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Atropine Induced Paradoxical Atrioventricular Conduction Block in a Jindo Dog

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Abstract : A 6-month-old intact male Jindo dog was underwent surgery for hip fracture caused by hit by a car. Routine laboratory tests performed prior to surgery found no significant abnormalities, which might increase risks associated with general anesthesia. The dog was premedicated with atropine, induced general anesthesia with thiopental sodium and maintained with isoflurane. Forty minutes after surgery, the dog was suddenly bradycardic. Atropine (18 ug/kg) was slowly infused intravenously to normalize heart rate. However, paradoxically the dog showed slower heart rate with intermittent atrioventricular block (2nd degree type I) after atropine infusion. The dog's rhythm was returned to normal rate 7 minutes after ephedrine was infused. This is a rare case of paradoxical atrioventricular block induced by high dose of atropine in a dog.

Key words **:** bradycardia, paradoxical, atrioventricular block, atropine

Introduction

Atropine is a well known pre-anesthetic agent used in preventing side-effects associated with anesthetic agents (i.e. prevent bradycardia and reduce airway secretion). Paradoxical sinus bradycardia induced by low-dose atropine (2 ug/kg, IV) is well-described in human medical literatures (4,7). Similar findings have been also described in veterinary literatures (11,14). Low-dose atropine can decrease heart rate (8,10) and increases respiratory sinus arrhythmia (13) in human, because it may paradoxically increase parasympathetic activity. However, high doses of atropine (15 ug/kg, IV) can induce parasympatholytic activities by blocking muscarinic receptors at the cardiac sinoatrial node. Therefore the heart rate can be markedly increased (5,12).

Atrioventricular (AV) block refers to conduction disturbances altering impulse conduction from the sinus node to the ventricles. First degree and second degree type I AV block can be occurred by increased vagal tone. The conditions which can increase parasympathetic activities (i.e. anesthetic drugs) cause these AV blocks. In clinic, atropine is often used to revert sinus bradycardia (often associated with low grade AV block) to normal rate of sinus rhythm. However, recent studies found that the effect of atropine to the heart rate is more likely dose-dependent (9).

Although atropine associated bradyarrhythmias have already been reported in human, no such report has been published in veterinary literatures. In this case report, we described paradoxical AV blocks induced by atropine in a dog

Case

A 6-month-old intact male Jindo dog was presented at Veterinary Teaching Hospital with primary complaint of hip fracture caused by automobile accident. In physical examination, the dog was mildly dehydrated, but was normal in other vital signs. Pre-operative blood pressure measurement and electrocardiogram revealed no abnormalities. In addition, routine laboratory tests including coagulation tests found no significant abnormalities, which might increase risks associated with general anesthesia. According to the referring veterinarian, the dog was unusually slow in recovering from general anesthesia and profoundly sedated after additional dose of intravenous atropine administration at 0.05 mg/kg. The dog was induced anesthesia with thiopental at 3 mg/kg IV without atropine premedication. After tracheal intubation, the anesthesia was maintained by isoflurane at 1.5-2.5% concentration in 100% oxygen. Dogs were mechanically ventilated at a rate of 20-30 times per minute using a volume-cycled respirator (MDS Matrix 3000, Hallowell, USA) with tidal volume set at 10-20 ml/kg so as to maintain eucapnia as monitored by a capnograph (Datex Capnomac Ultima, Finland).

Forty minutes after general anesthesia, the dog's HR gradually decreased to 50 beats minute (sinus bradycardia). However, no other abnormalities were found in continuous lead II rhythm strips. In order to normalize heart rate, atropine at 0.03 mg/kg was administered slowly IV. However, immedi-

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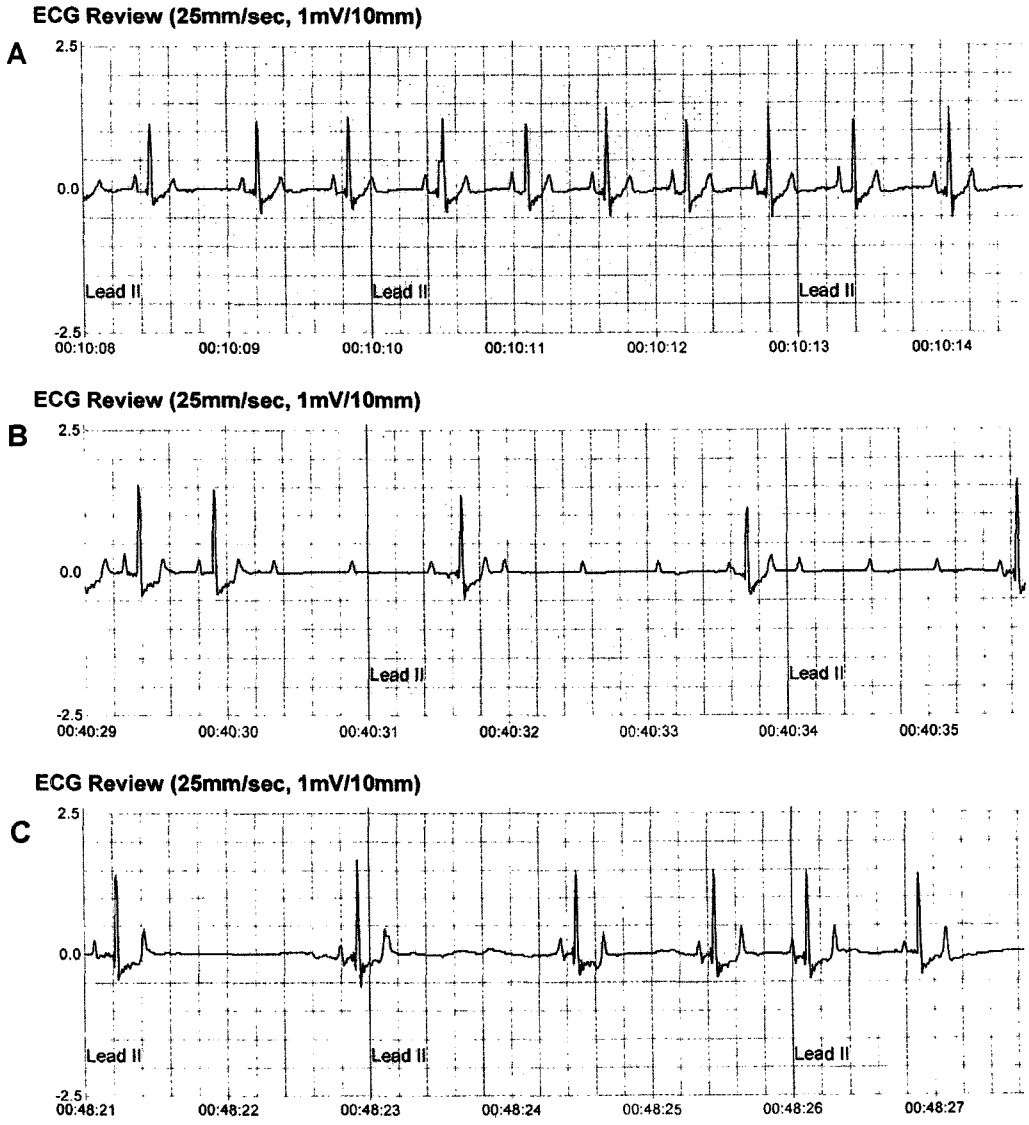

Fig 1. Lead II ECG rhythm strip recorded during surgery. A: Recorded at 10 minutes after general anesthesia. ECG strips showed normal sinus rhythm at 100 bpm of heart rate. A: Recorded at 30 seconds after atropine (0.018 mg/kg) administration. ECG strips showed high-grade atrioventricular (AV) block at atrial rate 130 bpm and ventricular rate 50 bpm. C: Recorded at 7 minutes after ephedrine administration. ECG strips showed that heart rhythm gradually returned to normal sinus rhythm at 60 bpm of heart rate.

ately after atropine infusion, the heart rate was paradoxically decreased further and sinus rhythm was changed to intermittent high grade atrioventricular heart blocks (Fig 1). This bradyarrhythmia was progressed over the next 1-2 minutes to high-grade AV heart block. Although the atrial rate had increased to 130 beats per minute, the ventricular rate decreased to 50 beats per minute. Ephedrine was administered IV to maintain the systolic blood pressure above 80 mmHg. Approximately 7 minutes after the onset of the bradycardia, the atrioventricular heart block reverted to sinus rhythm at a rate of 60-70 beats per minute. The recovery time to awareness was markedly lengthened, almost twice longer than other dogs.

Discussion

A paradoxical response to atropine with development of AV block has been described in humans (4,7). Atropine is frequently used for blockade of parasympathetic activity in emergency cases with severe bradycardia, particularly for high degree AV block, especially associated with general anesthesia. Atropine is also frequently used for the inhibition of salivation in premedication. In addition, low-dose atropine is often used in preventing spinal anesthesia-induced hypotension in humans (6). A recent human clinical study found that the administration of atropine (0.015 mg/kg, IV) induced cardiac

syncope in 2 of 23 patients having heart transplantation. Since atropine increases the sinus rate without affecting the delayed infranodal conduction, it can increase the frequency of AV block in patients with His-Purkinje disease (1). Although the effect of atropine on heart rate seems to be dosage-dependent, a recent study found that low-dose (0.002 mg/kg, IV) atropine causes bradycardia either by acting on the sinoatrial node or by its effects on central muscarinic receptors increasing vagal activity (2). In contrast, high-dose (0.015 mg/kg, IV) atropine causes tachycardia by blocking muscarinic receptors at the cardiac sinoatrial node. Nevertheless, paradoxical AV block by atropine administration is not a clearly understood phenomenon.

In the current reported case, the dog was administered with atropine at 0.02 mg/kg intravenously to increase heart rate during surgery. Because the dog was mechanically ventilated in order to maintain eucapnia, either respiratory suppression or poor oxygenation would not have contributed to the paradoxical atropine response. In humans with acute myocardial infarction, exaggerated ischemia caused by tachycardia can induce paradoxical AV block by atropine administration (3). However, this would have been an unlikely cause for the paradoxical atropine response, because the dog had no pre-existing myocardial diseases. The dog was induced with general anesthesia by routine dosage of thiopental, 15 mg/kg IV. Thiopental is an ultra-short acting barbiturate and is most commonly used in the induction phase of general anesthesia. As with nearly all anesthetic drugs, thiopental causes cardiovascular and respiratory depression resulting in hypotension, apnea and airway obstruction in a dose dependent manner. However, the dog's heart rate was maintained in normal range in the first 40 minutes after the induction of anesthesia, and the induction dose of thiopental would have been worn off by this time to contribute any significant cardiac effect associated with its use. In addition, no report has demonstrated conclusively that thiopental might exacerbate atropine mediated paradoxical bradycardic response. Furthermore, isoflurane maintenance of anesthesia in this case is unlikely to decrease heart rate in healthy animals that are free of preexisting cardiac diseases. Therefore, adverse effect of atropine in this case may not have been related to direct anesthetic drug effects. We carefully examined the lead II ECG rhythm strips for the first 40 minutes following general anesthesia. However, no cardiac rhythm disturbances were identified during this period, e.g., sick sinus syndrome, preexisting high-grade heart block, or ventricular premature contractions (e.g., sick sinus syndrome, preexisting high-grade heart block, or ventricular premature contractions etc). It is speculated that the dosage-dependent action of atropine may be the cause for paradoxical response for this case. Dose of 0.02 mg/kg is considered high concentration in human patients unlikely causing a paradoxical bradycardia, but this dose in dogs as observed in this report is considered a low dose that may be associated with paradoxical bradycardia. It appears a wide species variation exists as to at what dose of atropine, occurrence of paradoxical bradycardia may be prevented. Further study is warranted to establish doses of atropine not only for specific species but also different breeds among the species as to what doses are most likely to cause paradoxical bradycardia. Although further doses of atropine will be administered in order to correct low dose paradoxical bradycardia in clinical situation, it is imperative, in treating a life threatening bradycardia, to dose correctly in initial resuscitation in order to achieve optimal therapeutic outcome.

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진도종 개에서 아트로핀에 의해 발생한 역설적 방실 전도 차단

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요 약 : 6 개월령 수컷 진도종 개가 교통사고에 의한 골반 골절 교정술을 위하여 내원하였다. 일반적인 수술 전 검사에서 마취와 관련해 위험성 있는 이상은 발견되지 않았다. 이 개는 아트로핀으로 전처치하고, 유도마취로 thiopental을 주사하였으며 유지 마취 약물로 isoflurane을 사용하였다. 수술 시작 40분 후 갑자기 서맥이 발생하여 아트로핀(18ug/kg)을 천천히 정맥주사 하였으나 즉시 맥박이 증가하지 않고 오히려 heart rate가 감소하며 방실 전도 차단(2^{nd} degree type I)이 발생하였다. 따라서 ephedrin을 즉각적으로 주사하였으며, 투여 7 분 후 정상 심박으로 회복되었다. 본 증례는 개에서 고용량 atropine 투여로 드물게 발생하는 역설적 방실전도 차단 임상예이다.

주요어 : 서맥, 역설적인, 방실 전도 차단, 아트로핀