Medications that cause Prolonged (Q – T) interval on the electrocardiogram (E.C.G) increased risk of developing life- threatening condition

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Abstract

Applied clinical work has been carried out and obtained the most important results, the most important threat to human life are heart disorders, especially irregular heart rate and slow side effects caused by some drugs when given and focused on research on the most commonly used therapeutic drugs in our city are anti-irregular heart drugs (Amiadaron), and anti-Depression (amitriptyline), and antibiotic (erythromycin) that increase the QT interval period in ECG (Electrocardiogram) (normal distance: for men less than 450 milliseconds and for women less than 470 msc) these drugs that cause certain doses slow down the heart and press Torsades de pointes (Tdp) , ventricular tachycardia) VT

Our goal is to remove the risk from people where there are more than 100 types of drugs that prolong QT for the longest period and cause the most serious torsades de pointes. we worked through the monitoring of analyzes and (ECG, Echo and effort, radiation and patient history of patients and risk factors and physiological changes that occur and monitor patients carefully and cautiously Prevention of side effects will avoid the patient reaching the ventricular fibrillation (VF) threatened with sudden death, and we selected patients greater than > 40 years as follows: (total patients is 340 patients 200 men and 140 women) and for a period (9 months 2018-2019) we have divided patients in terms of age and sediment Factor (risk factors) More than 40 years (age 40-55 years Rsk 1) and (Rsk 2 of 55-65 years) and (65 years and above Rsk 3) are divided into three spheres of the first Group : Anti-arrhythmic (Amiadaron). Group II: Anti-depressants Anti-depressants (Amitriptyline) Group III: Anti-biotic (erythromycin) so the result was: - * Group I: men 52 - women 40): Amiadaron used cautiously in the form of Oral (mouth) tablets 200 Mg 2 times a day depending on the patient's condition and stability or emergency and ECG monitoring) and electrolyte analysis Risk 1 age of 40-55 years rarely seen slowing the heart heart block (cut the electrical conductivity of the heart) and the length of the QT less than 500 msc and the rate (360 - 480 msc) The amine did not occur problem, either cases who take high dose or in the world Concentrated infusion (Nutrient infusion), ie, those with the second and third rusk and risk factors The length of the Q-T period is more than 500 msc, who are at risk of seizures, especially the electrolyte disorder associated with them and their lives are threatened with death by 9% in intensive care. By controlling the dosage that preserves the patient's life, * Group II: Antidepressants amitriptyline we used the dose (25 -100 mg) per day ... the first 6 days of treatment until after 30 days and control QT in the dose less than 100 mg the result is there The length of the QT is confined between (360-480 msc) less than m 500 msc or 96% Nothing happened to be endangered and without reliable electrolyte disturbances and is safe for Risk 1, Risk 2 , 3 If the dose is greater than 100 mg and the electrolyte disturbance, QT length of more than 500 msc is threatened by death SCD. tdp, 6% confined between (1.04 - 6.12) The drug should be discontinued immediately ... * Group III: erythromycin at a dose (1000 mg) by mouth and by infusion (intravenous infusion) Patients Risk 1.. No risk change (360-450) Either in the case of giving the patient or the presence of allergies in patients, ectopic disorders (migrating heartbeat) and irregular heart, especially in the The high QT is more than 1500 mg and the length of QT is greater than 500 msc. The VT. Torside de Point Tdp .. So not to exceed the dose to preserve the safety of the patient .. And the safe dose that does not put the patient at risk of death and save their lives.

Keywords: Prolonged (Q – T), electrocardiogram (E.C.G), life- threatening
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Introduction
This scientific research was carried out in the educational hospital in Iraq Al- Samawah on the academic practical side of the most important threaten-life human is the heart disorders, especially the arrhythmia\(^{[1]}\), leading to sudden death through the use of drugs that work prolonged (Q –T) interval, The normal Q-T interval is longer in women than in men, and increases with age\(^{[2]}\) as (450 mc) for adult men and (470 mc) for adult women in the electrocardiogram (E.C.G) according to the preferred equation\(^{[3]}\) (Bezetts correction Formula), and there are groups of medicines. The work in this research on the most frequently traded drugs are\(^{[4]}\) 1) Anti-arrhythmic drug class (III) (Amiodarone) group block potassium channels, Its dominant effect is prolongation of the action potential duration and the refractory period.\(^{[5]}\) Amiodarone has antianginal as well as antiarrhythmic activity.\(^{[27]}\) 2) Anti-depressants tricycle (Amitriptyline) (TCAs) block norepinephrine and serotonin reuptake into the neuron effective in treating moderate to severe major depression, migraine headache and chronic pain syndromes\(^{[27]}\) 3) Anti-biotic-group Macrolides (Erythromycin) bacteriostatic, work inhibiting the translocation steps of protein synthesis, It is used the first choice and as an alternative to penicillin in individuals who are allergic, effective against Homophiles influenza, Chlamydia, Legionella, Moraxella, and Ureaplasma species and Helicobacter pylori, similar to that newer members of this family, brown 85 The baseline study Other reasons work along the\(^{[9]}\) (Q-T) interval congenital comprises a distinct group of cardiac channelopathies characterized by delayed repolarization of the myocardium, patients with some \(^{[7]}\) electrolyte abnormalities, some drugs, An implantable cardiac defibrillator and increased risk ventricular tachycardia (VT) Complain patient palpitation, dizziness, chest discomfort or breathlessness, syncope, seizures and sudden cardiac death\(^{[8]}\) (SCD), sometimes lethal arrhythmia of torsades de pointes\(^{[11]}\) (TdP) The sinus node acts as a pacemaker and its intrinsic rate is regulated by the autonomic nervous system\(^{[12]}\); vagal activity slows the heart rate, and sympathetic activity accelerates it via cardiac sympathetic nerves and circulating catecholamine.\(^{[10]}\) The main objective reduce mortality the incidence of malignant Arrhythmia\(^{[13]}\) (disorders of heart rate, rhythm and conduction)\(^{[14]}\) clinical diagnosis depends mainly on a patient history and physical examination, the Electrocardiogram (ECG) evidence to support a diagnosis And Laboratory tests, chest-x-ray and ECO-Study.
Measurement of the QT interval:

Time and speeds (ECG) machines record changes in electrical activity by drawing a trace on a moving paper strip. ECG machines run at a standard rate of 25 mm/s and use paper with standard-sized squares. Each large square (5mm) represents 0.2 second (s) i.e. 200 milliseconds (ms). Therefore, the speed of the ECG is important in the calculation of (Q-T) interval. If the speed of the device is 50 mm/second (usually written below the monitor chart sheet), this means the small box is 0.02 ms or (20 / second) and the large box containing 5 small squares (20 x 5 = 100 milliseconds (ms)). But if the speed of the device is 25 mm/second, the small box is 0.04 (i.e. 40 ms). The large box containing 5 small squares (5 x 40 = 200 milliseconds (ms)) on this is the exact calculation (Q-T) interval.

We record the length of the time period either the pathological greater then of the man > 460 (ms), The woman is > 470 (ms). And by using the preferred equation of the famous account (QTc):

\[ \text{Finger (3)} : \text{Measurement on paper ECG} \]

Aim: The Research is limited to work and early detection prolong Q-T and the extent of the effect of the therapeutic drugs used on the patient and the change in the ECG. In addition to the impact of cardiovascular and other drugs associated with the patient and the risk of the patient to have other heart disease, and the risk factors surrounding it, the goal is real to reduce the incidence of mortality and complication for the patients and to avoid danger.
Materials and methods
In the study of randomized patients in the (Academic Teaching Hospital in Iraq-Samawah) and (Specialized Center for Diabetes and Endocrinology) the study was based on patients over >40 years. According to risk factors from 40-55 years old Who do not have concomitant diseases it's called (risk I): And 55-65 years old who have hypertension, heart disease and diabetes (risk II); And the > 65 years who have heart failure, Kidney disease and liver disease (risk III). Generally Q-T interval prolongation is considered when the QTc (Corrected QT interval) interval is greater than >450 mc (men) and > 470 mc (women), although arrhythmias are most often associated with values of 500 mc or more. Directly collect Complete history, physical examination, Electrocardiogram (ECG), Treadmill, Eco-study, holter, Bicycle voltage, chest x-Ray, In addition to laboratory analysis And we took the patients in all aspects of emergency medical safety for stable cases and unstable situations and the admission of the hospital, and taking the safety of the patient is the first step in the work had divided into three groups work took 9 months between (2018-2019): (Group: 1 Antiarrhythmia Amiodarone tablet 200mg oral ph= 4.08 bioavailability 35-50% to systemic circulation or I.V ample 150mg BV 100% Number of patients 92:(mal: 52 female: 40) : (Group: 2 Antidepressants (Amitriptyline) tablet(25-100mg) ph= 7.4 oral BV 33-62% Number of patients 280:(mal: 190 female: 90): (Group: 3: Erythromycin capsule 500mg oral ph= 7.8 BV 15-45% Number of patients 340( mal: 200 female: 140) , *Group 1: Amiodarone is a potent antiarrhythmic agent that is used to treat ventricular arrhythmias and atrial fibrillation. The drug prevents the recurrence of life-threatening ventricular arrhythmias and produces a modest reduction of sudden deaths in high-risk patients. Amiodarone is more effective a rhythm-control strategy is chosen, amiodarone do not peak until seven weeks after the initiation of concomitant therapy. With our differential diagnosis (Q-T) between hereditary, genetic (congenital cardiac channel (LQTs), implantable cardioverter-defibrillators (ICDs)), Carefully given to the patient drug amiodarone 200mg One dose or two per day depended on situation patient Stable or unstable or emergency, in ECG observation. Traditionally, lead II has been used for Q-T interval measurement because in this lead, the vectors of repolarisation usually result in a long single wave rather than discrete T and U waves. digital ECGs with simultaneous 12-channel recording, (12 Lead) QT measurement, Bradycardia and heart block occur in 0.2% percent of patients, but incidence Only in the high doses we see or high risk factor QT interval < 500ms in oral dose, Work was done with confidence and safety. Hospitalized patients, particularly those in intensive care units (ICUs), are at higher risk factor increases > 500ms QT interval prolongation incidence. Torsades de pointes (TdP) may result in sudden cardiac death specific elderly risk III because of a greater preponderance of risk factors, in patients in ICUs ranges from 3% to 18%; the average as 9% of patients in ICUs, In comparison with patient risk factor 1 odds ratio (In comparison with patients) 95% confidence safety, the odds ratio increases markedly in patients with 2 or ≥3 risk factors (6.4% -9%) incidence (TdP) depended dose drug, medication contacted the physician to discuss obtaining more frequent ECGs for QTc interval monitoring, assuring the correct dose and maintenance of adequate serum electrolyte concentrations or substituting a drug that does not prolong the QTc interval, where possible and appropriate. , * Group 2: Amitriptyline drug (25mg-100mg) is a highly lipophilic molecule has an elimination half life of 25 hours give the patient tablet oral monitoring throughout the course of treatment is necessary because QT interval prolongation can occur anywhere from the first 6 days of treatment to after 30 days, Monitoring the QTc, we used a drug less than 100 mg Amtriptyline. Q-T interval was no more than 460 ms in males and 480 ms in females, generally less than 500 ms, (incidence rate ratio [IRR], 0.96; 96% confidence interval [CI] safety, While after over dose more than 100mg plus 2 ≥3 risk factor and heart disease Q-T interval >500 and disturbance electrets the patient is at real risk SCD or (TdP) equivalents IRR, (3.53; 92% CI, 1.04-6.12). Those threatened must withdraw the drug, *Group 3: Erythromycin has a large volume of distribution and is lipophilic with extensive penetration.
in body tissues and fluids, including cardiac tissue. The time to reach peak serum is 2 to 4 hours. And our knowledge drug interaction cytochrome p450 inhibitor in liver is caused when part of the patients potentially toxic compound CYP3A4 inhibitors, oral and intravenous (IV) erythromycin-related QTc interval prolongation (500 mg)/capsule oral 1x2 per day (course 7 day) Cardiac monitor rhythm risk I, II confidence interval [CI] safety interval at baseline (423 ± 70 ms, range 300–493 ms) without complication. As for risk III elderly arrhythmia from Ischemic heart disease. But when you give slow IV infusion of erythromycin lactobionate 500 mg injection every six hours (8.9 ± 3.5 mg/minute, range 3.9–12.5 mg/min) in fluid after infusion QTc interval (423 ± 96 ms, range 300–550 ms) short course 3 day followed by oral administration only 2 patient woman and 1 man elderly risk III polymorphic ventricular tachycardia (VT) associated with QTc interval prolongation > 500 ms which is most commonly associated with myocardial infarction, myocardial ischemia or heart failure, with attention and caution stop drug and rapidly management Avoiding risk ventricular fibrillation (VT) or sudden cardiac death (SCD), QT interval–prolonging medication contacted the physician to discuss obtaining more frequent ECGs for QTc interval monitoring, assuring the correct dose and maintenance of adequate serum electrolyte concentrations or substituting a drug that does not prolong the QTc interval, where possible and appropriate.

Results and Discussion:
QT Interval and Significance in cardiology, the time between the Q and T waves of an ECG is the QT interval. The emergence of a state of arithmetic is Torsades de pointes (TdP) may result in sudden cardiac death. Exist more than 100 drugs available including widely used antibiotics, antidepressants, cardiovascular drugs and many others, may cause QTc interval prolongation and TdP. Anti-arrhythmic agents were the first drugs associated with QT prolongation and ventricular arrhythmias. Recently, there has been an increased incidence of arrhythmia caused by noncardiac medications, generating significant concern and, in some cases, the QT interval is generally due to blocking of the potassium channels of the heart. QT-prolonging drugs should be avoided in patients with pre-existing heart disease, history of ventricular arrhythmias or with metabolic abnormalities such as hypokalemia. Hospitalized patients come under high risk for developing TdP than outpatients with the same QT prolonging drugs. Hospitalized patients are often elderly people with underlying heart disease who may also have renal or hepatic dysfunction, electrolyte abnormalities, or bradycardia and to whom drugs may be administered rapidly via the intravenous route. Concomitant administration of drugs that inhibit the cytochrome P450 especially antifungal, macrolide antibiotics or those that can prolong the QT interval or drugs that cause electrolyte disturbance should be avoided. It is recommended to perform surveillance ECG before and after initiation of QT-prolonging drugs. Routine monitoring of electrolytes especially potassium is also recommended in those who are on diuretics and QT-prolonging drugs. Through study:

Finger(4):
Normal sinus rhythm (ECG)
Torsades de pointes (Tdp) compared with Normal sinus rhythm (The difference ECG)

Finger(5):

Finger(6):
Effect of Drug on QT

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Parameter</th>
<th>Baseline</th>
<th>After Drug</th>
<th>(P) Wave</th>
<th>Blood Pressure</th>
<th>Heart Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Amidaron</td>
<td>Q-Tc</td>
<td>422±28</td>
<td>432±27</td>
<td>Sinus Rhythm</td>
<td>140/80</td>
<td>75±10</td>
</tr>
<tr>
<td>Lv Amidaron</td>
<td>Q-Tc</td>
<td>422±28</td>
<td>422±38</td>
<td>Extrasystol</td>
<td>130/75</td>
<td>75±20</td>
</tr>
<tr>
<td>Amtriptylin oral</td>
<td>Q-Tc</td>
<td>420±30</td>
<td>422±28</td>
<td>Sinus Rhythm</td>
<td>120/75</td>
<td>70±10</td>
</tr>
<tr>
<td>Erythromycin oral</td>
<td>Q-Tc</td>
<td>420±25</td>
<td>420±25</td>
<td>Sinus Rhythm</td>
<td>120/75</td>
<td>80±10</td>
</tr>
<tr>
<td>Erythromycin l.v</td>
<td>Q-Tc</td>
<td>422±25</td>
<td>422±25</td>
<td>Ectopic</td>
<td>125/80</td>
<td>85±10</td>
</tr>
</tbody>
</table>

Finger (7):

- QTc is prolonged if > 450 mc in men or > 470 mc in women.
- QTc > 500 mc is associated with increased risk of torsades de pointes.
- QTc is abnormally short if < 350 mc.

Clinical receiving a drug of the study population:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Age:</th>
<th>Normal</th>
<th>S. potisi</th>
<th>S. calcium</th>
<th>S. magne</th>
<th>S. sodi</th>
<th>S. Chlor</th>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amidaron</td>
<td>&gt; 40y</td>
<td>72%</td>
<td>4.3±0.7</td>
<td>2.25±12</td>
<td>0.73±0.9</td>
<td>128±15</td>
<td>95±7</td>
<td>1</td>
</tr>
</tbody>
</table>
The average population drugs prolonged QT interval

**Recommendation**

From the necessary electrolyte analysis hypomagnesemic or has a normal serum magnesium concentration. In patients unresponsive to intravenous magnesium, intravenous isoproterenol or Atropin (β₁- & β₂-Adrenergic compromise) Drugs known to prolong the QTc interval should be discontinued immediately. Serum potassium and/or magnesium should be replaced if the patient is hypokalemic or hypomagnesemic. If the patient is hemodynamically unstable (systolic blood pressure <90 mmHg, heart rate >150 bpm, unconscious or losing consciousness and/or experiencing chest pain), asynchronous defibrillation should be performed, rather than synchronized electrical cardioversion, as synchronization of shocks to the QRS complex/T wave is often impossible in patients with polymorphic ventricular arrhythmias. In patients with hemodynamically stable TdP, intravenous magnesium 1 to 2 g administered over 15 minutes may terminate the arrhythmia, regardless of whether the patient is rapid overdrive pacing via a temporary transvenous pacemaker may be used if the patient has TdP that is associated with bradycardia. Increasing the heart rate via isoproterenol or rapid pacing facilitates restoration of sinus rhythm. In patients with hemodynamically stable TdP unresponsive to magnesium and, where appropriate, isoproterenol or rapid pacing, sedation...
followed by elective defibrillation may be indicated. Sotalol-associated TdP that is unresponsive to conventional therapy has been managed with hemodialysis or peritoneal dialysis.

**Conclusion**

Applied clinical work has been carried out and the most important results, The most important thing about patients' life is the heart disorders, especially the Arrhythmia, (Irregularity heart) and the bradycardia (slow heart), block heart (disorders conduction) and complication symptoms caused by some medications when given and focused in the search for the most used therapeutic drugs in our city, 1) Antiarrhythmics drug (Amiodarone) , 2) Antidepressants (Amitriptyline) 3) Macrolides ((Erythromycin) bacteriostatic , Which works to increase the prolonged (Q–T) interval in ECG (Electrocardiogram ) - drugs that cause the bradycardia and most heart disturbance (Normal interval Q-T (420 – 470 mc) And the most dangerous arrhythmia, (VT )ventricular tachycardia , (TdP ) torsades de pointes polymorphic ventricular tachycardia , Our goal dimensions are danger to people where There are more than 100 types of drugs that work Which leads to sudden death, from our research work by monitoring the analyzes, and (ECG) , Echo, tredmal, halter, chest x-ray , And the history and pathology of patients, risk factors, physiological changes that occur, and careful monitoring of patients and prevention of complication. Preventing patient access to VF (ventricle fibrillation ) as well as those at risk of death so we chose patients are greater than 40 years of age: (The total number of patients is 340 patients, 200 men and 140 women.) We divided the patients in terms of age and risk factors (40-55 year) risk 1 And (55-65 year) risk 2 and (65 years and above) risk 3) divided into three group: So the result was (men 52 - women 40) (92) patients Group I: Use Antiarrhythmics drug (amidarone) with caution , In the form of Oral pills 200 mg first or twice a day, depending on the patient's condition and stability, (emergency as the case of the patient . ECG control, and laboratory analysis of the electrolyte risk 1,( age 40-55 years). We rarely see the bradycardia and heart block. The length of QT is less than 500 mc,(360 –480 mc) and his safe did not occur the problem, either cases that take high dose (loading-dose regimen is used) ,Or in intensive care unit with the second and third risk factors. Prolong QT more than 500 mc are those who have been at risk of seizures, especially the associated electrolyte disorder, and their lives are at risk of death at 9% in the center care depends on the skill of the doctor's decision to control the administration of the dose that maintains the patient's life. Group II: Anti-depressants tricycle (Amitriptyline) (TCAs).We used the dose (25 - 100 mg) per day. The first 6 days of treatment after 30 days and the control of QT in the dosage is less than 100 mg. The result is the length of the period QT is limited between (360-480 ms) In the case of a dose increase greater than 100 mg and the electrolyte disturbance, the QT length of more than 500 ms is at risk of dying from ( tdp) - 6% restricted between (1.04 - 6.12) The drug should be stopped immediately .. Group III: Anti-biotic-group Macrolides (Erythromycin) bacteriostatic (1000 mg) by oral and intravenous infusion in patients with risk factor 1 did not read any change in risk QT between (360-450 mc) .. In case of tender patient or the presence of sensitivity in patients, the disorders of ectopic (heartbeat migration) and irregular heart especially In the high dose, more than 1500 mg, the length of QT is greater than 500 ms. On the electrolyte disorders, it helps the arrhythmia , especially Rsik 2, 3, where he got two patient ectopic men and one woman, and thus the work was prevention and caution against getting venomous and (VT). Torsideed Point Tdp. So not to exceed maintenance dose . The dose was satisfied dose and the safe dose that does not endanger the lives of patients and save their lives.

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