EFFECT OF ATROPINE ON THE QT INTERVAL AND T-WAVE AMPLITUDE IN HEALTHY VOLUNTEERS

P. ANNILA, A. YLI-HANKALA AND L. LINDGREN

SUMMARY

Prolongation of the QT interval of the ECG represents an imbalance in cardiac autonomic function and may predict cardiac arrhythmia. Vagal activity protects against prolongation of the QT interval which may be associated with flattening of the T-wave of the ECG. The changes in QT interval, T-wave amplitude and respiratory sinus arrhythmia (RSA) were studied after i.v. administration of atropine 20 μg kg⁻¹ or placebo to 10 healthy volunteers in a cross-over study. After atropine, a decrease in RSA occurred in all volunteers, but remained at baseline values after placebo. Corrected QT interval (QTc) increased from 410 (20) ms to 454 (11) ms (P < 0.001) 5 min after atropine and remained prolonged for the entire study period (60 min). The T-wave flattened significantly (measured as R:T ratio) up to 30 min, without any changes in the R-wave. No changes in the ECG occurred with placebo. (Br. J. Anaesth. 1993; 71: 736-737)

KEY WORDS
Parasympathetic nervous system: atropine Heart: ECG.

Imbalance in cardiac autonomic function (increased sympathetic activity) prolongs the QT interval of the ECG, reflecting the rate of myocardial repolarization [1]. Prolongation of the QT interval has been shown to be a prognostic sign for cardiac arrhythmia. It occurs in the presence of increased concentrations of circulating catecholamines. When sympathetic tone predominates, vagal stimulation is believed to protect the ventricular myocardium by stabilizing the heart electrically [2]. Changes in the amplitude of the T-wave may be related to changes in the QT interval.

Cardiac arrhythmia has been reported after administration of atropine during induction of anaesthesia [3]. This may result from reduction in vagal protection and prolongation of the QT interval. The effect of atropine on the QT interval and on the T-wave amplitude has not been systematically evaluated, therefore we studied the effect of atropine on these variables in healthy volunteers in a placebo-controlled cross-over study.

METHODS AND RESULTS

The study was approved by the Ethics Committee of the Fourth Department of Surgery. Ten volunteers (four female and six male; mean age 31 (SD 3.4) yr (range 24–35 yr); weight 66 (11.4) kg) gave informed consent.

A vein of the dorsum of the hand was cannulated and the subject rested in the supine position for 10 min before beginning the study. The ECG was amplified from lead V₁ using an Olli 435D (Kone Ltd, Finland) monitor, recorded on tape (Racal FM tape recorder, Racal Ltd, England) and digitized offline at 200 samples s⁻¹ channel⁻¹ into a PC-compatible microcomputer.

A deep breathing test was used to evaluate respiratory sinus arrhythmia (RSA). The volunteer was asked to breathe with a maximal tidal volume at a rate of 6 b.p.m. The difference between the maximum and the minimum heart rates during a ventilatory cycle was calculated. The initial deep breathing test was followed by atropine 20 μg kg⁻¹ i.v. and was then repeated 5 min and 60 min later. The ECG was recorded until the last RSA test was performed. In seven of the 10 subjects, the trial was repeated using physiological saline as a placebo. All tests were performed between 15:00 and 18:00.

QT intervals were calculated from the ECG printed on paper. The corrected QT interval (QTc) was measured from four consecutive complexes according to Bazett’s formula (QTc = QT/√R—R') at rest, 5, 30 and 60 min after administration of atropine or placebo. The ratio of the amplitude of R-peaks and T-waves (R:T ratio) was calculated as a mean of three consecutive complexes. All amplitudes were measured during expiration (maximum R-peak amplitude) at rest, 5, 30 and 60 min after i.v. atropine or placebo.

Statistical evaluation between groups was performed using two-way analysis of variance. Changes within a group were tested with one-way analysis of variance corrected by Fisher PLSD test. Statistical analysis was performed using Stat View 512⁺ software (Brain Power Inc., Calabasas, CA, U.S.A.). P < 0.05 was considered statistically significant. Results are presented as mean (SD).

Heart rate increased from 64 (10) beat min⁻¹ to 94 (11) beat min⁻¹ 5 min after atropine (P < 0.001). At

P. ANNILA, M.D., Department of Clinical Sciences, University of Tampere, P.O. Box 607, 33101 Tampere, Finland. ARVI YLI-HANKALA, M.D., PH.D., Department of Anesthesiology, University of Louisville, School of Medicine, Louisville, KY 40292, U.S.A. LEENA LINDGREN, M.D., PH.D., Department of Anaesthesia, Fourth Department of Surgery, Helsinki University Central Hospital, Kasarmikatu 11, 00130, Helsinki, Finland. Accepted for Publication: May 6, 1993.

Correspondence to P.A.
30 min it was 92 (13) beat min⁻¹ and at 60 min 82 (11) beat min⁻¹ (P < 0.001). After atropine, the QTc interval increased significantly from baseline at each measurement point (P < 0.001) (fig. 1). Each subject had normal (> 12 beat min⁻¹) RSA before administration of the test drugs. Five minutes after atropine, RSA was greatly reduced (4 (1.6) beat min⁻¹) (P < 0.001); 60 min after atropine, it was 9.8 (3.8) beat min⁻¹ (P < 0.001). Five minutes after atropine, the R:T ratio increased from 1.15 (0.4) to 1.40 (0.6) (P < 0.01); at 30 min it was 1.51 (0.7) (P < 0.001) and at 60 min it was 1.33 (0.5) (P < 0.05). The R-wave amplitude was not affected by atropine. No changes in heart rate, QTc interval, RSA and R:T ratio occurred after placebo.

COMMENT

These data show that, in the presence of vagal block by atropine, the QTc interval increased significantly and the T-wave of the ECG was flattened. We chose a relatively large dose of atropine to ensure parasympathetic block as confirmed by the disappearance of RSA. Day, McCamp and Campbell [1] have suggested that QT dispersion (interlead variability) gives an indication of arrhythmogenicity and repolarization. We used a single lead V₂ which, according to the same group, provides the closest approximation to maximum QT interval [4]. They also accept the validity of a single lead value for QTc when changes are monitored. The flattened T-wave after atropine in our volunteers probably also reflected irregularity in repolarization.

Atropine has been shown to increase the incidence of cardiac arrhythmia during induction of anaesthesia [3]. In addition, i.v. atropine has been shown to cause ventricular tachycardia in a patient with a prolonged QT interval syndrome [5]. Inhibition of the sympathoadrenal tone by opioids shortens the QTc interval in patients with vagal block. Vagal stimulation protects the heart against arrhythmogenic vulnerability [2] and against prolongation of the QT interval. In our study, the QTc interval was prolonged, probably because sympathoadrenal tone became dominant after parasympathetic block by atropine.

In diabetic patients, vagal denervation develops gradually. Maintenance of remaining borderline vagal function by avoiding anticholinergics may be of value in diabetic patients, as serious cardiac arrhythmia has been described in these patients during anaesthesia and after atropine. Furthermore, ventricular fibrillation after i.v. atropine for bradycardia has been shown to occur in acute myocardial infarction [6]. The routine use of anticholinergics at induction of anaesthesia must be seriously questioned.

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REFERENCES