Progressive loss in circulating volume during haemodialysis can be monitored by time voltage integral area of QRS complex: pilot study

Mario Curione[1], Claudia Castro[1], Camillo Cammarota[2], Gianfranco Tonnarini[1], Marzia Pasquali[3]

[1]Department Internal Medicine and Medical Specialities – University "Sapienza", University of Rome, Italy
[2]Department of Mathematics, ''Guido Castelnuovo'' – "Sapienza", University of Rome, Italy
[3]Department of Internal Medicine and Medical Specialities, Nephrology Service – "Sapienza", University of Rome, Italy

Corresponding author:
Prof. Mario Curione
University of Rome
School of Medicine
viale del Policlinico 155
00164 Rome, Italy
Phone: 0390686207489,
0390649978443
E-mail:
mario.curione@uniroma1.it

Abstract

Introduction: Time voltage area of QRS is a parameter that showed a close association with modifications in endoventricular volume. The aim of the study was to investigate the efficacy of this parameter in identifying progressive reduction in circulating blood volume (BV) during haemodialytic treatment (HT).
Material and methods: Thirteen uraemic patients were studied. XYX like leads were monitored before, during and after HT. Summation of areas of each QRS complex was named QRS total area (TA).
Results: Increase in QRS TA and decrease in BV were found after vs. before HT. Progressive increase in QRS TA is strongly linked to a progressive reduction of BV during HT.
Conclusions: These findings encourage use of ECG monitoring during HT with a dual purpose: rhythm and haemodynamic control. In fact, excessive or insufficient subtractions of water, with consequent hypotensive or cardiorespiratory crisis, are the most frequent complications in these patients.

Key words: QRS area, haemodialysis, circulating volume.

Introduction

Time voltage area of QRS is closely linked to modifications in R-R interval length during stress time and during recovery time in normal subjects, probably as a consequence of endoventricular volume variations [1].

In the present study we want to investigate modifications in time voltage area of QRS during haemodialytic treatment (HT). Haemodialytic treatment represents a clinical experimental model in which progressive reduction in endoventricular volume represents *per se* the most important component affecting QRS voltage, in absence of significant variations in R-R interval length, diversely by the stress test model.

Increased QRS amplitude has been reported in a single lead (V5) or in XYZ Frank leads at the end, with respect to the start of HT [2, 3], except for Ojanen *et al.*, who monitored QRS vector difference changes during the entire HT [4]. To our knowledge, no study has evaluated the change in time voltage area during the entire HT.

The aim of the study was to investigate the efficacy of time voltage area of QRS in identifying the progressive decrease in blood volume (BV) in a group of patients who underwent to HT.

Material and methods

Thirteen chronic uraemic patients, 7 male, 6 female (mean aged 59 ±19 years) have been monitored during HT in the Haemodialysis Unit of Urology Department, University of Sapienza, Rome. Clinical characteristics of the population are shown in Table I.

Standard 12-lead ECG was continuously monitored before, during and after HT with a Norav Medical Ltd. device. Dedicated software was used to extract X, Y, Z like leads from standard 12-lead ECG. Subsequently time voltage area in each QRS complex in XYZ like leads was computed as the time integral from the onset to the offset of QRS [1]. Summation of areas of each QRS complex in XYZ like leads was named total area (TA). QRS TA values were obtained in each patient, as a mean of every minute beat-to-beat value. BV loss percentage was obtained from the difference of values measured every 15 min. Echocardiography was performed before HT in all patients to exclude pericardial effusion. Bundle branch block, ventricular pre-excitation, pacemakers, atrial fibrillation and acute myocardial ischemia during HT were considered exclusion criteria because they can affect, *per se*, with different mechanisms, QRS area [5-7]. Age, gender, race, and ventricular mass were not considered as our study concerns intra-individual variability of QRS area. To exclude change in heart's position, relative to the chest wall, the patients were maintained in the same decubitus during HT.

The variables reported in Table II were measured before and after the HT. Statistical evaluation was performed to exclude the influence during HT of variables able to modify QRS amplitude such as heart rate, haemoglobin, red cell number, and intra-myocardial conduction delay, in addition to BV loss [7, 8].

Statistical analysis

Mean values of variables listed in Table II at the start and at the end of HT were compared using Student's *t*-test. Statistical significance was considered for *p* value < 0.05. We considered the relationship between the following two variables: the QRS TA and the percentage of BV loss. The statistical analysis was performed with the software R: A language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org).

Results

A significant increase in QRS TA and a significant decrease in circulating BV were found after vs. before HT. QRS TA increase is gradual during HT and closely related to the reduction of BV. A BV loss of 1% involves a QRS TA increase of 10 units.

No statistical difference was found between all other variables, i.e. heart rate, QRS length, red cell number and haematocrit value before and after HT (Table II).

Discussion

It is difficult to find a unitary pathogenetic interpretation to explain changes in QRS amplitude during stress test or during HT or in heart failure, blood transfusion, myocarditis, and pericarditis and in myocardial ischaemia. In clinical models, many factors are able to modify QRS amplitude.

Proposed pathogenetic mechanisms are often in contrast with theoretical analysis (Brody effect) [9]. Recently, Madias has proposed a "3-Compartment Mechanistic Model" to explain the attenuation of the electrocardiographic QRS complexes

Table I. Clinical characteristics of patients undergoing haemodialytic treatment

Number of patients	13
Male	7
Female	6
Mean age [years]	56 ±19
Duration of HT [years]	1-15
HT length [h]	3-4
Types of nephropathies, *n*:	
Glomerulonephritis	4
Polycystic kidney	2
Berger disease	1
Goodpasture syndrome	1
Urethral stenosis	1
Diabetic nephropathy	1
Nephroangiosclerosis	1
Cancer kidney	1
Systemic lupus erythematosus	1
Associated pathologies, *n*:	
Hypertension	13
Hypothyroidism	4
Secondary hyperparathyroidism	2
Paroxysmal atrial fibrillation	1
Drugs: diuretics, anticoagulants, calcium channel blockers, ACE inhibitors, angiotensin receptor blockers, l-thyroxine, vitamin D, calcium carbonate, erythropoietin	

Mario Curione, Claudia Castro, Camillo Cammarota, Gianfranco Tonnarini, Marzia Pasquali

Table II. Statistical significance of differences in mean values of variables evaluated before and after haemodialytic treatment in 13 chronic uraemic patients

Variable	Pre HT	Post HT	Value of p
Total area QRS [mV × ms]	333	403	< 0.01
Blood volume [%]	100	91.1	< 0.0001
Weight [kg]	69.5	66.5	< 0.003
Blood pressure [mm Hg]	140/83	135/79	NS
Heart rate [bpm]	77	77	NS
Red cells [million/mm^3]	3.2	3.1	NS
Haemoglobin [g/dl]	12.4	13.9	NS
Haematocrit [%]	80	83	NS
QRS length [ms]	40.3	42.3	NS
PH	7.33	7.44	< 0.0001
Creatinine [mg/dl]	10.1	4.1	< 0.0001
Azotaemia [mg/dl]	73.07	28.77	< 0.002
Ca^{2+} [mg/dl]	8.16	9.84	< 0.005
K$^+$ [mEq/l]	5.52	3.77	< 0.0008
Na$^+$ [mEq/l]	134.32	141.55	< 0.0001
Phosphataemia [mg/dl]	6.122	2.65	< 0.0001

observed in patients with blood volume overload [10]. This pathogenetic hypothesis could be able to explain our results.

The 1st compartment, according to Madias, includes the effects of increased intraventricular blood volume and decreased haematocrit, due to blood dilution, the 2nd compartment includes the heart's alteration in electrogenesis, due to possible ischaemia or inflammation, leading to myocardial oedema, and the 3rd compartment includes the passive volume conductor of tissue and organ constituents of the thorax and the entire body (pulmonary and peripheral oedema).

In the absence of a significant increase of haematocrit value at the end of HT vs. before HT, only the reduction in BV would influence the QRS TA increase in our patients. The lack of difference in heart rate after vs. before HT allows us to exclude modifications in left ventricular diastolic filling as a cause of increased QRS TA value.

The influence of the 2nd compartment can be excluded by the absence of ischaemic symptoms with typical ECG abnormalities and by the absence of intraventricular conduction delay during HT.

The influence of the 3rd compartment can be excluded by the absence of pericardial effusion before HT. We cannot exclude "tegument oedema", as a possible variable influencing QRS TA, despite the patients in chronic dialysis having mild generalized oedema. Moreover, a redistribution of generalized oedema in such a short time (mean HT time 4 h) seems unlikely.

In conclusion, changes in QRS TA, observed during the HT treatment, should reflect variations in intraventricular volume, since we excluded many of the possible confounding factors listed in Madias' model. We found a strong inverse correlation between the increase in QRS TA and the reduction of BV (BV loss of 1% leads to a QRS TA increase of 10 units).

The results of this pilot study, despite the small number of patients, encourage to use monitoring of QRS TA during haemodialysis to prevent excessive or insufficient subtractions of water with consequent hypotensive or cardiorespiratory crisis, frequent complications in these patients.

References

1. Curione M, Cammarota C, Cardarelli G, et al. QRS area monitoring during stress test: a novel index to separate normal to ischaemic patients? Arch Med Sci 2008; 4: 51-6.
2. Vitolo E, Madoi S, Palvarini M, et al. Relationship between changes in R wave voltage and cardiac volume. A vector-cardiographic study during hemodyalisis. J Electrocardiol 1987; 20: 138-46.
3. Fuenmayor AJ, Vasquez CJ, Fuenmayor AM, Winterdaal DM, Rodriguez D. Hemodialysis changes the QRS amplitude in the electrocardiogram. Int J Cardiol 1993; 41: 141-5.
4. Ojanen S, Koobi T, Koronen P, et al. QRS amplitude and volume changes during hemodialysis. Am J Nephrol 1999; 19: 423-7.
5. Madias JE. Attenuation (augmentation) of intrinsic and paced QRS complexes before (after) hemodialysis. Pacing Clin Electrophysiol 2008; 31: 1656-60.
6. Ojanen S, Kööbi T, Koivisto AM, Korhonen P, Mustonen J, Pasternack A. Hemodialysis causes changes in dynamic

vectorcardiographic ischemia monitoring parameters. Clin Nephrol 2000; 54: 227-33.

7. Madias JE. Low QRS voltage and its causes. J Electro-cardiol 2008; 41: 498-500.

8. Oreto G, Luzza F, Donato A, et al. Electrocardiographic changes associated with haematocrit variations. Eur Heart J 1992; 13: 634-7.

9. Brody DA. A theoretical analysis of intracavitary blood mass influence on the heart-lead relationship. Circ Res 1956; 4: 731-8.

10. Madias JE. QRS voltage changes in heart failure: a 3-compartment mechanistic model and its implications. Indian Pacing Electrophysiol J 2010; 10: 464-73.