

# Heart Block and Prolonged Q-Tc Interval Following Muscle Relaxant Reversal: A Case Report

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*Heart block and Q-Tc interval prolongation have been reported with several agents used in anesthesia, and the US Food and Drug Administration mandates evaluation of the Q-T interval with new drugs. Drug-induced Q-T interval prolongation may precipitate life-threatening arrhythmias, is considered a precursor for torsades de pointes, and may predict cardiovascular complications.*

*In the patient described in this article, heart block occurred and the Q-Tc interval became prolonged after muscle relaxant reversal with neostigmine; both were considered to be related to the combination of agents used in the case, as well as to other predisposing fac-*

*tors such as morbid obesity. The agents used that affected cardiac conduction were neostigmine, desflurane, droperidol, dolasetron, and dexmedetomidine.*

*Although the heart block was resolved after 2 doses of atropine, prolonged P-R and Q-Tc intervals persisted into the immediate postoperative period but returned to baseline within 4 hours. Clinical implications of this report include increasing awareness of the multitude of factors affecting Q-T interval prolongation during anesthesia.*

**Key words:** Dexmedetomidine, heart block, neostigmine, Q-T interval prolongation.

**D**rug-induced Q-T interval prolongation may precipitate life-threatening arrhythmias and is considered a precursor for torsades de pointes. Several drugs used during anesthesia are known to affect the Q-T interval, including inhalation agents and antiemetics such as droperidol and the 5-hydroxytryptamine<sub>3</sub> antagonists.<sup>1,2</sup> Several predisposing physical conditions have also been associated with Q-T prolongation, including morbid obesity and genetic predisposition, and females are more at risk. In addition, along with effects on heart rate and cardiac conduction, Q-T interval prolongation may occur during reversal of muscle relaxation using combinations of glycopyrrolate and neostigmine.<sup>3,4</sup>

In a patient undergoing gastric bypass, dexmedetomidine was being used along with desflurane as the primary anesthetics, supplemented by fentanyl, 5 µg/kg. During reversal of the muscle relaxant, second-degree heart block and Q-T prolongation developed 5 minutes after administration of a combination of glycopyrrolate and neostigmine. Although the heart block resolved after 2 doses of atropine, the P-R and rate-corrected Q-T interval (Q-Tc) on the electrocardiogram (ECG) remained prolonged for 4 hours postoperatively. Due to the refractory nature of the Q-Tc interval prolongation, the heart rhythm and conduction changes were considered to have been related not only to neostigmine but also to the concomitant use of other drugs affecting conduction and the Q-Tc interval.

## Case Report

The patient was a 41-year-old, 165-kg, morbidly obese woman undergoing a gastric restrictive procedure with short-limb Roux-en-Y gastroenterostomy. Her medical history was significant for smoking, pseudotumor cerebri with shunt placement, and use of phentermine for weight loss. Current medications included furosemide for ankle edema, with physical examination revealing 3+ pitting edema in both legs. The neurologic findings were unremarkable, and the cardiovascular examination demonstrated regular rate and rhythm, with no rubs or murmurs. An ECG revealed normal sinus rhythm, with left axis deviation, a P-R interval of 0.186 seconds, and a Q-T interval of 0.386 seconds. The preoperative laboratory values were normal, with a serum potassium level of 4.4 mEq/L and a hematocrit value of 45%.

Induction of anesthesia was accomplished with propofol, 150 mg; lidocaine, 100 mg; and desflurane. Rapid-sequence induction with cricoid pressure was used with 200 mg of succinylcholine. Maintenance of neuromuscular relaxation was achieved with vecuronium (total dose, 24 mg), and anesthesia was maintained with desflurane and a dexmedetomidine infusion. The initial bolus of dexmedetomidine was 124 µg (based on 1 µg/kg for 75% of body weight), and the initial infusion dose was 0.4 µg/kg per hour, with a total dose of 324 µg. Fentanyl, 5 µg/kg (600 µg), was administered with induction, and desflurane was titrated for hemodynamic control and to maintain the bispectral monitoring index between 40 and

P-R interval: 231 s  
QRS duration: 94 s

Q-T interval: 403 s  
Q-T interval corrected: 441 s

Axes: P wave: 75°  
Mean QRS vector: -58°

ST segment: 84°  
T wave: 60°



**Figure 1.** Electrocardiographic impression: sinus rhythm; rate, 72 beats per minute. First-degree atrioventricular block. Left anterior fascicular block. Late transition. Borderline low voltage in frontal leads.

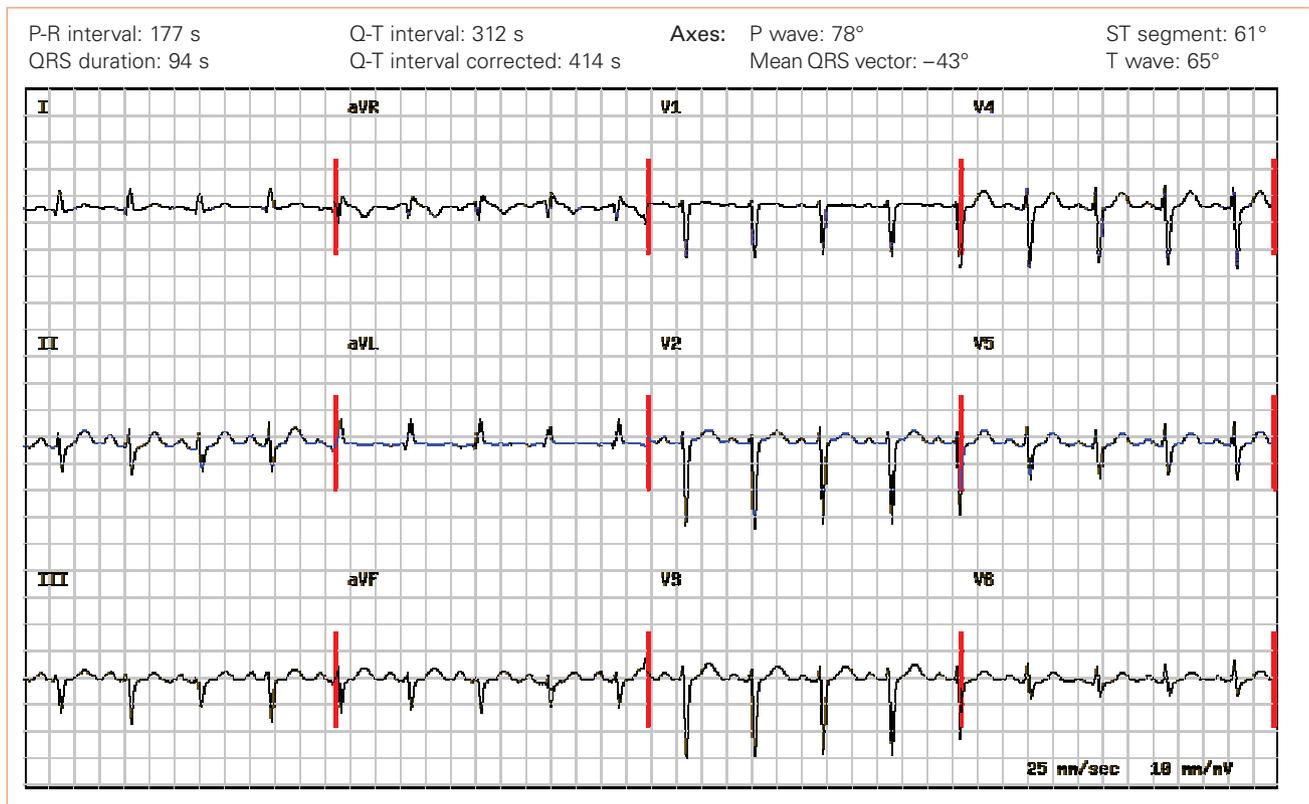
60. Intraoperatively, vital signs were stable, with the heart rate ranging between 60 and 98 beats per minute and ST segments showing no signs of ischemia. The systolic blood pressure ranged between 96 and 160 mm Hg, and the diastolic blood pressure ranged between 50 and 92 mm Hg. The oxyhemoglobin saturation was maintained between 96% and 100% with a mixture of oxygen and air, an inspired oxygen concentration (fraction of inspired oxygen [ $FI_{O_2}$ ]) of 0.60 to 0.64, and an end-tidal carbon dioxide ( $ETCO_2$ ) level of 32 to 40 mm Hg.

After closure of the fascia, the dexmedetomidine infusion rate was increased to 0.7  $\mu$ g/kg per hour according to the protocol for this anesthetic technique, and droperidol, 0.625 mg, was administered intravenously for prevention of postoperative nausea and vomiting. Desflurane was discontinued and nitrous oxide initiated at 60%. Train-of-four testing revealed 2 of 4 twitches, and reversal of neuromuscular blockade was accomplished with 0.6 mg of glycopyrrolate and 4 mg of neostigmine.

The initial vital signs after reversal revealed a sinus rhythm with heart rate of 74 beats per minute, blood pressure of 112/54 mm Hg, an oxyhemoglobin saturation of 95%, and an  $ETCO_2$  level of 39 mm Hg. However, 5 minutes after reversal medications were administered, the heart rhythm suddenly converted into second-degree heart block with a ventricular rate of 31 beats per minute and a prolonged P-R interval (0.24 seconds). Vital signs revealed a blood pressure of 82/42 mm Hg, an oxygen sat-

uration of 92%, and an  $ETCO_2$  level of 40 mm Hg. This rhythm persisted for 4 minutes and 24 seconds, during which time 0.4 mg of atropine was administered, and the rhythm subsequently returned to normal with 1:1 conduction. The blood pressure improved to 101/65 mm Hg, the  $ETCO_2$  measured 36 mm Hg, the oxyhemoglobin saturation was 95%, and the ST segments remained comparable to baseline. The dexmedetomidine infusion and nitrous oxide were immediately discontinued, the  $FI_{O_2}$  was increased to 1.0, desflurane was reinstated, and events preceding the rhythm deterioration were assessed for cause.

The ECG recording was examined for ST changes suggestive of myocardial ischemia, but no change greater than a 0.2 decrease in lead II had occurred before the event. Although vasovagal influences could have had a role in the development of heart block, such influences were not considered the primary factor because the fascia was almost closed. In addition, because desflurane had just been discontinued and nitrous oxide introduced, light anesthesia could have been a factor; however, bispectral monitoring index had remained within 40 to 60 and expired desflurane concentrations were consistent with previous readings. The blood pressure had been within the range of previous readings, and the oxyhemoglobin saturation had been 95% or higher so that inadequate myocardial oxygenation was an unlikely cause. The only changes in the conduct of the anesthetic were an in-



**Figure 2.** Electrocardiographic impression: sinus tachycardia; rate, 106 beats per minute. Left axis deviation, consider left anterior fascicular block. Late transition.

crease in the dexmedetomidine infusion rate, administration of droperidol and dolasetron, and reversal of vecuronium with neostigmine.

Closure of the skin ensued, and preparations were made for emergence and extubation. Spontaneous ventilation was assisted, and no further medications or anesthetic modifications were used. Two minutes and 36 seconds after return to sinus rhythm, second-degree heart block reoccurred with an atrial rate of 74 beats per minute and a ventricular response of 37 beats per minute. Another dose of atropine, 0.4 mg, was administered, and within 72 seconds, the rhythm had again converted to 1:1 conduction. At this time, other vital signs revealed a blood pressure of 106/54 mm Hg, an  $\text{ETCO}_2$  of 35 mm Hg, an oxyhemoglobin saturation of 95%, and a P-R interval of 0.24. Hemodynamic parameters remained unchanged until the procedure was complete, at which time the desflurane was discontinued.

On emergence, the patient's neurological signs were intact, and she had an adequate respiratory effort and was subsequently extubated. No cardiovascular symptoms were noted, with an initial postoperative blood pressure of 140/70 mm Hg, a heart rate of 74 beats per minute, a respiratory rate of 16 breaths per minute, and an oxyhemoglobin saturation of 95%. The patient remained mildly sedated, and no additional pain medications were required until discharge from the postanesthesia care unit.

The troponin and creatine kinase-MB fraction levels were normal, and a 12-lead ECG revealed sinus rhythm and a heart rate of 72 beats per minute. However, the P-R interval was 0.231 seconds, the Q-T interval was 0.403 seconds, and the Q-Tc interval was 0.441 seconds, in comparison with preoperative values of 0.186, 0.386, and 0.407, respectively (Figure 1). No further episodes of heart block occurred during the patient's hospital stay, and the 12-lead ECG done 4 hours after dexmedetomidine infusion was discontinued revealed a P-R interval of 0.177, a Q-T interval of 0.312, and a Q-Tc interval of 0.414 (Figure 2).

## Discussion

Morbid obesity (body mass index,  $> 35 \text{ kg/m}^2$ ) is associated with sleep apnea, decreased functional residual capacity, decreased lung compliance, and increased work of breathing.<sup>5-7</sup> Morbidly obese patients undergoing gastric bypass surgery may be sensitive to the respiratory depressive effects of opioid analgesic drugs and are more likely to require postoperative ventilation to avoid hypoxia and hypercarbia.<sup>8,9</sup> Alternative drugs such as clonidine and ketamine have been used to potentiate analgesia and decrease the risk of respiratory effects by lowering the needed dose of opioids.<sup>10,11</sup> Dexmedetomidine is an  $\alpha_2$ -adrenergic agonist similar to clonidine with sedative, analgesic, and anxiolytic properties. Intraopera-

tive anesthetic requirements are decreased, as are postoperative opioid requirements,<sup>12</sup> and it has a more than 7- to 8-fold affinity for  $\alpha_2$  receptors compared with clonidine.<sup>13</sup> Dexmedetomidine has been advocated to minimize the risk of respiratory depression in morbidly obese patients by decreasing inhalation and opioid requirements during surgery, along with catecholamine levels.<sup>10,14-19</sup> In this institution, the standard protocol for gastric bypass includes desflurane at or below the minimal alveolar concentration (ETCO<sub>2</sub> < 6%) and dexmedetomidine administration at a rate of 0.4 to 0.7  $\mu\text{g}/\text{kg}$  per hour.

Along with the use of antiemetics, reversal of muscle relaxation is routinely performed with glycopyrrolate and neostigmine near the end of the procedure. As mentioned previously, reversal of muscle relaxation may be associated with rhythm disturbances ranging from mild bradycardia to asystole.<sup>20</sup> In addition, reversal of the muscle relaxant may be associated with cardiac conduction changes ranging from Q-Tc interval changes to heart block.<sup>1</sup> Although the patient described herein received 0.6 mg of glycopyrrolate along with 4 mg of neostigmine, these doses may be considered low,<sup>4,21</sup> contributing to any effect neostigmine may have had on rhythm and conduction.

Along with neostigmine, volatile anesthetic agents such as sevoflurane have also been associated with Q-Tc interval prolongation, and desflurane is associated with a higher degree of Q-T interval prolongation.<sup>22</sup> In addition, ancillary agents commonly used for the prevention of postoperative nausea and vomiting, such as droperidol and dolasetron, have also been demonstrated to cause Q-Tc prolongation.<sup>23</sup> Although the dose of droperidol used in the present case has not been associated with significant increases in the Q-Tc interval, higher doses may prolong the Q-T interval and may increase any predisposition to heart block or conduction defect.<sup>24,25</sup> Although the dose of droperidol used in the present case was much smaller than doses cited in most case studies, its use may have further impaired conduction in this patient. In addition, the serotonin antagonist, dolasetron, may have had a role in the prolongation of the Q-T interval. Although prolongations in the Q-T interval are small, reversible, and clinically insignificant,<sup>26</sup> the effects may have been additive.

Although the occurrence of clinically significant respiratory depression is uncommon with dexmedetomidine, cardiovascular effects are quite common and include moderate decreases in blood pressure and heart rate, conduction defects, and severe bradycardia that is refractory to standard doses of glycopyrrolate.<sup>18,19</sup> In addition, dexmedetomidine and other  $\alpha_2$  agonists have been shown to depress atrioventricular nodal conduction and prolong the P-R interval, so they must be used cautiously in patients with existing prolongation of the P-R interval or spontaneous bradycardia.<sup>27,28</sup> Asystole in a patient receiving high doses of anticholinesterase (ie, pyridostigmine,

Drug or risk factor	Effect
Desflurane	Prolonged Q-T interval
Fentanyl	Prolonged Q-T interval
Succinylcholine	Prolonged Q-T interval
Neostigmine	Prolonged Q-T interval
Dolasetron	Prolonged Q-T interval
Droperidol	Prolonged Q-T interval
Dexmedetomidine	Prolonged Q-T interval?
Vagal influences	Bradycardia, heart block?
Female gender	Prolonged Q-T interval
Morbid obesity	Prolonged Q-T interval

**Table.** Drugs and Risk Factors With Known Effects on the Q-T Interval

120 mg 3 times a day) was attributed to dexmedetomidine, and severe bradycardia in a 5-week-old infant was attributed to an interaction between digoxin and dexmedetomidine infusion.<sup>29,30</sup> Dexmedetomidine has the potential to augment bradycardia induced by vagal stimulation, which may result from closing of the fascia, and its effects may have been additive.<sup>31</sup>

The use of fentanyl has also been associated with bradycardia<sup>32</sup> and, in the present case, may have contributed to decreases in the heart rate and sympathetic outflow. Although no fentanyl had been administered within the previous 105 minutes, the fentanyl dose was 600  $\mu\text{g}$  (3.6  $\mu\text{g}/\text{kg}$ ), and its effect on heart rhythm, rate, and Q-T interval would have been minimal but may have resulted in an additive effect.<sup>33</sup> Morbid obesity may be associated with increases in the maximum Q-T interval,<sup>34,35</sup> with up to 47% of patients demonstrating abnormally prolonged Q-Tc intervals. Women are twice as susceptible as men to acquired Q-T interval prolongation, especially when under the influence of anesthesia.<sup>36,37</sup>

Heart block and Q-Tc interval changes in this patient most likely represent multifactorial influences of the anesthetic used (Table). Although the initial episode of heart block could have been ascribed to neostigmine because 1:1 conduction was restored with anticholinergic, the refractory nature of the Q-T interval prolongation would seem to be related to longer lasting agents such as droperidol, dolasetron, and dexmedetomidine. Other physiologic variables, including obesity and gender, may have had a role, but clearly, because the Q-Tc interval was within normal limits before induction of anesthesia and 4 hours after emergence, the anesthetic technique seems to have had a major role. Implications of this particular case involve awareness of the potential of Q-T interval prolongation when using multiple agents associated with Q-Tc prolongation. In addition, if Q-T interval prolongation is recognized, consideration should be given to immediate substitution of propofol for agents associated with this effect.<sup>38,39</sup>

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