

# Analysis on diagnostic value of esophageal electrophysiological examination for positive atropine test

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**Abstract:** To discuss the cause of positive atropine test and the possible reason for false positive atropine test, providing a certain aids for clinical diagnosis and treatment. Eighty patients, conducted atropine test due to sinus bradycardia, with positive results from January 2010 to June 2013, were selected. Sinus heart rate were calculated and the changes in heart rhythm were observed by tracing electrocardiogram. Esophageal electrophysiological examination and atropine test were administrated. SPSS 10.0 statistical software was adopted and  $\chi^2$  test was applied for comparison. The positive results of atropine test and results of esophageal electrophysiological examination in different ages showed that as age grows, false positive rate of atropine test was significantly reduced, presenting statistically significant difference ( $\chi^2=6.2821$ ,  $p<0.05$ ); The positive results of atropine test and results of esophageal electrophysiological examination in different heart rates showed that false positive rate of atropine test on those with bradycardia was smaller than those with significant bradycardia, presenting statistically significant difference ( $\chi^2=5.1792$ ,  $p<0.05$ ). Simple sinus bradycardia is mostly caused by the increase of vagus nerve tension, almost negative in atropine test. Sick sinus syndrome (SSS) leads to abnormality in pacemaking and conduction induced by organic lesions in sinus nodes. Moreover, as the disease progresses, it is able to cause severe and persistent sinus bradycardia, almost positive in atropine test. Therefore, to identify the increase in vagus nerve tension or sinus bradycardia induced by SSS has a crucial clinical significance. Furthermore, the false positive and false negative profiles in atropine test can easily lead to misdiagnosis and mistreatment in clinic.

**Keywords:** Atropine test; Positive; Sick sinus syndrome; Esophageal electrophysiological examination

## INTRODUCTION

Sick sinus syndrome (sick sinus syndrome, SSS) called sick sinus syndrome or sinus disease, sick sinus syndrome is due to sinus node or its surrounding tissue (also including the atrium, atrioventricular junctions, etc.) organic disease, leading to arrhythmia generated by the disorders of sinus impulse formation and impulse outgoing, mainly showed by sinus bradycardia, sinoatrial block, sinus arrest, and bradycardia - tachycardia syndrome was also performed.

Atropine test is the basic drug experiment to diagnose sick sinus syndrome (SSS), with convenient and safe operation, an important method to preliminarily diagnose SSS. Simple sinus bradycardia is mostly caused by the increase of vagus nerve tension, almost negative in atropine test. Esophageal cardiac electrophysiology is a technology by transesophageal pacemaker for electrophysiological diagnosis and treatment. The method used the characteristics of close relationship among the esophagus with cardiac anatomy, sent the electrode catheter into esophagus through the nose, adopted Cardiac Stimulator to issuance DC pulse, stroke atrial or ventricular through esophagus electrode which close to the heart. Meanwhile, surface and esophagus electrocardiogram were recorded to get the electrophysiological parameters of each heart part, thus

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revealing the mechanism, diagnosis and treatment of certain arrhythmias. The method was simple and relatively safe (Li ZJ, Xu Y, *et al*, 2011).

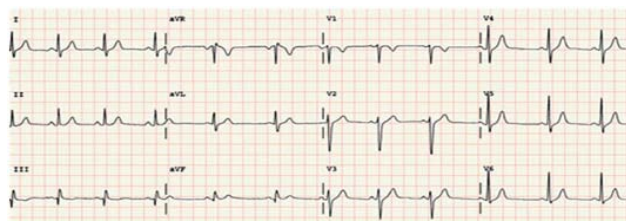
Sick sinus syndrome (SSS) leads to abnormality in pacemaking and conduction induced by organic lesions in sinus nodes. Moreover, as the disease progresses, it is able to cause severe and persistent sinus bradycardia, almost positive in atropine test. Therefore, to identify the increase in vagus nerve tension or sinus bradycardia induced by SSS has a crucial clinical significance. Meanwhile, the false positive and false negative profiles in Atropine test can easily lead to misdiagnosis and mistreatment in clinic. This study, through the esophageal electrophysiological examination on patients with positive atropine test in Xinxiang Central Hospital and the comparison analyses on results, is to discuss the cause of positive atropine test and the possible reason for false positive atropine test, thus providing a certain aids for clinical diagnosis and treatment.

## MATERIAL AND METHODS

### General information

Eighty patients, conducted Atropine test due to sinus bradycardia, with positive results from January 2010 to June 2013, were selected from Xinxiang Central Hospital. Among those, there were 59 males (73.75%) and 21 females (26.25%), with age ranging from 33 years to 74

years (an average age of  $47.2 \pm 8.3$  years). Besides, 54 cases were less than 60 years and 26 cases were no less than 60 years. Through clinical diagnoses, there were 41 cases (51.25%) in coronary heart disease, 14 cases (17.5%) in syncope, 21 cases (26.25%) in cholecystitis and cholelithiasis and 4 cases (5.0%) in radiotherapy and chemotherapy for tumors. After conventional electrocardiogram, it showed that 62 cases were with bradycardia (heart rate of 46-59 times/min) and 18 cases were with significant bradycardia (heart rate no larger than 45 times/min). The study was approved by the institutional research ethics committee of Xinxiang Central Hospital, and written informed consent was obtained from each subject.



**Fig. 1:** Electrocardiogram (ecg) map in the control group.

## Methods

### Atropine test

(1) Stop drugs (such as propanolol and atropine) affecting heart rate for 2-3 days before experiment. (2) Lay decubitus, tracing II electrocardiogram as control. (3) 2mg (0.02-0.04mg/kg) Atropine, add 2ml normal saline for dilution, intravenously quickly. (4) To trace electrocardiogram at 1, 3, 5, 10, 20, 25 and 30 min after drug use respectively for calculating sinus heart rate and observing the changes in heart rhythm. Diagnosis criteria (Wang *et al.*, 2013) After intravenous injection with atropine, the maximum heart rate was less than 90 times/min or there appeared arrhythmia, such as atrioventricular junction heart arrhythmia, sinoatrial block and sinus arrest, diagnosed as positive; on the contrary, the heart rate was larger than 90 times/min and the previous cardiac arrhythmia was disappeared, diagnosed as negative.

### Esophageal electrophysiological examination

Esophageal electrophysiological examination was performed on the patients with positive atropine test. Esophageal stimulation was performed by type DF-6A cardiac electrophysiology stimulator (Oriental Electronic Instrument Factory of Suzhou City), the esophagus atrial adjustable stroke recorded with 8 lead ECG physiological instrument (NIHON KOHDEN). (1) Stop drugs (such as propanolol and atropine) affecting heart rate for 2-3 days before examination. (2) Intubate according to conventional esophageal electrophysiological examination in order to detect basic sinus node recovery time (SNRT), corrected sinus node recovery time (CSNRT) and sinus atrial conduction time (SACT).

Positive criteria: SNRT > 2000ms, CSNRT > 550ms and SACT > 180ms, diagnosed as sinus node dysfunction, suggesting SSS.

## STATISTICAL ANALYSIS

SPSS 10.0 statistical software was adopted. Percentages were used for presenting count data and  $\chi^2$  test was applied for comparison of measurement data.

## RESULTS

### Comparison between the positive results of atropine test and results of esophageal electrophysiological examination in different ages

From table 1, the results of esophageal electrophysiological examination showed that after esophageal electrophysiological examination on 80 patients with positive atropine test, 16 cases were performed with false positive atropine test, with 80% coincidence rate in positive atropine test and esophageal electrophysiological examination. Moreover, there were 4 cases in false positive coronary heart disease, 4 cases in false positive syncope, 7 cases in false positive cholecystitis and cholelithiasis and 1 case in false positive radiotherapy and chemotherapy of tumors. With age growing, false positive rate of atropine test was significantly reduced, presenting statistically significant difference ( $\chi^2=6.2821$ ,  $p<0.05$ ).

### Comparison between positive results of atropine test and results of esophageal electrophysiological examination in different heart rates

From table 2, the results of esophageal electrophysiological examination showed that false positive rate of atropine test on those with bradycardia was smaller than those with significant bradycardia, presenting statistically significant difference ( $\chi^2=5.1792$ ,  $p<0.05$ ).

## DISCUSSION

SSS can be divided into internal nodal and extra nodal type. Internal SSS is always accompanied with organic heart disease and induced by the organic lesion in sinoatrial node and its surrounding tissues, with relatively severe symptoms; Extra nodal SSS is almost not with organic heart disease, which is greatly influenced by autonomic nerve, induced by abnormal increase of vagus nerve tension and belonged to functional alteration. Atropine, as the acetylcholine receptors blocker, not only can block the negative frequency of acetyl choline on cardiac muscles and facilitate the epinephrine in sinoatrial node region have a relatively advantage domination, but also can induce the enhance of heart auto rhythmicity, speed conduction and augment the myocardial contractility. Literature was reported that during

**Table 1:** Comparison between the positive results of Atropine test and results of esophageal electrophysiological examination in different ages (cases (%))

Esophageal electrophysiological examination	<60 years (n=54)	≥60 years (n=26)
Abnormal in sinus node function	39 (72.22)	25 (96.15)
Normality in sinus node function	15 (27.78)	1 (3.85)

**Table 2:** Comparison between the positive results of Atropine test and results of esophageal electrophysiological examination with different heart rate (cases (%))

Esophageal electrophysiological examination	Bradycardia (n=62)	Significant bradycardia (n=18)
Abnormal in sinus node function	53 (85.48)	11 (61.11)
Normality in sinus node function	9 (14.52)	7 (38.89)

diagnosing SSS, the positive rate of atropine test was 78% - 95%, while 89% in sensitivity and 80% in specificity (Li *et al*, 2008). The results in this experiment indicated that the esophageal electrophysiological examination in 80 cases with positive atropine test suggested 64 cases in SSS, with 80.00% positive rate.

SSS is more common in middle - aged and elderly individuals, and coronary heart disease accounts for 20% -53% (Li *et al*, 2008). In this study, the results of esophageal electrophysiological examination suggested that in 64 cases with SSS, 37 cases were with coronary heart disease, accounting for 57.81%. Sinoatrial node blood supply is from the artery of sinoatrial node. Meanwhile, 55% blood supply is from right coronary artery while the rest from left coronary artery. Due to the sinoatrial artery is the terminal artery, it is difficult in establishing an effective collateral circulation once occurring lesions. Hence, coronary heart disease is the main cause of SSS. Rubenstein (1972) reported sick sinus syndrome associated with symptoms in 26 to 90 years (mean age 65 years) has two peaks occurred, namely 21 to 30 years old and 61 to 70 years old. The mainly cause of the elderly group was ischemic heart disease, the young group set mainly for cardiomyopathy and infectious heart disease. But more authors believe that there was only one peak in a lifetime, 60 to 69 years old maximum, followed by 70 to 79 years old, and then was 50 to 59 years old. In China, there were few young patients, but elderly patients with coronary heart disease was most common. Meanwhile, this study also found that with growth in age, the accurate rate of positive atropine test on SSS diagnoses was significantly increased, the coincidence rate among positive atropine test with esophageal electrophysiological examination was 96.15%, which indicating a close relationship between age factors and the property of sinus bradycardia. The reasons are maybe that: (1) Patients with a rather older age are suffering more various predisposing factors, such as hypertension, diabetes and coronary heart disease. (2) As age grows, the sinoatrial node itself is aging, the component of connective tissues in sinoatrial node and atrioventricular node is augmented, more distinct changes in sinoatrial node, making abnormality in the pacemaking function of

sinoatrial node. Therefore, sinus bradycardia in older individuals is relative to the function of sinoatrial node.

The reasons for false positive in atropine test are probably that: (1) the individual difference in patients and the different degree at bradycardia, especially the young adults usually taking physical activity are performing outstandingly in vagus nerve hyperfunction. (2) In the thoracic 4 - 5 nerve, there was an intersection between the sensory nerve dominating heart and the sensory nerve dominating gall bladder. When there were hepatobiliary system diseases like cholecystitis and cholelithiasis, the cardiomotility imbalance and arrhythmia can be induced by nervous reflex; At the same time, the enhance of bilirubin and bile acid concentration in blood also can activate the vagus nerve. The above two aspects can significantly exacerbate the effect of vagus nerve on heart chronotropismus, thus weakening the effect of atropine in heart. (3) One highest dosage in atropine test is 2mg. However, it may highly reached 3-4mg of atropine dosage to completely block vagus nerve. It is not able to completely block vagus nerve in atropine test and individuals' tension reflects are different towards the remaining vagus nerve. (4) The individual difference of different atropine sensitivities in different patients can induce the different degrees during atropine is suppressing vagus nerve tension. Whether there are other reasons is still needed to be confirmed with further studies.

As a screening method in SSS, atropine test is characterized by simplicity and practicability as well as economy and safety. However, negative atropine test is not able to completely exclude SSS and positive atropine test also cannot mean that all are SSS. For patients with positive atropine test, clinicians should comprehensively evaluate ages, working features, history diseases and other profiles. Moreover, they can make judgement by combining esophageal electrophysiological examination in necessity. At the same time, due attentions should be paid that after atropine is intravenously injected, the heart rate is significantly quickened, further enhancing the myocardial oxygen consumption, and having a potential threat on patients with cardiac insufficiency. The various arrhythmia and serious adverse effects induced by

atropine have been reported at home and abroad (Wang and Ci, 2008; Tian *et al*, 2009), which should be attached importance. Other literature has been reported that atropine combined with sit up exercise is able to remarkably reduce the false rate of atropine test, showing values in improving sinoatrial node function (Xu *et al*, 2009).

## CONCLUSION

The results determine of atropine test in the auxiliary diagnosis pathological antrum room knot syndrome, needed synthesize clinical data and esophageal electrophysiological examination. Atropine test was suitable as a means of preliminary check in the case of limited medicine conditions.

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