

INFLUENCE OF EXERCISE TESTING IN GASTROESOPHAGEAL REFLUX IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE

Influência do teste de esforço no refluxo gastroesofágico em portadores de doença do refluxo gastroesofágico

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ABSTRACT - Background: Gastroesophageal reflux disease is a worldwide prevalent condition that exhibits a large variety of signs and symptoms of esophageal or extra-esophageal nature and can be related to the esophageal adenocarcinoma. In the last few years, greater importance has been given to the influence of physical exercises on it. Some recent investigations, though showing conflicting results, point to an exacerbation of gastroesophageal reflux during physical exercises. **Aim:** To evaluate the influence of physical activities in patients presenting with erosive and non erosive disease by ergometric stress testing and influence of the lower esophageal sphincter tonus and body mass index during this situation. **Methods:** Twenty-nine patients with erosive disease (group I) and 10 patients with non-erosive disease (group II) were prospectively evaluated. All the patients were submitted to clinical evaluation, followed by upper digestive endoscopy, manometry and 24 h esophageal pH monitoring. An ergometric testing was performed 1 h before removing the esophageal pH probe. During the ergometric stress testing, the following variables were analyzed: test efficacy, maximum oxygen uptake, acid reflux duration, gastroesophageal reflux symptoms, influence of the lower esophageal sphincter tonus and influence of body mass index in the occurrence of gastroesophageal reflux during these physical stress. **Results:** Maximum oxygen consumption or VO₂ max, showed significant correlation when it was 70% or higher only in the erosive disease group, evaluating the patients with or without acid reflux during the ergometric testing (p=0,032). The other considered variables didn't show significant correlations between gastroesophageal reflux and physical activity (p>0,05). **Conclusions:** 1) Highly intensive physical activity can predispose the occurrence of gastroesophageal reflux episodes in gastroesophageal reflux disease patients with erosive disease; 2) light or short sessions of physical activity have no influence on reflux, regardless of body mass index; 3) the lower esophageal sphincter tonus does not influence the occurrence of reflux disease episodes during exercise testing.

HEADINGS - Gastroesophageal reflux. Exercise testing. Exercise. Gastrointestinal motility

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Financial source: none
Conflicts of interest: none

Received for publication: 06/08/2013
Accepted for publication: 28/11/2013

RESUMO - Racional: A doença do refluxo gastroesofágico é afecção com elevada prevalência em todo o mundo, que apresenta grande variedade de sinais e sintomas esofagianos ou extra-esofágico, podendo ter entre suas complicações o adenocarcinoma esofágico. Nos últimos anos, maior importância tem sido dada à influência dos exercícios físicos na sua patogênese. Algumas investigações recentes, embora com resultados conflitantes, apontam para agravamento do refluxo gastroesofágico durante eles. **Objetivos:** Avaliar a influência da atividade física em pacientes com doença erosiva e não erosiva através do teste ergométrico de esforço, e ainda, a relevância do tônus do esfíncter esofágico inferior e do índice de massa corpórea durante esta situação. **Métodos:** Vinte e nove pacientes com doença do refluxo erosiva (grupo I) e 10 com não-erosiva (grupo II) foram avaliados prospectivamente. Todos foram submetidos à avaliação clínica, seguida pela endoscopia digestiva alta, manometria e pH-metria esofágica de 24 horas. Um teste ergométrico foi realizado uma hora antes de retirar a sonda de pH-metria. Durante ele as seguintes variáveis foram analisadas: eficácia do teste, o consumo máximo de oxigênio ou VO₂ max, tempo de refluxo ácido, sintomas de refluxo gastroesofágico, influência do tônus do esfíncter esofágico e do índice de massa corporal na ocorrência de refluxo gastroesofágico durante esta situação. **Resultados:** VO₂ max apresentou correlação significativa, quando foi maior ou igual a 70%, apenas no grupo doença erosiva, avaliando os pacientes com ou sem refluxo

DESCRITORES - Refluxo gastroesofágico. Teste de esforço. Exercício. Motilidade gastrointestinal

ácido durante o teste ergométrico ($p=0,032$). As demais variáveis consideradas não demonstraram correlação significativa entre a ocorrência de refluxo gastroesofágico e a atividade física ($p>0,05$). **Conclusões:** 1) Atividade física de alta intensidade pode predispor à ocorrência de episódios de refluxo gastroesofágico em pacientes em portadores da forma erosiva; 2) atividade física de baixa intensidade ou de curta duração não exercem influência, independentemente do índice de massa corpórea; 3) o tônus do esfíncter esofágico não influencia na ocorrência de episódios de refluxo gastroesofágico durante atividade física.

INTRODUCTION

Gastroesophageal reflux disease (GERD) was defined by the consensus of Montreal as a condition developed when the reflux of stomach contents causes uncomfortable symptoms and complications²⁵. It has important medical-social feature due high prevalence rates, estimated at 20% in the USA adult population and similar rates in Europe²³. In Brazil, a population study shows a prevalence around 12%¹⁶.

The pathophysiology of GERD is multifactorial, highlighting the transient lower esophageal sphincter (LES) relaxation and changes in its tone (hypotonia).

Several studies^{5,6,21,22} have shown that depending on the intensity of physical activity performed symptoms related to the upper digestive tract (heartburn, regurgitation, belching,) are common, being present in up to 58%⁶. How physical exercise influences on its occurrence, however, remains unclear. Publications suggest three possible mechanisms: gastroesophageal motor disorders resulting from reduced mesenteric blood flow^{21,22}, endocrine-metabolic changes²⁰ and increased abdominal pressure correlated to some physical activity⁶. Other possible causes have been evaluated, such as changes in the esophagogastric junction and the LES tone (hypotonia)¹⁹.

Most studies on the subject were made in athletes and healthy, asymptomatic individuals, and few recent evaluations of the exercise training effects in patients with GERD¹². The hypothesis of the authors is that symptoms and reflux episodes induced by exercise are more frequent and symptomatic in patients with GERD, when compared to those that occur during their usual activities.

The primary objective of this study was to evaluate the influence of physical activity, through the ergometric stress testing (EST) in the occurrence of gastroesophageal reflux (GER) in patients with GERD, comparing the erosive and non-erosive forms of the disease. A secondary objective was evaluate the influence of the lower sphincter pressure and body mass index (BMI) in their occurrence.

METHODS

The study was conducted in accordance with the principles of the Declaration of Helsinki. The protocol was approved by the ethical-scientific committee of the Department of Gastroenterology and review committee of research projects at the Hospital das Clínicas (Cappesq), with the assent No 0615/07. After the study, patients continued to be followed as outpatient of the Department of Gastroenterology, Hospital das Clínicas, FMUSP.

In a prospective study, were evaluated 39 adult patients aged between 18 and 50 years old, both genders, coming from the ambulatory of esophageal and gastric diseases from the Hospital das Clínicas, School of Medicine, University of São Paulo São Paulo, SP, Brazil, with typical symptoms (heartburn or regurgitation more than three times a week). According to the endoscopic findings, they were divided into two groups: Group I - 29 patients with erosive esophagitis and Group II - 10 patients with the non-erosive reflux disease.

Based on BMI, patients were weighted and classified according to the classification of the World Health Organization², namely: normal or healthy individuals - those with BMI between 19 and 24.9 kg/m²; overweight - those with BMI between 25-30 kg/m²; considered obese - those with BMI >30 kg/m². In this study, patients had only grade I obesity.

The occurrence of GERD was assessed by performing pH monitoring, comparing the occurrence of this phenomenon during the patients' daily activities (excluding the sleeping period) and during the EST.

The patients were submitted to the following procedures: on the first day it was conducted an upper endoscopy to confirm or refute the presence of peptic erosions; on the second, it was performed esophageal manometry to localize LES precisely for correct positioning of the pH-metry probe and to discard the presence of esophageal dysmotility; on the third, the patient performed treadmill stress test with the pH probe monitoring, using the modified Heck protocol. The procedure was performed one hour after breakfast, and was concluded when all stages were performed (eight

RESULTS

total), and stopped when the heart rate reached the maximum pre-determined, or at the request of the patient. To calculate the maximum oxygen consumption (VO₂ max) pre-determined standard formulas were used and described by the national consensus ergometry, which are: VO₂=1.11x(60 - 0.55 x age) for men, and 1.11x(48 - 0.37 x age) for women⁷.

To calculate the maximum heart rate pre-determined, was used the Karvonen formula¹⁷, subtracting 220 from the patient's age; submaximal was considered as 85% of this figure. The test was considered successful when the patient reached at least the submaximal heart rate⁷. After the procedure, the patient remained seated one hour in recovery, and then the pH probe was removed, for data analysis.

To performed manometry and pH-metry a Alacer® equipment was chosen. For data analysis in the period in which the patient has exercised its usual activities, on periods analysis so supine and during the implementation of EST (considered artifacts); to analyze only during the EST, all other periods were considered artifacts. Drugs that interfere on the motility and/or gastrointestinal secretion - such as prokinetics, calcium channel blockers, antispasmodics, histamine H₂ receptor blockers and proton pump inhibitors - were suspended 10 days earlier the beginning of the study. Patients were instructed to use antacids (aluminum hydroxide) if they presented typical dyspeptic symptoms of GERD.

Were analyzed the following variables: 1) if the effectiveness of EST would influence the occurrence of GER episodes; 2) if the VO₂ max level attained would influence the occurrence of reflux episodes during the EST; 3) if during the EST, the individual would experience GER episodes compared to usual activities (excluding periods in the supine position); 4) if during the EST there would be more clinical symptoms suggestive of GERD, compared to usual activities; 5) if the hypotonia of the LES would influence the occurrence of GER during EST; 6) if the overweight or mildly obese have influence on the occurrence of GER episodes during the EST.

Statistical analysis

To compare categorical variables by group, was used the Fisher exact test, and except for analysis of the symptoms' occurrence at rest and at EST, when nonparametric Wilcoxon was used. To analyze the influence of BMI in the two groups together, it was utilized the likelihood ratio test. In every analysis was adopted the significance level of 5% (p<0.05).

Influence of the EST effectiveness in determining episodes of GER during the same

As shown in Table 1 the efficiency of EST does not influence the occurrence of GER in the two groups (p>0.05).

TABLE 1 - Correlation of the effective exercise testing to predispose gastroesophageal reflux episodes in comparison to the test which was not effective

| Reflux | Effective | Ineffective | p ¹ |
|-----------------|-----------|-------------|----------------|
| Group I | | | |
| Absent | 14 | 6 | 0,382 |
| Present | 8 | 1 | |
| Grupo II | | | |
| Absent | 8 | 1 | 1,000 |
| Present | 1 | 0 | |

¹Fisher's exact test

Evaluation of correlation between reflux episodes and physical intensity achieved, as measured by maximum oxygen consumption

The influence of physical intensity to produce an episode of GER in EST, obtained by indirect measurement of VO₂ max pre-determined, was evaluated in each group and are shown in Table 2, where it appears that there was influence of the intensity of physical activity on the occurrence of GER only in patients of Group I, who achieved a VO₂ greater than or equal to 70%. They had at least one episode of GER in EST compared with those who have not reached the same group (p=0.032). This correlation was not observed when analyzing Group II (p>0.05).

TABLE 2 - Correlation between maximum oxygen uptake during exercise testing and the presence of gastroesophageal reflux episodes

| Reflux episodes | VO ₂ ≥ 70% | VO ₂ <70% | p ¹ |
|-----------------|-----------------------|----------------------|----------------|
| Group I | | | |
| Absent | 4 | 16 | 0,032* |
| Present | 6 | 3 | |
| Grupo II | | | |
| Absent | 5 | 4 | 1,000 |
| Present | 1 | 0 | |

¹Fisher's exact test

Time percentage comparison of acid reflux during exercise testing and in usual activities

Was assessed whether, in the period in which the patient underwent the EST, there was a proportional increase in the percentage of acid reflux time compared to the same in the usual activities. Table 3 shows that in Group I the vast majority of patients had a percentage of acid reflux time higher in the usual activities; in Group II, this was true in all. Statistical correlation was not significant (p>0.05).

TABLE 3 - Acid reflux time during exercise testing and usual activities

| | % acid reflux time in ergometric testing higher than acid reflux time in usual activities | | p ¹ |
|---------|---|----|----------------|
| | Yes | No | |
| Grup I | 22 | 7 | 0,158 |
| Grup II | 10 | 0 | |

¹Fisher's exact test

Evaluation of clinical symptoms suggestive of gastroesophageal reflux during exercise testing and in usual activities

Was assessed whether, during the EST, the patient reported symptoms of GER and compared with the number of complaints reported in the acid reflux time. Table 4 shows that patients in both groups had a frequency of clinical symptoms suggestive of GER increased in usual activities compared to the period of the EST. There was, in this case, a significant statistical correlation (p=0.026).

TABLE 4 - Number of symptoms during exercise testing and in usual activities

| | Number of symptoms in daily activities (NSDA) X number of symptoms in ergometric testing (NSET) | | | | p ¹ |
|---------|---|-----------|-----------|-------|----------------|
| | NSDA<NSET | NSDA=NSET | NSDA>NSET | Total | |
| Grup I | 3 | 10 | 16 | 29 | 0,026 |
| Grup II | 0 | 4 | 6 | 10 | |

¹Nonparametric Wilcoxon test

Evaluation of the influence of tone of LES in the presence of gastroesophageal reflux episodes during exercise testing

The influence of the lower sphincter pressure in episodes of GER in EST was evaluated in both groups. Table 5 shows that there was no significant correlation between the presence of hypotonia of the LES and the presence of GER episodes during EST in the two groups (p>0.05).

TABLE 5 - Evaluation of the influence of tone of LES and the presence of gastroesophageal reflux episodes during exercise testing

| | Tone of LES | | | p ¹ |
|---------|-------------|-----------|--------|----------------|
| | Reflux | Hypotonia | Normal | |
| Grup I | Absent | 6 | 14 | 0,106 |
| | Present | 6 | 13 | |
| Grup II | Absent | 1 | 8 | 0,200 |
| | Present | 1 | 0 | |

¹Fisher's exact test

Evaluation of the influence of BMI in the presence of gastroesophageal reflux episodes during exercise testing

The influence of BMI in determining episodes of GER in the two groups together during EST was

evaluated and is shown in Table 6. Patients with excess weight (overweight and obesity) had no more episodes of reflux related to EST when compared with patients with weight within the normal range (p>0.05). All patients were obese in the classification of mild obesity (grade I).

TABLE 6 – Presence of reflux during exercise, compared to normal-weight individuals and those with overweight or obesity

| | Reflux | | Total | p ¹ |
|------------------|----------------|------------------------|----------|----------------|
| | Without reflux | Reflux during exercise | | |
| Normal-weight | 8 (88,9%) | 1 (11,1%) | 9(100%) | 0,3994 |
| Overweight/obese | 20 (66,7%) | 10 (33,3%) | 30(100%) | |
| Total | 28 (71,8%) | 11 (28,2%) | 39(100%) | |

¹Likelihood ratio test

DISCUSSION

In the recent years, several studies have shown that physical activity causes symptoms of GERD^{5,6,21,22}. On one hand this correlation seems to be well documented when performed at strenuous levels¹³, controversy exists regarding the issue when it comes to everyday activities, such as a simple walk. Avidan et al¹ in a randomized trial found that a light walk accelerates gastric emptying and reduces the duration of esophageal exposure to acid in reflux agents. Another aspect still controversial is how the exercise would provide the occurrence of reflux episodes.

In this study, was chosen to evaluate patients with both presentation of GERD disease (erosive and non-erosive form) who did not exercise regularly (most). The physical practice was chosen as the treadmill exercise test, which was the method available in the hospital and could be easily used in this population, whose profile was varied.

Being an original study, was found in the literature review no other paper correlating GER with EST; thus was not possible to compare these results with those of other authors regarding the influence of effectiveness. In this study, the vast majority of patients, both in Group I (75.86%) and Group II (90%), performed an EST considered effective. Correlation between this variable and the occurrence of GER episodes was not found (p>0.05). On the other hand, the VO2 max is considered the most important physiological measure of cardiorespiratory functional capacity⁷. In this study, was observed a significant correlation between the presence of GER episodes and EST when VO2 was reached at least 70% (p=0.032) only in Group I. This finding is consistent with those reported by Soffer et al^{21,22}, which demonstrated that the higher the level of physical activity, the

higher the time percentage and number of reflux episodes observed. The importance of intensity of physical activity was also demonstrated in the study of Kraus et al, which found an increase total time at reflux for racing (during 1 h), over the same period at rest, being the physical effort performed with a frequency close to the maximum heart rate in individuals conditioned¹⁵. In this study, were compared proportionally the time percentage when the pH was less than 4 (acid reflux time %) during the EST with that observed during their usual activities prior to the procedure. The period in which the individual was in the supine position was excluded from the analysis, understanding that any activity was being conducted and as an attempt to standardize the analysis, not taking the influence of that position into account, since five out of nine (55.55%) patients who had GER during EST reflux agents were supine or in combination. Only seven out of 29 patients in Group I (24.13%) and none in Group II had proportionately increased percentage of acid reflux time during physical exercise. It is believed that the observation period of intraesophageal pH variations has been much longer in this situation than during the EST performed may have favorably influenced a time in GER proportionately larger than in usual activities.

Evaluation of daily activities influence is subject in few papers in literature. Józkow et al in a study involving a larger number of patients (n=100) patients with GERD, compared pH-metric parameters of GER and symptoms, level of daily physical activity performed during a week with the same variables and activities during 24 h of pH monitoring completion, and concluded that the usual activities are not associated with changes in these parameters¹². In this study, patients from both groups had symptoms of GER in higher number in usual activities compared to the period in which underwent EST, this analysis also excluded the period during which the patient was supine. In Group I, of the 29 patients, only three (10.34%) reported more clinical complaints during the EST, while in Group II this has not been verified. Statistical significance (p=0.026) to the inverse of the hypothesis to be proven (number of symptoms frequently during the EST). Again, the much longer period of monitoring the usual activities may also have influenced this variable.

Few studies refer symptoms during physical activity and do not compare the frequency of symptoms between the two periods, not allowing a comparison with this study. In relation to clinical complaints reported during exercise, Kraus et al¹⁵ noted as most frequent complaint episodes of belching. In this study the most frequent symptom

of GERD was heartburn during EST in Group I (n=6). In Group II, only one patient had clinical complaints (reported regurgitation) in EST.

In this study, hypotonia of the LES did not influence the occurrence of GER during EST in two groups (p=0.106 and p=0.200 in Groups I and II respectively). This finding is similar to that reported by Pandolfini et al¹⁹, a study conducted by pH monitoring catheter free system (Bravo), which found no influence of the lower sphincter pressure in GERD during exercise, despite having found the influence of esophagogastric junction morphology. Another study in conditioned individuals and no complaints of GER showed no statistical difference in the average resting pressure of LES of those who have had reflux during physical activity¹⁵. In these two cases, there was none suffering from LES hypotonia in the evaluated groups. In this study, 14 patients had LES hypotonia, with the majority (76.92%) being overweight or obese. Although the statistical analysis did not show correlation, this finding may have exerted some influence on this variable due to the increased frequency of defects and higher incidence of transient relaxation of lower esophageal sphincter^{2,3}.

In this study, BMI did not contributed to determine episodes of GER during EST. When analyzed together 33.3% of overweight or mildly obese patients had at least one episode of GER related to exercise, while it occurred in normal individuals with 11.1% of patients. Those who did not have GER at EST, 66.7% were overweight or mildly obese, and 88.9% were healthy. Statistical analysis did not show significance (p>0.05). In the literature review conducted was found no studies considering BMI as a precursor of GER during physical activity. Most studies were conducted in subjects conditioned and/or athletes, and it is therefore impossible to compare with the profile of the population included here.

The correlation between physical activity and GERD needs further investigations with larger populations. This study had limitations, especially given to the short time allowed by EST exertion in people of a higher age group and other sedentary. In spite of this restriction, it confirms what has been reported by other authors, the fact of the relationship between physical activity and GER is highly dependent.

CONCLUSIONS

Exercise of greater intensity, characterized by a EST with $VO_2 \geq 70\%$ of pre-determined, predisposes to episodes of GER in patients with erosive GERD, while lower intensities did not; the lower sphincter

pressure does not influence the occurrence of GER in patients with GERD during exercise; overweight or mild obesity did not influence the occurrence of GER during exercise.

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