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Estudo das Alterações Eletrocardiográficas com o Uso de Antidepressivos Tricíclicos em Pacientes com Dor Crônica*

A Study on Electrocardiographic Changes Secondary to the Use of Tricyclic Antidepressants in Patients with Chronic Pain

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RESUMO

Cunha Jr RJ, Barrucand L, Verçosa N — Estudo das Alterações Eletrocardiográficas com o Uso de Antidepressivos Tricíclicos em Pacientes com Dor Crônica.

JUSTIFICATIVA E OBJETIVOS: *Os antidepressivos tricíclicos (ADT) são amplamente utilizados como analgésicos para lombalgias crônicas e dores neuropáticas. O objetivo deste estudo foi avaliar as alterações eletrocardiográficas dos pacientes com dor crônica em uso de amitriptilina ou imipramina.*

MÉTODO: *Foram estudados 40 pacientes com idade entre 26 e 81 anos (57,27 ± 13,65 anos), de ambos os gêneros (feminino 19, masculino 21), com síndromes neuropáticas (lombociatalgias, síndromes pós-laminectomia, neurites pós-herpética, entre outras); 60% com doenças cardiovasculares; 30% tinham ECG alterado (BRD, BRE, BAV 1º grau, HBAE ou extra-sístoles). Foram realizados e analisados três ECGs: antes do início dos ADT, 30 e 60 dias após o início do tratamento, avaliando os parâmetros PR, QRS, QT, QTc, DQT, DQTc e FC. Trinta e dois pacientes fizeram uso de amitriptilina e oito de imipramina. A dose média ao final do estudo foi de 54,29 mg de amitriptilina e de 46,87 mg de imipramina.*

RESULTADOS: *A análise das variáveis eletrocardiográficas após o uso dos ADT apresentou a amitriptilina com aumento na frequência cardíaca transitoriamente no gênero feminino (p = 0,049) e a duração do QRS nos pacientes com idade igual ou maior que 60 anos e nos cardiopatas na segunda avaliação (p = 0,01). Nos pacientes que receberam amitriptilina, doses de 75 mg, o intervalo QTc foi maior quando comparado com doses de 25 mg (p = 0,0044). O aumento desses parâmetros evidenciou o efeito da amitriptilina sobre a condução cardíaca; no entanto, não houve comprometimento clínico, pois os valores permaneceram dentro dos limites de normalidade (QRS < 110ms e QTc < 470ms).*

CONCLUSÕES: *O uso clínico dos ADT em dores crônicas mostrou-se seguro e eficaz, não apresentando distúrbio da condução cardíaca com repercussão clínica.*

Unitermos: DOR, Crônica: neuropática; DROGAS, Antidepressivos tricíclicos; EXAMES COMPLEMENTARES: eletrocardiograma.

SUMMARY

Cunha Jr RJ, Barrucand L, Verçosa N **—** A Study on Electrocardiographic Changes Secondary to the Use of Tricyclic Antidepressants in Patients with Chronic Pain.

BACKGROUND AND OBJECTIVES: *Tricyclic antidepressants (TCAs) are widely used as analgesics in chronic lumbar pain and neuropathic pain. The objective of this study was to evaluate the electrocardiographic changes in patients with chronic pain treated with amitriptyline or imipramine.*

METHODS: *Forty patients, ages 26 to 81 years (57.27 ± 13.65 years) of both genders (female 19, male 21), with neuropathic syndromes (lumbosciatalgia, postlaminectomy syndromes, and postherpetic neuritis, among others) participated in this study; 60% had cardiovascular diseases; 30% had changes in the ECG (RBBB, LBBB, first-degree AVB, LAHB, or PVCs). Three ECGs were done in each patient: one ECG was done before beginning treatment, and 30 and 60 days after beginning treatment evaluating PR, QRS, QT, QTc, DQT, DQTc, and HR. Thirty-two patients were on amitriptyline and eight on imipramine. The mean dose at the end of the study was 54.29 mg of amitriptyline and 46.87 mg of imipramine.*

RESULTS: *Analysis of electrocardiographic parameters after the use of TCAs showed that amitriptyline caused a transitory increase in heart rate in females (p = 0.049), and the duration of the QRS in patients 60 years or older and patients with cardiopathies (p = 0.01). In patients who received 75 mg of amitriptyline, the QTc interval was greater when compared to that of patients who received 25 mg of the drug (p = 0.0044). The increase in those parameters demonstrated the effects of amitriptyline on cardiac conduction; however, clinical compromise was not seen, since they remained within normal limits (QRS < 110 msec and QTc < 470 msec).*

CONCLUSIONS: *The chronic use of TACs proved to be safe and effective, and it did not show changes in cardiac conduction with clinical repercussion.*

Key Words: COMPLEMENTARY EXAMS: electrocardiogram; DRUGS: tricyclic antidepressants; PAIN, chronic: neuropathic.

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ções quanto à segurança em baixas doses, refere-se à metanálise com seis estudos comparando os ADT em baixas doses (< 100 mg), com doses-padrão para depressão (> 100 mg), mostrando menor incidência de efeitos colaterais nas doses baixas [1].

Neste estudo prospectivo longitudinal, os antidepressivos foram utilizados em doses analgésicas máximas de 75 mg por dia, em uma amostra representativa da população-fonte no que diz respeito a distribuição por gênero, quadro clínico doloroso e dose média de ADT empregada.

A interferência na frequência cardíaca, com discreto aumento dos valores, foi observada após 30 dias de uso dos fármacos (M_1), mas com significância estatística (Tabela II). O aumento da frequência cardíaca surge com o início da terapêutica, tendendo a adaptação em torno de quatro semanas. Essa variação ocorreu apenas com o gênero feminino. Ao final do acompanhamento (M_2) houve um retorno aos valores basais (p = 0,01). Esse efeito transitório não teve importância clínica, sendo, porém, relatado na literatura [18].

A duração do complexo QRS evidenciou discreto aumento em M_1, com pequena significância estatística (p = 0,049 e IC = 0,014-6,58). Em M_2, porém, os valores se elevaram um pouco mais em relação ao basal (M_0), com p-valor de 0,003 (IC 2,02-8,90), sem repercussão clínica (Tabela II). Essa pequena variação do QRS foi observada em idosos e cardiopatas (Tabelas IV e V). Nenhum paciente registrou QRS maior ou igual a 120 ms ao final do acompanhamento, valor que indicaria maior tendência à arritmia, registrada na literatura [19]. Neste trabalho, não foi evidenciada nenhuma arritmia no eletrocardiograma.

No que diz respeito ao ECG prévio, ocorreu variação no QRS tanto nos pacientes com ECG iniciais alterados quanto nos normais (Tabela VI). Nesta pesquisa os pacientes com distúrbio de condução prévia não apresentaram maior variação do QRS diferindo da literatura consultada, quando os ADT são usados em doses antidepressivas [20].

Ficou constatado que a variação do QRS ocorreu no momento em que era utilizada a dose mais elevada. Isso corrobora a idéia de que a influência desse grupo de fármacos na eletrofisiologia cardíaca é sobretudo dose-dependente.

Na avaliação dos efeitos dos ADT nas diversas doses utilizadas foi comprovado, neste trabalho, aumento significativo do QTc durante o uso da amitriptilina na dose de 75 mg (p = 0,004). Quanto ao uso da imipramina, foi observada redução do QTc com a dose de 50 mg, porém sem importância estatística significativa.

O aumento do QT pode levar à arritmia ventricular grave conforme citação de Antzelevitch [21]. A dispersão do QT (DQT) reflete as diferenças regionais do tempo de despolarização ventricular. Quando a heterogeneidade intrínseca do miocárdio ventricular é ampliada, ela se reflete em um maior DQT. Nos pacientes estudados a dispersão do QT não aumentou de forma significativa durante o tratamento (Tabela III). Nesta pesquisa, não foi detectada nenhuma disritmia apesar de haver relatos na literatura comprovando a presença de complicações cardiovasculares, inclusive bloqueios cardíacos, com doses antidepressivas de ADT [22,23].

Quando havia uma diferença em relação à dose utilizada, pode-se constatar que houve influência sobre o QTc em vigência apenas de amitriptilina (Tabela III). Contudo, o número reduzido de pacientes em uso de imipramina (oito pacientes) não permitiu concluir que esse fármaco não interfira nesse intervalo. Idosos e mulheres são mais propensos ao aumento do intervalo QT induzido pelos ADT [24], o que não foi demonstrado nas doses aqui empregadas.

O estudo concluiu que os antidepressivos tricíclicos mostraram atuação no sistema de condução, porém sem comprometimento clínico nos pacientes cardiopatas e idosos, porque as doses utilizadas para analgesia das dores neuropáticas foram menores que 100 mg.

A Study on Electrocardiographic Changes Secondary to the Use of Tricyclic Antidepressants in Patients with Chronic Pain

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INTRODUCTION

Tricyclic antidepressants (TACs) are used worldwide in psychiatric patients and in the treatment of chronic pain syndromes. In the United Kingdom, a 40% increase in the prescription of those drugs was seen from 1991 to 1996. In the USA, data from 2000 and 2001 demonstrated that those drugs are prescribed more often than serotoninergic drugs [1]. They are indicated in the treatment of neuropathic pain [2], fibromyalgia, irritable bowel syndrome, migraines (prophylaxis) and headaches of cervical origin, and in chronic myofascial pain. Those syndromes are common in patients treated in pain clinics and are difficult to treat, even in state-of-the art centers requiring, frequently, a pharmacological and non-pharmacological approach by the multidisciplinary team.

The main side effects of TACs include: dry mouth, constipation, somnolence, weight gain, mental confusion, urinary retention, postural hypotension, and cardiac arrhythmias. Some authors, based on studies during psychiatric treatment in which they are used in higher doses than the doses used in the treatment of chronic pain syndromes (25 to 100 mg) recommend that TACs should be avoided in the elderly and patients with cardiomyopathies.

It is known that, in Brazil [4] and in the rest of the world [5], the incidence of neuropathic pain, as well as cardiovascular diseases, increases with age. Therefore, we have, on one hand, a drug with a good analgesic response in neuropathic pain,

and on the other hand, the concern about possible deleterious cardiovascular effects. However, the literature lacks evidence proving the incidence of those effects in the doses used for pain relief.

The objective of this study was to evaluate the use of TACs in chronic pain syndromes and their electrocardiographic repercussions.

METHODS

After approval by the Ethics on Research Committee of the Hospital Universitário Clementino Fraga Filho da Universidade Federal do Rio de Janeiro (HUCFF/UFRJ) and signing of the informed consent, 40 patients of the Pain Treatment and Palliative Care Program (PTDCP, from the Portuguese), ages 18 years or older, with neuropathic pain were included in this study. Exclusion criteria were as follows: patients on class Ia anti-arrhythmic drugs (pro-arrhythmic action); consumptive syndromes, liver disease, unstable cardiomyopathies, major mood disturbances (depression, bipolar) disorders, and altered cognition. Fifty-two patients were enrolled in the study; however, 12 were excluded for the following reasons: the dose was reduced in four patients due to a non-cardiac collateral effect (somnolence); one presented persistent palpitation and the drug was discontinued; four did not attend follow-up appointments, and three started TACs before the baseline ECG. Twenty one patients were males and 19 females. Patients on amitriptyline or imipramine on doses equal or greater than 25 mg/day for relief of neuropathic pain participated in this study. Patients underwent three electrocardiograms (ECG), which were analyzed posteriorly: before beginning TACs, and 30 and 60 days after its onset. Standard 12-lead ECG, at a speed of 25 $mm.sec^{-1}$, was done with the patient at rest. The following parameters were measured and analyzed: HR (heart rate), PR, QRS, QT, QTc, QT dispersion, and QTc dispersion. As for the PR interval, measured from the beginning of the P wave to the beginning of the QRS, the highest value among the bipolar derivations in the frontal plane (D_1, D_2, D_3) was considered, and 0.21 sec was the upper normal limit [6]. A QRS of up to 0.10 sec was considered normal. For the QT interval, it was established a value of up to 0.46 sec, in V_2 or V_3, by the Lepeschkin method [7]. For the QT dispersion (normal up to 60 msec), it was calculated the difference between the lower and higher QT of the 12 leads. The Bazett formula ($QTc = QT/RRsec^{1/2}$) was used to calculate the QTc (QT interval corrected for the mean heart rate) [8]. The QTc dispersion (DQTc – QTcmax – QTcmin) was also calculated. For the statistical analysis, the results obtained for each parameter were evaluated by the Kolmogorov-Smirnov test, which did not reject the hypothesis of normalcy. Mean standard deviation and standard error were calculated. Analysis of Variance (ANOVA) for repeated measures was used to compare measurements along time (pre-, and 30 and 60 days of treatment). Paired Student *t* test was used to evaluate the progression of the doses of the drugs along the study. A level of significance of 5% was established for all statistical tests. The SPSS statistical program version 13.0 was used.

RESULTS

Table I shows the characteristics of all 40 patients regarding gender, age, use of imipramine or amitriptyline, preexisting diseases, and pattern of prior ECGs. Amitriptyline was used at a mean dose of 54.3 mg, and imipramine, 46.8 mg. Painful syndromes included: herniated intervertebral disk (17.5%), post-traumatic neuritis (17.5%), lumbosciatalgia (10%), post-herpetic and post-leprosy neuritis (7.5% each), and post-laminectomy syndrome, central pain and postoperative neuroma (5.0% each).

Heart rate, PR, QRS, QT, QTc, DQT, and DQTc of all 40 patients during the eight weeks of treatment with TACs were analyzed and the results only showed statistically significant differences in the variation of the HR and duration of the QRS (Table II).

Table I – Patient Characteristics

Parameters	n	%
Gender		
Male	21	52.5
Female	19	47.5
Age		
< 60 years	24	60
≥ 60 years	16	40
Preexisting diseases		
None	10	25
Hypertension	23	57.5
Non-insulin dependent diabetes	4	10
Insulin-dependent diabetes	3	7.5
Ischemic heart disease	2	5.0
Others	4	10
Normal baseline ECG	28	70
Abnormal baseline ECG	12	30
Left ventricular hypertrophy	3	7.5
Right bundle branch block	3	7.5
Left bundle branch block	3	7.5
1st degree atrioventricular block	1	2.5
Left anterior hemiblock	1	2.5
PVCs	1	2.5
TOTAL	40	100

ECG - electrocardiogram.

When compared with the dose of the TACs, the QTc demonstrated statistically significant differences with the use of amitriptyline (Student *t* test – Table III). Due to the reduced number of patients on imipramine, confirmation of this information was not possible. Stratified analysis was done for: gender, age, baseline cardiomyopathy, baseline ECG, and type of TCA used (Tables IV, V, and VI).

Table II – Antidepressant Actions of Tricyclic Antidepressants *versus* Time

	Amitriptyline + Imipramine (n = 40)			
Parameters	M_0	M_1	M_2	p
HR (bpm)	72.76 ± 13.21	76.79 ± 15.48	76.48 ± 14.52	< 0.05
PR (ms)	150.15 ± 27.04	155 ± 26.27	151.90 ± 31.17	NS
QRS (ms)	82.30 ± 10.61	85.60 ± 10.30	87.77 ± 9.49	< 0.05
QT (ms)	377.78 ± 28.82	371.05 ± 34.82	370.33 ± 28.98	NS
QTc (ms)	412.71 ± 27.06	414.80 ± 21.80	413.50 ± 26.53	NS
DQT (ms)	34.70 ± 14.05	36.10 ± 14.02	35.23 ± 14.80	NS
DQTc (ms)	37.74 ± 14.75	40.77 ± 16.11	39.30 ± 16.18	NS

ANOVA
M_0 – pre-medication ECG; M_1 – ECG 30 after beginning TACs; M_2 – ECG 60 days after beginning TACs.

Table III – Effects of the Different Doses of Tricyclic Antidepressants

	amitriptyline				imipramine			
Dose	25 mg (n = 15)	50 mg (n = 59)	75 mg (n = 22)	p	25 mg (n = 12)	50 mg (n = 11)	75 mg (n = 1)	p
HR	68	75	71.5	NS	70.2	83		NS
PR	161.6	146	146.3	NS	178.8	154	-	NS
QRS	82	84	82	NS	80	80	-	NS
QT	360	380	400	NS	380	360	-	NS
QTc	397.8	412.2	428.1	0,0044	417.4	407.3	-	NS
DQT	26	36	40	NS	28	40	-	NS
DQTc	34.9	37.5	39.9	NS	31.3	46.5	-	NS

Student *t* test.
p < 0,05 – significant; NS – non-significant.

Table IV – Effects of Tricyclic Antidepressants on Mean QRS Duration *versus* Age

Parameter	Age < 60 years (n=24)			Age ≥ 60 years (n=16)		
QRS (ms)	Δ mean	p	CI 95%	Δ mean	p	CI 95%
$M_1 - M_0$	1.75	0.30 (NS)	-1.69; 5.19	5.62	0.09 (NS)	-1.17; 12.42
$M_2 - M_0$	3.70	0.07 (NS)	-0.45; 7.86	8.12	0.01	1.79; 14.45
$M_2 - M_1$	1.95	0.25 (NS)	-1.47; 5.39	2.50	0.18 (NS)	-1.37; 6.37

ANOVA; NS – non-significant.
Δ mean – mean difference; M_0 – before TACs; M_1 - 30 days after the beginning of TACs; M_2 - 60 days after the beginning of TACs; CI – confidence interval.

Table V – Effects of Tricyclic Antidepressants on Mean QRS *versus* Heart Disease

Parameter	Absence of heart disease (n = 16)			Heart disease (n = 24)		
QRS (ms)	Δ mean	p	CI 95%	Δ mean	P	CI 95%
$M_1 - M_0$	4.00	0.08(NS)	-0.57; 8.57	2.83	0.23 (NS)	-1.98; 7.65
$M_2 - M_0$	4.56	0.07(NS)	-0.47; 9.59	6.08	0.01	1.12; 11.04
$M_2 - M_1$	0.56	0.66(NS)	-2.14; 3.27	3.25	0.09 (NS)	-0.54; 7.04

ANOVA; NS – non-significant.
Δ mean – mean difference; M_0 – before TACs; M_1 - 30 days after beginning TACs; M_2 - 60 days after beginning TACs; CI – confidence interval.

Table VI – Effects of Tricyclic Antidepressants on the Mean Duration of the QRS *versus* Baseline ECG

Parameter	Normal baseline ECG (n = 28)			Abnormal baseline ECG (n = 12)		
QRS (ms)	Δ mean	P	CVC 95%	Δ mean	p	CI 95%
$M_1 - M_0$	4.00	0.02	0.55; 7.44	1.66	0.67 (NS)	-6.77; 10.11
$M_2 - M_0$	4.28	0.02	0.51; 8.09	8.25	0.01	0.01; 16.48
$M_2 - M_1$	0.28	0.82 (NS)	-2.40; 2.97	6.58	0.01	1.57; 11.59

ANOVA; NS - non significant.
Δ mean – mean difference; M_0 – before TACs; M_1 - 30 days after the beginning of TACs; M_2 - 60 days after the beginning of TACs; CI – confidence interval.

DISCUSSION

The Pain Clinic of the Hospital Universitário Clementino Fraga Filho da Universidade Federal do Rio de Janeiro was opened in 1983 and it has a multidisciplinary team that includes anesthesiologists, psychiatrists, clinicians, physical therapists, and social workers. It treats oncology patients undergoing palliative care and patients with non-oncologic chronic pain. Tricyclic antidepressants are prescribed for approximately 40% of the patients with chronic pain followed-up by the Program, which justifies the importance of the present study.

Tricyclic antidepressants have been used for more than 40 years in the treatment of depression, and more than 20 years in the treatment of neuropathic pain, starting with the studies of Watson [9], Max [10], and Leijon [11]. In the decade of 1960, when their use became more common, heart block or arrhythmias were the main cause of death in cases of overdose.

As for their cardiac effects, they interfere with conduction, which can be seen in the electrocardiogram and electrophysiological studies, with increases in PR, QRS, and QTc intervals. However, those increases are seldom symptomatic in patients without heart disease [12]. More recently, it has been speculated that low doses of those drugs are not associated with additional risks, even in the elderly and patients with heart disease [13]. The results of the present study corroborate those in the literature. However, it should be emphasized that the doses used in psychiatry are higher than those used for analgesia [14,15], what can affect patients with heart disease [16] and the elderly [17]. One of the rare publications on their safety in low doses is a meta-analysis of six studies comparing low doses of TACs (< 100 mg) with standard doses used in the treatment of depression (> 100 mg), showing the lower incidence of side effects in low doses [1].

In this longitudinal, prospective study, antidepressants were used in maximal analgesic doses of 75 mg/day in a representative sample of the population as far as gender, pain syndrome, and mean dose of TACs are concerned.

Interferences with the HR, with a mild increase, were observed after 30 days of treatment (M_1), and this was statistically significant (Table II). The increase in heart rate begins at the onset of treatment, with a tendency for adaptation in approximately four weeks. This variation only affected females. At the end of the follow-up (M_2), a return to baseline levels was observed (p = 0.01). This transitory effect was not clinically significant, but it has been reported in the literature [18].

The duration of the QRS complex was discretely increased in M_1, with a small statistical significance (p = 0.049 and CI = 0.014-6.58). However, values in M_2 increased further when compared to baseline levels (M_0), with a p = 0.03 (CI 2.02-8.90) and without clinical repercussion (Table II). This small variation of the QRS was seen in elderly patients and patients with cardiomyopathies (Tables IV and V). QRSs complexes equal or greater than 120 msec were not observed until the end of the follow-up; this level according to the literature would indicate greater tendency for arrhythmia [19]. In the present study arrhythmias were not observed on the electrocardiogram.

As for the baseline ECG, QRS changes were observed in patients whose baseline ECG was altered as well as in those with normal ECGs (Table IV). In this study, patients with prior conduction changes did not have greater variation of the QRS, which is not supported by the literature when TACs are used in antidepressant doses [20].

It was demonstrated that change in the QRS occurred at the moment the highest dose was used. This supports the notion that the influence of this group of drugs on cardiac electrophysiology is mainly dose-dependent.

Evaluating the effects of different doses of TACS, this study demonstrated a significant increase in QTc during the use of 75 mg of amitriptyline ($p = 0.04$). On the other hand, a reduction in the QTc was observed with the use of 50 mg of imipramine, but this was not statistically important.

An increase in QT can lead to severe ventricular arrhythmias, according to Antzelevitch [21]. QT dispersion (DQT) reflects regional differences in ventricular depolarization time. When the intrinsic heterogeneity of the ventricular myocardium is widened, it is reflected on a greater DQT. In the present study, QT dispersion did not increase significantly during treatment (Table III). Despite reports in the literature, which demonstrate the presence of cardiovascular complications, including heart blocks, with antidepressant doses of TACS, arrhythmias were not detected in this study [22,23].

In cases of differences in the dose used, one could demonstrate an influence on the QTc, but only in cases treated with amitriptyline (Table III). But the reduced number of patients treated with imipramine (eight) did not allow the conclusion that this drug does not interfere with the QT interval. Elderly patients and women are more prone to TAC-induced increases of the QT interval [24], which was not demonstrated in the present study.

To conclude, tricyclic antidepressants affect the conduction system, but without clinical significance in patients with heart disease and the elderly, because the doses used for analgesia of neuropathic pain were lower than 100 mg.

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RESUMEN

Cunha Jr RJ, Barrucand L, Verçosa N **—** Estudio de las Alteraciones Electrocardiográficas con el Uso de Antidepresivos Tricíclicos en Pacientes con Dolor crónico.

JUSTIFICATIVA Y OBJETIVOS: *Los antidepresivos tricíclicos (ADT) son muy utilizados como analgésicos para lumbalgias crónicas y dolores neuropáticos. El objetivo de este estudio fue evaluar las alteraciones electrocardiográficas de los pacientes con dolor crónico que usan amitriptilina o imipramina.*

MÉTODO: *Se estudiaron 40 pacientes con edad entre 26 y 81 años (m = 57,27 ± 13,65 años), de los dos sexos (mujeres 19, hombres 21), con síndromes neuropáticos (lumbociatalgias, síndromes pos-laminectomía, neuritis pos-herpética, entre otras); un 60% con enfermedades cardiovasculares; 30% tenían ECG alterado (BRD,*

BRE, BAV 1°G, HBAE o extra-sístoles). Se realizaron y se analizaron tres ECGs: antes del inicio de los ADT, 30 y 60 días después del inicio del tratamiento, evaluando los parámetros PR, QRS, QT, QTc, DQT, DQTc y FC. Treinta y dos pacientes usaron amitriptilina y ocho imipramina. La dosis promedio al final del estudio fue de 54,29 mg de amitriptilina y de 46,87 mg de imipramina.

RESULTADOS: *El análisis de las variables electrocardiográficas después del uso de los ADT arrojó lo siguiente: la amitriptilina aumentó la frecuencia cardíaca transitoriamente en el sexo femenino (p = 0,049) y la duración del QRS en los pacientes con edad igual o superior a los 60 años y en los cardiópatas en la segunda evaluación (p = 0,01). En los pacientes que recibieron amitriptilina, dosis de 75 mg, el intervalo QTc fue mayor cuando se le comparó a las dosis de 25 mg (p = 0,0044). El aumento de esos parámetros mostró el efecto de la amitriptilina sobre la conducción cardíaca, sin embargo, no se registró comprometimiento clínico, pues los valores permanecieron dentro de los límites de la normalidad (QRS < 110ms y QTc < 470ms).*

CONCLUSIONES: *El uso clínico de los ADT en dolores crónicos, arrojó resultados seguros y eficaces, y no presentó disturbio de la conducción cardíaca con repercusión clínica.*