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Effects of Bioarginina® C supplementation on physical performance during Cardiac Rehabilitation in patients with heart failure.

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Background: One of the main symptoms of heart failure is reduced ability to exercise, therefore physical training is recommended to improve physical capacity, quality of life and prognosis (reduction in hospitalizations for heart failure). Therefore, physical exercise causes changes in arginine metabolism with increased NO production. Furthermore, reduced exercise capacity in heart failure may be caused by reduced exercise-induced hyperemic blood flow response arising from the endothelium dysfunction in heart failure. There is no evidence regarding changes in plasma concentrations of arginine derivatives during physical exercise in patients with heart failure. There is evidence that nutritional support with L-arginine and liposomal vitamin C, improve the perceived tolerance to effort. We hypothesized that Bioarginina® C supplementation during a program of Cardiac Rehabilitation in patients with heart failure, enhances its response. **Aim of the study**: to evaluate the effects of the use of combination of oral L-arginine + liposomal vitamin C (Bioarginina®C, 1.66 g 2 bottles/day) on perceived exertion measured Borg modified scale (BMS) and the functional capacity measured with the six minute walking test (6MWT) of subjects with heart failure during CR. **Methods:** The routine data of patients with reduced (HFrEF) admitted to Rehabilitation of S. Gennaro Hospital (Naples) were analysed. 73 patients (55 M and 18 F), with mean age 63 ± 9 years, (Group A) undergoing integration with two bottles of L arginine and liposomal vitamin C were examined above for 90 days during the CR cycle. As a control population, the results obtained with standard treatment in 36 patients with high cardiovascular risk (24 M and 13 F) (mean age 61 ± 6 years) (Group B), were examined. The entire study lasted 3 months. In all patients at baseline and after 3 months, routine blood pressure and M and B mode echocardiogram were performed. The ability to perform normal daily activities was analyzed with the six minute walk test (6MWT) which measures the distance that a subject can run on a flat surface, walking as fast as possible in six minutes, including any interruptions that patient deems necessary. The perception of the tolerance to the effort was measured by Borg modified 0–10 Rate of Perceived Exertion (BRPE) scale. Thirty minutes after each 6MWT, the nurse asked the patient to rate his/her level of effort at performing the exercise on the BRPE scale. The BRPE was used to measure the physical activity intensity level. BRPE is a personalized exertion grading since it gives a good estimate of heart rate during physical activity. 6 minute walk test was performed and after that patient BRPE level was graded based on Modified Borg scale grading 1-10 with 1 as “nothing”, 2 as “very easy” 3 as “Easy “,4 as “comfortable”,5 as “somewhat difficult”,6 as “difficult”,7 as “hard”, 8 as “very hard”,9 as “extremely hard”,10 as “maximal exhaustion”. **Statistical Analysis:** Normally distributed variables are presented as mean ± standard deviation (SD) and were compared by Student’s t-test for paired data for differences in the same group and with the Student's T test for unpaired data for differences between the two groups. Categorical variables are summarized in terms of number and percentages and were compared by using Chi-square test. A p-value ≤0.05 was considered statistically significant. **Results:** The basal characteristics of patients are shown in Tables 1. At 3 months, improvement in 6MWT values was observed in both groups in Group A: 248 ± 132 m vs 307 ± 124 m (p <0.0001) - Group B: 231 ± 126 m vs 241 ± 140 m (p <0.021). However in group A, these was more significant. In the BRPE score was a significant improvement in A group but not in B group. In Group A: 3,5 ± 3,1 vs 2,8 ± 3,1 (p <0.031) - Group B: 3,1 ± 2,8 vs 2,9 ± 2,4 (p <0.41). After the CR cycle, the increase in the 6MWT distance in group B was not accompanied by a statistically significant reduction in the BRPE score, denoting a persistent muscle load. Our data indicate that functional capacity, significantly reduced in patients with HFrEF, may improve after physical training. The simultaneous administration of L-arginine potentiates the response to CR, independently of age,

baseline functional capacity, and comorbid conditions, so that after 3 months CR program, we were able to detect a statistically and clinically significant increase in the 6MWT distance. **Conclusion:** We hypothesized that a supplementation combining L-Arginine (to improve endothelial function) and Vitamin C (to reduce oxidation) could have favorable effects on ventricular function and HRQoL in patients with post ischemic HFrEF. This study also, suggest that oral L-arginine + liposomal vitamin C supplementation could improve cardiac recovery and function.

Tab. 1: Baseline Characteristics

	A group 73 pts	B group 36 pts	P value
Age (yrs)	63 ± 9	61 ± 6	0,35
M/F	55/18	24/13	---
BMI	26±3	25±3	0,11
Hypertension	67 (91)	24 (64)	0,002
Hypercholesterolemia	58 (79)	29 (78)	0,89
Current smoker	5 (6)	7 (19)	0,04
Diabetes	38 (67)	13 (36)	0,11
GFR<60 ml/min	31 (42)	19 (52)	0,16
History PCI	59 (80)	30 (83)	0,75
History of prior MI	65 (89)	31 (86)	0,65
ICD	21 (28)	9 (25)	0,67
CRT	16 (21)	4 (11)	0,17
ACEi	31 (42)	11(30)	0,22
ARBs	3 (4)	6 (16)	0,02
ARNI	39 (53)	19 (53)	0,94
MRA	66 (90)	27 (75)	0,03
SGLT1 i	58 (79)	25 (69)	0,24
Diuretics	61 (83)	22 (61)	0,009
Beta Blockers	70 (95)	31 (86)	0,06
Statins	66 (90)	28 (77)	0,07
Ezetimibe	54 (73)	19 (53)	0,02
PCSK9i	9 (12)	2 (5)	0,0001