mortality and have a proven safe pharmaceutical profile.20 It is yet to be determined if the increased use of antifibrinolytic agents actually reduces the rate of blood transfusions, but TXA has been shown to reduce the degree of blood loss perioperatively. This inexpensive and safe drug is increasingly being used since aprotinin went off the market and because it is more potent than EACA. Further research is needed to differentiate possible alternate mechanisms of action of TXA, procedure-specific dosing regimens, and even use of TXA in traumatic brain injuries, including hemorrhage. In addition, future research should involve larger trials that definitively prove the effectiveness of TXA because existing smaller trials may be biased.
REFERENCES


38. Yuan C, Zhang H, He S. Efficacy and safety of using antifibrinolytic...


42. Lawson JH, Murphy MP. Challenges for providing effective hemostasis in surgery and trauma. *Semin Hematol.* 2004;41(1 suppl 1):55-64.


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American Association of Nurse Anesthetists

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July 11-14, 2016, Massachusetts; Northwest Seminars - 20 CEC. “Topics in Emergency Medicine: Emphasis on Pediatrics.” Sea Crest Beach Hotel, North Falmouth (Cape Cod), MA. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; fax (509) 547-7065; email, info@nwas.com; www.nwas.com.

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July 11-15, 2016, Montana; Northwest Anesthesia Seminars - 20 CEC. “Current Anesthesia Practice.” The Lodge at Whitefish Lake, Glacier National Park, Whitefish, MT. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; fax (509) 547-7065; email, info@nwas.com; www.nwas.com.

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July 14-17, 2016, Missouri; Northwest Anesthesia Seminars - 20 CEC. “Current Topics in Anesthesia.” Hilton Branson Convention Center Hotel, Branson, MO. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; fax (509) 547-7065; email, info@nwas.com ; www.nwas.com.

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July 18-21, 2016, California; Northwest Seminars - 20 CEC. “Topics in Emergency Medicine.” Disney’s Grand Californian Hotel & Spa, Anaheim, CA. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; email, info@nwas.com; www.nwas.com.


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August 9-12, 2016, California; Northwest Anesthesia Seminars - 24 CEC. “Relevant Topics in Anesthesia.” Hotel Solamar, San Diego, CA. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; fax (509) 547-7065; email, info@nwas.com; www.nwas.com.

August 15-18, 2016, North Carolina; Northwest Anesthesia Seminars - 20 CEC. “Topics in Anesthesia.” The Omni Grove Park Inn Resort, Asheville, NC. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; fax (509) 547-7065; email, info@nwas.com; www.nwas.com.

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August 30, 2016, Florida; Gulfcoast Ultrasound Institute - 7.25 CEC. “Ultrasound-Guided Regional Anesthesia.” Gulfcoast Ultrasound Institute, St. Pete Beach, FL. Lori Green, 4615 Gulf Blvd Ste 205, St. Pete Beach, FL 33706; (727) 363-4500; email, lori.green@gcus.com; www.gcus.com.


September 5-8, 2016, Nevada; Northwest Anesthesia Seminars - 20 CEC. “Topics in Anesthesia.” The Cosmopolitan, Las Vegas, NV. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.


September 10, 2016, Florida; Twin Oaks Anesthesia - 8 CEC. “Twin Oaks Anesthesia 2016 Cardiac Conference.” Renaissance Tampa International Plaza Hotel, Tampa, FL. Jonathan Kline, 26714 Winged Elm Drive, Wesley Chapel, FL 33544; (813) 837-5559; email, twinoaksanesthesia@gmail.com; www.twinoaksanesthesia.com.


September 12-16, 2016, California; Northwest Anesthesia Seminars - 20 CEC. “Clinical Anesthesia Update.” Tenaya Lodge, Fish Camp, CA. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

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September 26-29, 2016, California; Med City Anesthesia Seminars - 20 CEC. “A Taste of Anesthesia in Wine Country.” The Lodge at Sonoma Renaissance Resort & Spa, Sonoma, CA. Karissa Goodrich, CRNA, PO Box 711, St. Charles, MN 55972; (800) 538-0217; email, mail@medcityanesthesiaseminars.com; www.medcityanesthesiaseminars.com.

September 26-29, 2016, Rhode Island; Northwest Anesthesia Seminars - 20 CEC. “Current Topics in Anesthesia.” Hyatt Regency Newport Hotel & Spa, Newport, RI. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@northwestseminars.com; www.northwestseminars.com.

September 30-October 2, 2016, Florida; EverWont, Inc. - 20 CEC. “Topic in Anesthesia Practice.” SamiBel Harbour Resort & Spa, Fort Myers, FL. Kendall Pease, 3337 Crescent Oaks Blvd., Tarpon Springs, FL 34688; (619) 892-2467; email, kpease@everwont.com; www.everwont.com.

September 30-October 2, 2016, Massachusetts; Airway Management Education Center - 18.5 CEC. “The Difficult Airway Course: Anesthesia.” Hyatt Regency Boston, Boston, MA. Registration Office, 333 South State Street, Suite V-324, Lake Oswego, OR 97034; (866) 924-7929; fax (404) 795-0711; email, registrations@theairwaysite.com; www.theairwaysite.com.
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October 3-6, 2016, Bahamas; Northwest Anesthesia Seminars - 20 CEC. “Current Anesthesia Topics.” Atlantis Resort, Paradise Island, Bahamas. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

October 3-6, 2016, Florida; Northwest Anesthesia Seminars - 20 CEC. “Anesthesia Update.” Ritz Carlton Amelia Island, Fernandina Beach, FL. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

October 3-6, 2016, Maine; Encore Symposiums - 21 CEC. “Autumn in Bar Harbor & Acadia National Park 2016 Anesthesia Encore Symposiums.” The Harborside Hotel, Spa & Marina Resort, Bar Harbor, ME. Nancy LaBré, RN, 1907 Loch Lomond Court, Winston-Salem, NC 27106; (336) 768-9095; fax (336) 768-9055; email, nancy@escrnas.com; www.escrnas.com.

October 4-12, 2016, Spain; Northwest Anesthesia Seminars - 20 CEC. “Clinical Concerns in Anesthesia.” Celebrity Equinox, sailing from Barcelona, Spain. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

October 6-9, 2016, Tennesse; Northwest Anesthesia Seminars - 20 CEC. “Anesthesia Spectrum.” The Park Vista, a Doubletree Hotel, Gatlinburg, TN. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

October 7-9, 2016, New Mexico; Institute For Post Graduate Education - 15 CEC. “The Annual Balloon Fiesta Anesthesia Meeting.” Sheraton Albuquerque Uptown Hotel, Albuquerque, NM. Bernard Kuzava, CRNA, PO Box 28, Hastings, MI 49058; (877) 692-0433; fax (269) 948-2507; email, info@mideasttrvl.com; www.mideasttrvl.com.

October 7-9, 2016, Oregon; Oregon Association of Nurse Anesthetists - 17 CEC. “2016 ORANA Annual Conference.” Marriott Portland Downtown Waterfront, Portland, OR. Evelyn Bloomhart, PO Box 4444, Salem, OR 97302; (503) 874-1105; email, elyn@orregan-crna.org; www.orregan-crna.org.

October 15-18, 2016, Florida; Valley Anesthesia - 20 CEC. “CE for the CRNA.” Naples Grande Beach Resort, Naples, FL. Scott Schaus, 2583 Alpine Dr., Woodbury, MN 55125; (651) 395-0777, fax (651) 846-5034, email, scott@valleyanesthesia.com; www.valleyanesthesia.com.

October 17-20, 2016, Rhode Island; Encore Symposiums - 21 CEC. “Newport Mansions Fall Foliage Experience 2016 Anesthesia Encore Symposiums.” Hotel Viking, Newport, RI. Nancy LaBré, RN, 1907 Loch Lomond Court, Winston-Salem, NC 27106; (336) 768-9095; fax (336) 768-9055; email, nancy@escrnas.com; www.escrnas.com.

October 17-21, 2016, Colorado; Northwest Anesthesia Seminars - 20 CEC. “Clinical Anesthesia Update.” Gateway Canyons Resort, Gateway, CO. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

October 21-23, 2016, Kansas; Core Concepts Review - 24 CEC. “Core Concepts Anesthesia Review/Refresher Course.” University of Kansas at KUMC, Kansas City, KS. Marianne S. Cosgrove, CRNA, DNSAP, APRN, 64 Signal Hill Road, Madison, CT 06443; (203) 567-0272; email, support@ccanesthesiareview.com, www.ccanesthesiareview.com.


October 30-31, 2016, Hawaii; Northwest Anesthesia Seminars - 20 CEC. “Anesthesia Topics.” Hyatt Regency Maui, Lahaina, HI. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

November 2, 2016, Illinois; American Association of Nurse Anesthetists - 8 CEC. “Essentials of Obstetric Analgesia/Anesthesia Workshop.” AANA Foundation Learning Center, Park Ridge, IL. 222 S. Prospect, Park Ridge, IL 60068; (847) 655-8797; email, meetings@aana.com; www.aana.com/meetings.

November 3-5, 2016, Illinois; American Association of Nurse Anesthetists - 21 CEC. “Spinal and Epidural Workshop.” AANA Foundation Learning Center, Park Ridge, IL. 222 S. Prospect, Park Ridge, IL 60068; (847) 655-8797; email, meetings@aana.com; www.aana.com/meetings.

November 3-6, 2016, Florida; Northwest Anesthesia Seminars - 20 CEC. “Keys in Anesthesia.” Westin Resort & Marina, Key West, FL. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

November 4-6, 2016, Nevada; Airway Management Education Center - 18.5 CEC. “The Difficult Airway Course: Anesthesia.” Bally's Resort Las Vegas, Las Vegas, NV. Registration Office, 333 South State Street, Suite V-324, Lake Oswego, OR 97034; (866) 924-7929; fax: (404) 795-0711; email, registrations@theairwaysite.com; www.theairwaysite.com.

November 4-6, 2016, Tennessee; Focus Nurse Anesthesia Review - 15 CEC. “The Basics and Beyond Session 1: Focus in Music City.” Sheraton Nashville Downtown Hotel, Nashville, TN. Lindsay Studt, 5031 Timber Lake Trail, Clarkston, MI 48346; (248) 618-3481; email, info@focusnar.com; www.focusnar.com.

November 5-6, 2016, Florida; Northwest Anesthesia Seminars - 14 CEC. “Ophthalmic Regional Block Hands-On Workshop.” The Hyatt Grand Cypress, Orlando, FL. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

November 5-20, 2016, India; Spieckermann Travel - 20 CEC. “Current Issues in CRNA Practice.” India. Michael Rieker, DNP, CRNA, Nurse Anesthesia Program, Medical Center Boulevard, Winston-Salem, NC 27157; (800) 645-3233; fax (586) 775-9556; email, info@mideasttrvl.com; http://www.mideasttrvl.com/.

November 6, 2016, Arizona; Encore Symposiums - 8 CEC. “Sedona Ultrasound Workshop 2016 by Encore Symposiums.” Hilton Sedona Resort at Bell Rock, Sedona, AZ. Nancy LaBré, RN, 1907 Loch Lomond Court, Winston-Salem, NC 27106; (336) 768-9095; fax (336) 768-9055; email, nancy@escrnas.com; www.escrnas.com.
November 6-9, 2016, South Carolina; Wake Forest School of Medicine - 19 CEC. “22nd Annual Advances in Physiology & Pharmacology in Anesthesia and Critical Care.” The Westin Hilton Head Island Resort & Spa, Hilton Head Island, SC. Pam Martin, Medical Center Blvd., Winston-Salem, NC 27157; (336) 716-2712; Fax (336) 716-8190; email, pdmartin@wakehealth.edu; www.Wakehealth.edu/anest-cme-annual-meeting.

November 7-10, 2016, Arizona; Encore Symposiums - 21 CEC. “Sedona Red Rock & Grand Canyon Adventure 2016 Anesthesia Encore Symposiums.” Hilton Sedona Resort at Bell Rock, Sedona, AZ. Nancy LaBrie, RN, 1907 Loch Lomond Court, Winston-Salem, NC. 27106; (336) 768-9095; fax (336) 768-9055; email, nancy@escrnas.com; www.escrnas.com.

November 7-10, 2016, Florida; Institute For Post Graduate Education - 20 CEC. “Discussions in Clinical Anesthesia.” Westin Key West Resort & Spa, Key West, FL. Bernard Kuzava, CRNA, PO Box 28, Hastings, MI 49058; (877) 692-0430; fax (269) 948-2307; email, ipgeseminars@ipge.com; www.ipge.com.

November 7-10, 2016, Virginia; Nurse Anesthesiology Faculty Associates - 22 CEC. “40th Annual Anesthesia Conference.” Williamsburg Lodge, Williamsburg, VA. Michael Fallacaro, PO Box 980226, Richmond, VA 23298; (804) 828-6734; email, nafa@vcu.edu; www.nafa-va.org.

November 11-13, 2016, California; University of California, Davis Health System - 20.75 CEC. “27th Annual UC Davis Anesthesiology Update.” Monterey Plaza Hotel, Monterey, CA. Beng Salud, 4150 V Street, PSSB Suite 1200, Sacramento, CA 95817; (916) 734-1574; fax (916) 734-2975; email, bsalud@ucdavis.edu; www.ucdmc.ucdavis.edu/anesthesiology/.

November 11-13, 2016, Florida; Frank Moya Continuing Education Programs - 20 CEC. “45th Annual Refresher Course for Nurse Anesthetists.” Hilton Orlando Walt Disney World Resort, Lake Buena Vista, FL. Frank Moya, MD, 1828 SE First Ave, Ft. Lauderdale, FL 33316; (954) 763-8811; fax (954) 762-9111; email, info@currentreviews.com; www.currentreviews.com.

November 14, 2016, Nevada; Northwest Anesthesia Seminars - 8 CEC. “Business Concepts in Healthcare: A Practical Approach for Healthcare Providers.” The Cosmopolitan, Las Vegas, NV. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

November 14-18, 2016, Costa Rica; Southwest Anesthesia and Medical Seminars - 20 CEC. “Medical Spanish for Health Professionals.” Playa Flamingo, Guanacaste, Costa Rica. Richard M. Saucier,CRNA, MBA, 4406 North Saddle View Drive, Tucson, AZ 85730; (614) 382-3393; email, saucier@saoil.com; www.swamseminars.com.

November 28-December 1, 2016, Florida; Nurse Anesthesiology Faculty Associates - 22 CEC. “35th Annual Anesthesia Meeting.” Disney’s Yacht and Beach Club Resort, Lake Buena Vista, FL. Michael Fallacaro, PO Box 980226, Richmond, VA 23298; (804) 828-6734; email, nafa@vcu.edu; www.nafa-va.org.

November 29-December 2, 2016, California; Northwest Anesthesia Seminars - 20 CEC. “Topics in Anesthesia.” Napa Valley Marriott Hotel and Spa, Napa, CA. Anna Hilliard, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

November 29-December 2, 2016 Georgia; Northwest Anesthesia Seminars - 24 CEC. “Current Topics in Anesthesia.” Hyatt Regency Savannah, Savannah, GA. Anna Hilliard, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

December 5-8, 2016, Bahamas; International Seminars, LLC - 20 CEC. “Nurse Anesthesia Update.” Atlantis, Paradise Island, Bahamas. Barbara McNulty, 1828 SE First Avenue, Ft. Lauderdale, FL 33316; (954) 763-8811; fax (954) 762-9111; email, info@nurseanesthetist.com; www.nurseanesthetist.com.

December 5-9, 2016, Christiansted, St. Croix, US Virgin Islands; Northwest Anesthesia Seminars - 20 CEC. “Applied Pharmacology Update.” The Buccaneer, Christiansted, St. Croix, US Virgin Islands. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.

December 13-16, 2016, Florida; Northwest Anesthesia Seminars - 20 CEC. “Current Topics in Anesthesia.” Eden Roc Miami Beach, Miami Beach, FL. NWAS, PO Box 2797, Pasco, WA 99302; (800) 222-6927; (509) 547-7065; fax (509) 547-1265; email, info@nwas.com; www.nwas.com.


January 16-20, 2017, Aruba; Frank Moya Continuing Education Programs - 20 CEC. “Caribbean Seminar in Anesthesiology.” Aruba Marriott Resort & Stellaris Casino, Palm Beach, Aruba. Frank Moya, MD, 1828 SE First Ave, Ft. Lauderdale, FL 33316; (954) 763-8811; fax (954) 762-9111; email, info@currentreviews.com; www.currentreviews.com.

February 4-10, 2017, Colorado; University of Florida - 25 CEC. “Concepts in Anesthesiology.” Steamboat Grand Hotel, Steamboat Springs, CO. Medical Seminars LLC, 2451 Cumberland Parkway, Suite 3366, Atlanta, GA 30339; (800) 871-0326; fax (770) 847-8655; email, info@conceptsinanesthesiology.com; www.conceptsinanesthesiology.com.

February 24-26, 2017, Florida; American Association of Nurse Anesthetists. “Assembly of School Faculty.” Westin Beach Resort, Fort Lauderdale, FL. (847) 655-8797; email, meetings@aana.com; www.aana.com/meetings.


February 16-18, 2018, Arizona; American Association of Nurse Anesthetists. “Assembly of School Faculty.” The Scottsdale Resort, Scottsdale, AZ. (847) 655-8797; email, meetings@aana.com; www.aana.com/meetings.
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<tr>
<th>Date</th>
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<tr>
<td>September 21-25, 2018</td>
<td>Massachusetts</td>
<td>American Association of Nurse Anesthetists</td>
<td>Hynes Convention Center, Boston, MA. (847) 655-8797; email, <a href="mailto:meetings@aana.com">meetings@aana.com</a>; <a href="http://www.aana.com/meetings">www.aana.com/meetings</a>.</td>
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<tr>
<td>April 5-9, 2019</td>
<td>Washington, DC</td>
<td>American Association of Nurse Anesthetists</td>
<td>Grand Hyatt, Washington, DC. (847) 655-8797; email, <a href="mailto:meetings@aana.com">meetings@aana.com</a>; <a href="http://www.aana.com/meetings">www.aana.com/meetings</a>.</td>
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<tr>
<td>August 9-13, 2019</td>
<td>Illinois</td>
<td>American Association of Nurse Anesthetists</td>
<td>Hyatt Regency Chicago Hotel, Chicago, IL. (847) 655-8797; email, <a href="mailto:meetings@aana.com">meetings@aana.com</a>; <a href="http://www.aana.com/meetings">www.aana.com/meetings</a>.</td>
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