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RESEARCH ARTICLE

PARASYMPATHETIC DEFICIENCY IN HEART FAILURE

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Abstract

In heart failure,it has been recognized that sympathetic hyperactivity occurs, which is well counteracted by beta-blockers. In addition, there is frequently parasympathetic deficiency, which in turn contributes to the deterioration of cardiac function. The aim of the study was to evaluate the parasympathetic function by the deep breathing test and to highlight the deficiency of this system in the heart failure patient. We conducted a descriptive cross-sectional study from March to August of 2019. Patients were subdivided into 2 groups:group 1 included 35 patients with chronic heart failure (left ventricular ejection fraction ≤49%) and group 2 (control group) included 32 patients without heart failure(left ventricular ejection fraction ≥50%). The exploration of the parasympathetic system in our patients was based on the deep breathing test. It revealed a vagal deficit in 60% of group 1 patients versus 20% of group 2 patients. This difference was statistically significant between the 2 groups with a p-value of 0.032 (<0.05). Theseresults showed a significant vagal deficiency in heart failure patients and were in line with the literature. Therefore, vagal stimulation in patients with heart failure may be a good therapeutic option to improve symptoms and cardiac functionas some studies have shown.

Introduction:-

In heart failure (HF), there is an autonomic imbalance consisting of sympathetic hyperactivity and vagal deficiency, which is known to lead to further worsening of the heart failure prognosis[1].For this reason,the inhibition of the activated sympathetic system with beta-blockers is recommended.There are fewer studies concerning parasympathetic deficiency versus sympathetic hyperactivity in heart failure. Therefore, its pathophysiology is less known, its diagnosis is not common and its treatment is not yet practiced despite some studies have demonstrated that vagal stimulation has beneficial effects on heart failure specifically on the improvement of quality of life and symptoms [2-3].The aim of our study is to highlight the parasympathetic deficiency in the heart failure patient by evaluating the vagal response with the deep breathing test.

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Material and Methods:-

The studywas a descriptive cross-sectionalstudyover a period of 6 monthsfrom March to August of 2019.Patients weresubdividedinto 2 groups: group 1 included 35 patients withchronicheartfailure (leftventricularejection fraction ≤49%) and group 2 (control group) included 32 patients withoutheartfailure (leftventricularejection fraction ≥50%).

All patients were in sinus rhythm.Weapplied the deepbreathing (DB) test to **assess** thevagal activity.This test evaluates changes in the instant heart rate (RR space variation on the electrocardiogram) thatisprovoked by "deep" breathingat 6 breaths/min. The test isperformed in supine position and startswith a restperiodthatgives patient time to relax.

The beta-blockers and vasodilatorswerestopped in all patients beforeat least 48 hours of the DB test.All patients underwent a completeclinicalexamination, electrocardiogram, echocardiography and DB test.

Statisticalanalysis of resultswasperformedusing SPSS software.

Results:-

The meanagewas 57+/-9 years in group 1 and 53+/-4 years in group 2. Wenoted a slightmalepredominance in both groups, 56% in group 1 with a sex ratio of 1.17 and 61% in group 2 with a sex ratio of 1.21.

The mostcommoncardiovascularrisk factor in both groups was smoking. In group1, diabetes and obesitywere second only to smoking, thenobesity and dyslipidemia (Table 1).The difference in cardiovascularriskfactorsbetween the two groups wasstatisticallysignificant for smoking (p-value: 0,043) and hypertension (p-value: 0,003).

Table 1:- Description of cardiovascular risk factors in both groups.

Cardiovascular risk factor	Group 1 n=35	Group 2 n=32	p-value
Chronic smoking	17 (48%)	13(40%)	0.043
Diabetes	12 (34%)	9 (28%)	0.7
Hypertension	8 (22%)	4 (12%)	0.03
Dyslipidemia	7 (20%)	9 (28%)	0.54
Android obesity	12 (34%)	10 (31%)	0.5

All patients in group 2 (control group) were asymptomatic except 3 patients with extracardiac symptoms including arthralgia, gastric ulcer and chronic low back pain of undetermined cause.

In group 1,according to the NYHA classification of dyspnea, 5 patients had stage I, 21 patients had stage II, 9 patients had stage III, and no patients had stage IV.

In group 1, two patients reported atypical precordialgia, 2 patients had palpitations and 1 patient had a syncopal episode. In the same group, 22 patients had no signs of heart failure (HF), 6 patients had isolated right-sided signs of HF, 3 patients had left-sided signs of HF, and 4 patients had global signs of HF.

In group 2, the echocardiography revealed a moderate left ventricular hypertrophy with slight dilatation of the left atrium in 2 patients. All patients had normal LVEF ≥50% with no significant valvulopathy. However, in group 1, 23 (66%) patients had LVEF between 35 % and 49% (Fig 1), 3 (8%) patients had severe aortic insufficiency and 2(5%) patients had severe mitral insufficiency.

The etiologies of heart failure in group 1 in descending order were ischemic heart disease (54%), valvular disease, primary dilated cardiomyopathy and hypertensive cardiomyopathy. (Fig 2). In Group 1 patients, evaluation of parasympathetic activity by deep breathing test showed that 21 patients (60%) had vagal deficiency and 14 patients had normal vagal response (Fig 3). However, in group 2, only 7 patients (21%) had vagal deficiency. Among these patients, 4 were hypertensive and 1 was diabetic.

The difference of deep breathing test between the 2 groups was statistically significant with a p-value of 0.032.

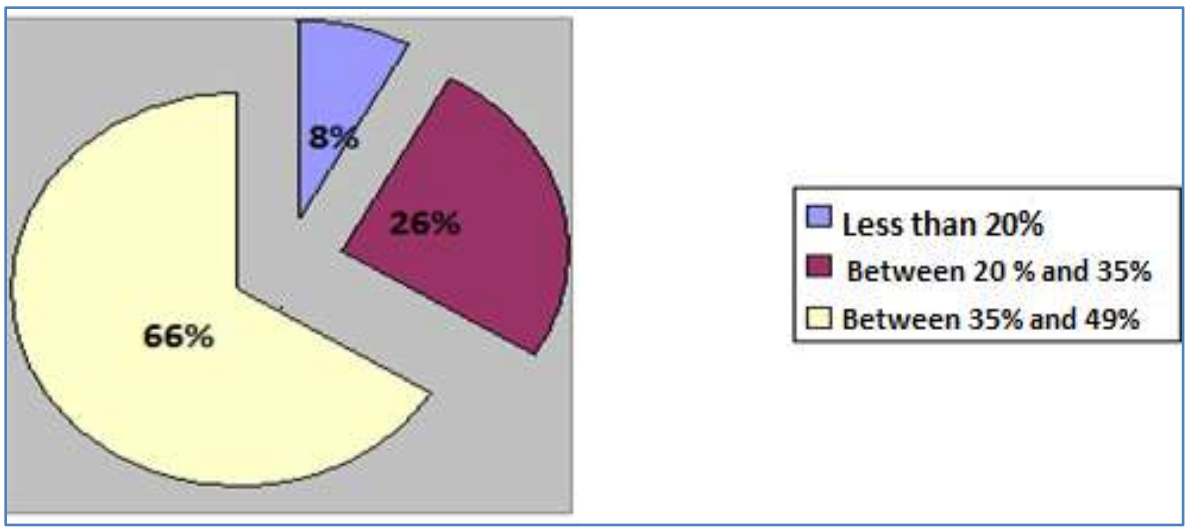

Figure 1:- Distribution of Group 1 patients according to LVEF.

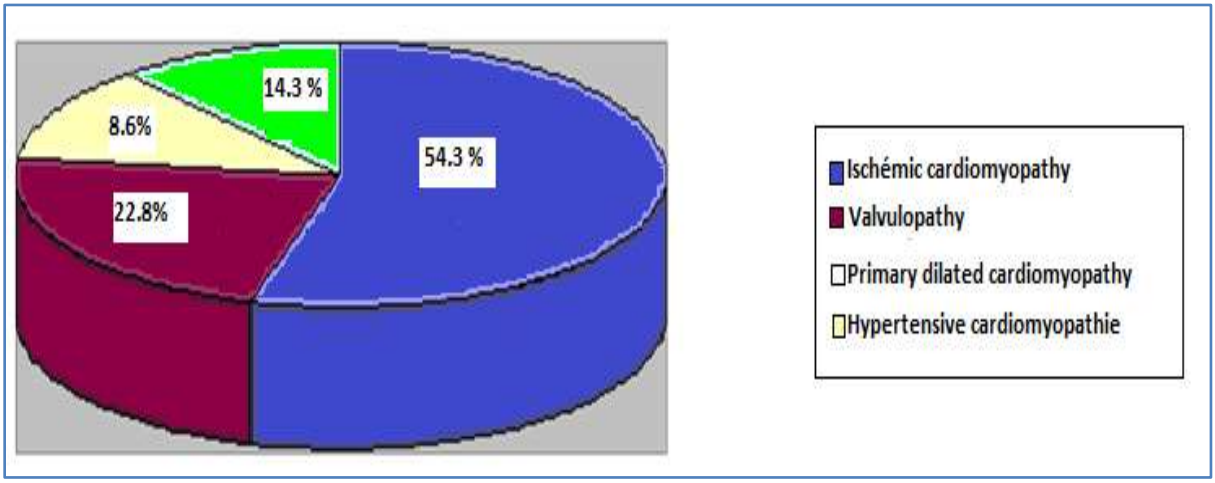

Figure 2:- Etiologies of heart failure in group 1 patients.

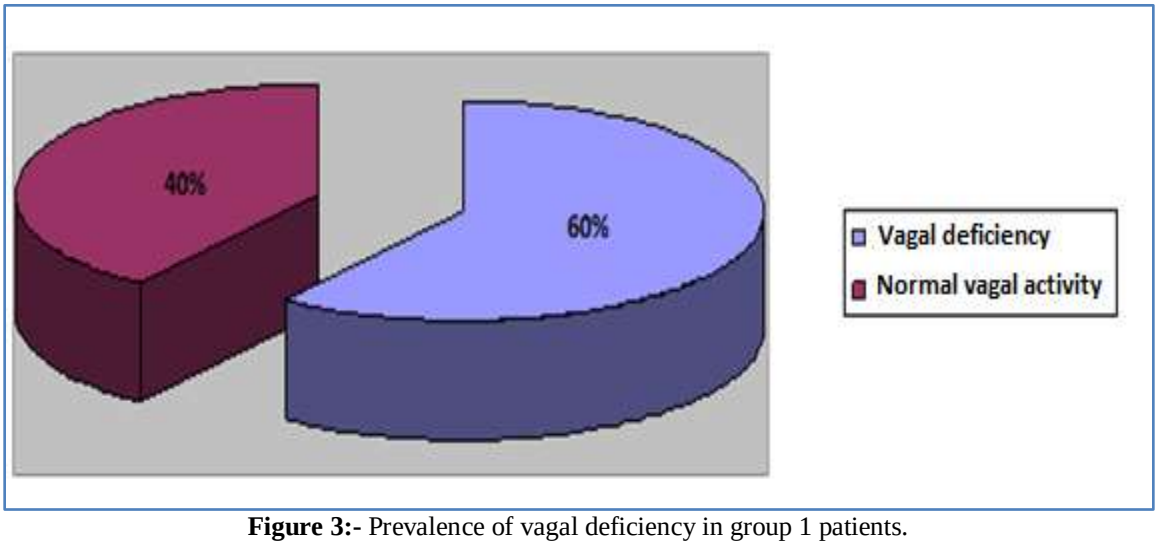

Figure 3:- Prevalence of vagal deficiency in group 1 patients.

Discussion:-

The concept of autonomic reflex dysfunction in human heart failure emerged from the demonstration by Eckberg **et al** of attenuated bradycardia in response to a drug-induced rise in systolic arterial pressure[4].Regardless of the etiology of heart failure,there are an almost constant parasympathetic deficiency and sympathetic hyperactivity that evolve over time[5].Indeed, when the heart dilates, vagal and sympathetic afferent cardiac fibers increase their firing, and this afferent sympathetic excitation leads to the tonic and reflex inhibition of cardiac vagal efferent activity.Therefore, heart failure should be considered as a disorder of autonomic and myocardial function [6].
The results of ourstudyshowed a significant vagal deficiency in heartfailure patients compared to patients withoutheartfailure .This resultsconcordwithmanystudies. Nolan et al conducted a study in heartfailure patients, using 24 hour Holter-ECG recordings, and demonstratedthattherewas a significantlinearcorrelationbetween the parameters of heart rate variability in relation to vagal deficiency and the severity of leftventriculardysfunction [7]. Musialik'sPolishstudyalsocompared the rate of leftventriculardysfunction and parameters of heart rate variability in heartfailure patients and concludedthattherewas a significantcorrelationbetweenthesetwoparameters [8].

Vagal deficiencyiscertainlyfound in heartfailure due to ventriculardysfunction, but there are other situations thatfavouritindependently of ventricularfunctionsuch as diabetes[9], hypertension [10], smoking[11], obesity[12], dyslipidemia[13], sedentarylifestyle[14]and somecardiacdiseasessuch as ischemicheartdisease[15],dilatedcardiomyopathy[16], and hypertensive cardiomyopathy.

In group 2 (control group) of ourstudy, 4 diabetic patients and one hypertensive patient had vagal deficiency, whichis in line with the literature data [10-15].

Thereforeparasympatheticdeficiency in the heartfailureis the result of ventriculardysfunction. This deficiencyisfavored or aggravated by the existence of cardiovascularriskfactors and someetiologies of heartfailure.

Vagus nerve stimulation (VNS)to restore vagal activity in heartfailure has garneredincreasinginterest in recentyears. The results of trials werepromising.TheAutonomic Neural Therapy to EnhanceMyocardialFunction in HeartFailure (ANTHEM-HF) studyevaluated the use of a VNS system in patient with HF[17]. In thisstudy,therewerestatisticallysignificantimprovements in the primaryefficacyendpoints of LVEF and leftventricle end-systolic volume (LVESV) as well as the secondaryefficacyendpoints of leftventricle end-systolicdiameter (LVESD), heart rate variability and 6-minute walk test (6MWT). Subsequent 12-month follow-up on 49 of the initial 60 patients showedthatimprovementspersistedduring longer follow-up and that the device implantation remainedsafe. Twootherstudies, NECTAR-HF Trial[2]and INOVATE-HF Trial[3], showedimprovement in NYHA class of dyspnea, patient quality of life and 6-minute walk test, but no improvement in mortality.

Consequently, vagal stimulation couldenhance the functionalprognosis as well as quality of life of heartfailure patients and itmaybe as effective as sympathetic inhibition. However,thereisstill no consensus or validatedprotocolregardingthis new therapeuticapproach.

Conclusion:-

Heartfailureisassociatedwithsignificantmorbidity and mortalitydespite the use of medicaltherapiesthattarget, in part, the neurohormonal axis. This diseaseischaracterized by autonomicimbalancewithincreasedsympatheticactivity and withdrawal of parasympatheticactivitywhichcontribute to the deterioration of cardiacfunction. Therefore, it'snecessary to carry out more studies on vagal deficiency to targetit in the treatment of heartfailure, especiallythatsome trials revealed a promisingeffect of vagal stimulation.

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