Coll. Antropol. **34** (2010) 3: 905–909
Original scientific paper

The Role of the Nutrition in the Pathogenesis of Gastroesophageal Reflux Disease, Barrett's Oesophagus and Oesophageal Adenocarcinoma

Marko Lukić[1], Ana Šegec[2], Igor Šegec[3], Ljerka Pinotić[4], Krešimir Pinotić[5], Bruno Atalić[6], Krešimir Šolić[7] and Aleksandar Včev[8]

[1] Department of Nutrition, Osijek University Hospital Center, Osijek, Croatia
[2] Department for Pathologic Anatomy and Forensic Medicine, Osijek University Hospital Center, Osijek, Croatia
[3] Clinic for Otorhinolaryngology and Maxillofacial Surgery, Osijek University Hospital Center, Osijek, Croatia
[4] Clinic for Paediatrics, Osijek University Hospital Center, Osijek, Croatia
[5] Clinic for Surgery, Osijek University Hospital Center, Osijek, Croatia
[6] Department of Physiology and Immunology, School of Medicine, »Josip Juraj Strossmayer« University, Osijek, Croatia
[7] Department of Biophysics, Medical Statistics and Medical Informatics, School of Medicine, »Josip Juraj Strossmayer« University, Osijek, Croatia
[8] Clinic for Internal Medicine, Osijek University Hospital Centar, Osijek, Croatia

A B S T R A C T

This paper aims at evaluating the role of improper nutrition in the pathogenesis of gastroesophageal reflux disease (GERD), Barrett's oesophagus (BE), and oesophageal adenocarcinoma (EADC). It also tries to examine the influence of the alcohol, nicotine and coffee consumption in the development of the mentioned diseases. There were 180 subjects included in the trial, 109 males and 71 females, which were divided in the four groups (70 patients with GERD, 20 patients with BE, 20 patients with EADC, and 70 healthy examinees composing a control group). Their dietary habits were investigated by the usage of the dietary questionnaires. The results show that the fast eating and the insufficient mastication were present in 64.3–85.0% patients with GERD, BE, and EADC in comparison with only 15% of the examinees from the control group. Furthermore, very hot was preferred by 25.0–42.9% of the mentioned patients in comparison with only 12.9% from the control group. Similarly, 60.0–75.0% of them preferred strongly spiced food on contrary with 17.1% of the healthy examinees. Moreover, strong alcoholic beverages were consumed three or more times per week by 55.0–75.0% of the mentioned patients in comparison with only 15.7% from the control group. Finally, there were 15.7–55.0% heavy smokers among the patients with GERD, BE, and EADC contrary to 1.4% in the control group.

Key words: *nutrition, dietary questionnaire, gastroesophageal reflux disease, Barrett's oesophagus, oesophageal adenocarcinoma*

Introduction

Improper nutrition has a significant place among the factors in the pathogenesis of different diseases. In this respect gastrointestinal diseases are the most represented ones. One of them is gastroesophageal reflux disease (GERD) as the most frequent oesophageal disease, which can be defined as any clinical symptomatic condition or histopathological change of oesophagus, which is a consequence of repeated episodes of gastroesophageal reflux[1]. Its frequency rises with the age and it is more frequent in men than women[2]. GERD begins to appear when aggressive factors such as the stomach acid overcome defending factors such as the mucous membrane[3]. The appearance of the already mentioned stomach acid in the oesophagus is the major event in its pathogenesis[4]. The mentioned acid may end up in the larynx, the mouth and the lungs as well[5].

The complications of the reflux could be divided in intraoesophageal and extraoesophageal ones. The pro-

Received for publication July 12, 2010

longed reflux can cause erosions and ulcers of the oesophageal mucosa. It can even lead to the narrowing of the oesophageal lumen, which can result in the obstruction of food passage. The next stage would be the development of the Barrett's oesophagus (BE), which is a precarcinomatous condition characterised with the metaplasia of the typical squamous epithel into the atypical cylindrical epithel[6]. The final stage is the development of the oesophageal adenocarcinoma (EADC) in the area of the metaplastic epithel[7]. The reflux of stomach acid can cause the complications in the other organs as well[8–10], such as coughing, laryngitis[11], teeth diseases, pneumonia[12], and asthma[13].

The conditions that help the reflux of the stomach acid are obesity, full stomach, lying after eating, body ante flexion, hard objects elevating, pregnancy, and untreated obstructive lung diseases[14]. Some drugs are also important in this respect like the muscle relaxators such as diazepam, the oral bronhodilatators such as teophilin, and the blockers of calcium channels[15]. The composition of food and the way of eating can have their effect as well[16]. Regarding the composition of food, chocolate, menthol and spicy food, as well as the consumption of tea, coffee and alcohol play significant role[17]. Nicotine especially causes the weakening of the lower oesophageal sphincter[18]. Taking into the consideration the way of eating, too hot food can be damaging as well[19].

The majority of scientific papers were looking at the constitutional factors as the necessary causes of the reflux conditions[20]. Springer et al were quantitatively assessing visceral adipose tissue (VAT) in order to determine whether GERD and lower oesophageal sphincter pressure (LESP) are related to the volume of visceral fat masses. 25 morbidly obese patients (nine male, 16 female) were examined by the combination of a multi-slice MRI for VAT, a standardized questionnaire for GERD, and an oesophageal manometry for LESP. Endoscopy of the upper gastrointestinal tract was performed to reveal pathologies of the gastroesophageal junction. The results have shown that waist-to-hip ratio and VAT were significantly higher ($p = 0.0021$) in males ($\overline{X}$=1.05+/–0.05; $\overline{X}$=8.89+/–2.33 l) than in females ($\overline{X}$=0.86+/–0.07; $\overline{X}$=6.04+/–1.28 l). Despite its obvious gender connection, VAT in the end was not correlated with either GERD, BMI or LESP, so they have concluded that neither GERD, BMI nor LESP were significantly influenced by the stage of morbid obesity[21]. Healy et al. were examining the connection between GERD, BE and EADC in order to determine the role of the obesity. 118 BE patients and 113 age- and sex-matched GERD controls were studied by metabolic syndrome screening, anthropometry studies including segmental body composition analysis, and laboratory tests including fasting lipids, insulin, and C-reactive protein. They have observed that the central obesity and the metabolic syndrome are common in both Barrett's and GERD cohorts, but not significantly different, suggesting that the central obesity and the metabolic syndrome does not by itself impact on the development of BE in a reflux population[22].

Basseri et al have evaluated the role of lymphocytes in the eosinophilic esophagitis, lymphocytic esophagitis and GERD, and have concluded that it blurs the line between these already clinically and histologically overlapping entities[23]. A number of scientific papers has examined GERD in children. Teitelbaum et al have analysed the body mass index of pediatric patients with gastrointestinal complaints and have observed a greater percentage of obese patients with constipation, gastroesophageal reflux, irritable bowel syndrome, encopresis, and functional abdominal pain compared with the healthy controls[24]. Wijk et al. have investigated the threshold amount of constantly infused feed needed to trigger lower oesophageal sphincter relaxation, and concluded that GERD is triggered at volumes unlikely to induce gastric distension, and more in the right lateral position and left lateral position[25].

Only a small number of authors were looking at dietary habits as either causes or cures of reflux conditions, but primarily by qualitative approach[26,27]. This was the main reason why this paper will try to examine the role of the nutrition in the pathogenesis of GERD, BE and EADC by semi-quantitative approach. It will also try to evaluate the influence of alcohol, nicotine and coffee consumption.

Examinees and Methods

The study lasted from September 2000 until June 2002. There were 180 subjects in the research, 71 women and 109 men, who were chosen randomly and divided into four groups (70 patients GERD, 20 patients with BE, 20 patients with EADC, and 70 healthy examinees as a control group). They ranged from youths to elders (=53.04±14.41 years, range=17–83 years). The subjects all lived in the region of Eastern Croatia. They underwent oesophagogastroduodenoscopy in the Department for Endoscopy at the Clinic for Internal Medicine of the Osijek University Hospital Centre, and an endoscopic diagnosis was made for each patient.

Dietetic research was conducted through the individual interview based on the dietary questionnaire. Its aim was to establish the possible influence of dietary habits in the development of the reflux conditions. It was organised as a semiquantitive questionnaire containing the questions on a type and quantity of food, the way of preparing food, the speed of consuming food, the warmth of consumed food, the quantity of spices in the food, the smoked food, as well as alcohol, nicotine and coffee consumption.

Statistical analysis

Data are presented as absolute and relative frequencies. Differences in categories (GERD, BE, EADC) were tested with Fisher's exact test. Statistical analyses were conducted using SAS software (version 8.02, SAS Institute Inc., Cary, NC, USA) with significance level set at $p<0.05$.

Results

The research on dietary habits was conducted in order to determine the role of the nutrition in the pathogenesis of GERD, BE and EADC (Table 1). Number of meals per day, food consumption speed, the most consumed food type, consumed food warmth, spiced food consumption, fat food consumption, barbecue food consumption, and smoked food consumption were analysed. The patients with GERD, BE or EADC tended to prefer irregular meals, fast food consumption speed, roasted food, very hot or cold food, very spiced food, very fat food, barbecue food consumption one to four times per month, and smoked food consumption three times and more per week. On contrary, the healthy examinees preferred three to four meals per day, normal food consumption speed, boiled food, medium warm food, medium spiced food, temperate fat food, and finally barbecue and smoked food consumption one to four times per month. The Fischer's exact test has showed that all the mentioned results were statistically significant with $p<0.001$. The only exception was barbecue food consumption with $p=0.065$.

TABLE 1
DISTRIBUTION OF ALL EXAMINEES REGARDING THEIR NUTTRITION HABBITS

	Gastroesophageal reflux disease / No (%)	Barrett's oesophagus / No (%)	Oesophageal adenocarcinoma / No (%)	Control group / No (%)	p*
Number of meals per day					
One to two times	25 (35.72)	7 (35.00)	5 (25.00)	7 (10.00)	
Three to four times	21 (30.00)	2 (10.00)	4 (20.00)	61 (87.14)	
Irregular	24 (34.28)	11 (55.00)	11 (55.00)	2 (2.86)	<0.001
Food consumption speed					
Fast	45 (64.29)	17 (85.00)	14 (70.00)	11 (15.71)	
Normal	16 (22.85)	2 (10.00)	1 (5.00)	38 (54.21)	
Slow	9 (12.86)	1 (5.00)	5 (25.00)	21 (30.00)	<0.001
The most consumed food type					
Boiled	16 (22.85)	3 (15.00)	2 (10.00)	40 (57.14)	
Roasted	36 (51.43)	10 (50.00)	11 (55.00)	5 (7.14)	
Industrial	6 (8.57)	1 (5.00)	1 (5.00)	0 (0)	
Mixed	12 (17.15)	6 (30.00)	6 (30.00)	25 (35.72)	<0.001
Consumed food warmth					
Very hot	30 (42.85)	8 (40.00)	5 (25.00)	9 (12.85)	
Medium warm	19 (27.15)	2 (10.00)	4 (20.00)	58 (82.85)	
Cold	21 (30.00)	10 (50.00)	11 (55.00)	3 (4.30)	<0.001
Spiced food consumption					
Very spiced	48 (68.57)	15 (75.00)	12 (60.00)	12 (17.14)	
Medium spiced	17 (24.28)	4 (20.00)	6 (30.00)	40 (57.14)	
Weakly spiced	5 (7.15)	1 (5.00)	2 (10.00)	18 (25.72)	<0.001
Fat food consumption					
Very fat food	38 (54.28)	10 (50.00)	9 (45.00)	9 (12.85)	
Temperate	25 (35.72)	9 (45.00)	11 (55.00)	36 (51.42)	
No fat food	7 (10.00)	1 (5.00)	0 (0.00)	25 (35.73)	<0.001
Barbecue food consumption					
3 times and more *per* week	6 (8.57)	0 (0.00)	5 (25.00)	2 (2.86)	
1–4 times *per* month	52 (74.28)	16 (80.00)	11 (55.00)	51 (72.86)	
No	12 (17.15)	4 (20.00)	4 (20.00)	17 (24.28)	=0.065
Smoked food consumption					
3 times and more *per* week	48 (68.57)	11 (55.00)	15 (75.00)	11 (15.71)	
1–4 times *per* month	20 (28.57)	8 (40.00)	5 (25.00)	53 (75.71)	
No	2 (2.86)	1 (5.00)	0 (0.00)	6 (8.58)	<0.001
Total	70 (100)	20 (100)	20 (100)	70 (100)	

*Fisher's Exact test

TABLE 2
DISTRIBUTION OF ALL EXAMINEES REGARDING ADDICTIVES CONSUMPTION

	Gastroesophageal reflux disease / No (%)	Barrett's oesophagus / No (%)	Adenocarcinoma oesophagus / No (%)	Control group / No (%)	p*
Alcoholic drinks consumption					
No	34 (48.57)	6 (30.00)	5 (25.00)	61 (87.14)	
0.3 dL *per* week	8 (11.42)	4 (20.00)	2 (10.00)	7 (10.00)	
0.5 dL *per* day	20 (28.57)	5 (25.00)	9 (45.00)	1 (1.43)	
More than 1 dL *per* day	8 (11.44)	5 (25.00)	4 (20.00)	1 (1.43)	<0.001
Wine or beer consumption					
No	23 (32.85)	1 (5.00)	6 (30.00)	53 (75.71)	
2–3 dL *per* week	16 (22.85)	8 (40.00)	4 (20.00)	16 (22.86)	
2–5 dL *per* day	21 (30.00)	11 (55.00)	7 (35.00)	1 (1.43)	
>6 dL *per* day	10 (14.30)	0 (0.00)	3 (15.00)	0 (0.00)	<0.001
Soft drinks consumption					
No	15 (21.42)	6 (30.00)	6 (30.00)	34 (48.57)	
5 dL *per* week	23 (32.85)	5 (25.00)	3 (15.00)	29 (41.43)	
5 dL *per* day	20 (28.57)	5 (25.00)	8 (40.00)	5 (7.14)	
>6 dL *per* day	12 (17.16)	4 (20.00)	3 (15.00)	2 (2.86)	<0.001
Cigarettes Smoking					
No	29 (41.43)	4 (20.00)	3 (15.00)	47 (67.14)	
Up to 10 cigarettes *per* day	9 (12.85)	1 (5.00)	0 (0.00)	15 (21.43)	
10–20 cigarettes *per* day	21 (30.00)	4 (20.00)	10 (50.00)	7 (10.00)	
More than 21 cigarettes *per* day	11 (15.72)	11 (55.00)	7 (35.00)	1 (1.43)	<0.001
Coffee Drinking					
No	7 (10.00)	0 (0.00)	0 (0.00)	19 (27.14)	
Less than 4 cups *per* day	26 (37.14)	5 (25.00)	7 (35.00)	47 (67.14)	
More than 5 cups *per* day	37 (52.86)	15 (75.00)	13 (65.00)	4 (5.72)	<0.001
Total	70 (100)	20 (100)	20 (100)	70 (100)	

*Fisher's Exact test

The consummation of alcohol, nicotine and coffee was taken into consideration as well (Table 2). The patients with GERD, BE or EADC consumed alcohol, nicotine and coffee more often than the healthy examinees. All the results were statistically significant according to the Fischer exact test with $p<0.001$.

Disscussion and Conclusion

This study represents a continuation of the half a century old tradition of nutritional studies in Croatia. Like the similar previous studies it is also composed as a multidisciplinary approach[28–30]. The results show that the unhealthy dietary habits were more represented among the patients with the reflux conditions, in comparison with the healthy examines from the control group. Both the irregular eating and the fast eating were more represented among the mentioned patients than among the healthy examines. The very hot food and the much spiced food were again equally highly consumed by the patients from all the three groups. Fat, barbecue and smoked food were as well more often consumed by the mentioned patients than by the healthy examines. While the patients with the reflux conditions tended to prefer roasted food, the healthy examinees preferred boiled food.

While alcoholic drinks were consumed mainly by the patients with the reflux conditions, soft drinks were consumed mainly by the healthy examinees. The greatest number of heavy smokers was among the patients with EADC (50%), while the greatest number of non-smokers was among the healthy examiners, which is in accordance with the studies on the carcinogenic effect of the cigarette smoking[31–33]. Coffee drinking was represented among the examinees from all the four groups, but it could be observed that it was represented with more than five cups per day among the patients with reflux conditions, and with less than four cups per day among the healthy examiners from the control group. In this respect this study could be used as a basis for a comparison of eating habits between Croatian and other populations[34,35].

All the results were statistically significant with $p<0.001$. The only exception was barbecue food consumption with $p=0.065$, which in context with all the other results, could be broadly interpreted as statistically significant as well. Although, the results have showed the differences in the dietary habits between the patients with GERD, BE and EADC on one hand, and the healthy examinees on the other hand, which could be interpreted as an evidence of their role in the pathogenesis of the mentioned diseases, they have not reflected the differences between the three mentioned diseases as the results of the various stages of the gastric acid reflux. Proper nutrition could have a prophylactic effect against the development of the reflux conditions, which should be more thoroughly, investigated in the future researches. On this track, a well chosen dietary therapy could effectively improve the life quality of the patients with GERD, BE and EADC, which should also be further researched.

REFERENCES

1. SONTAG S, Defining GERD. In: MODLIN I (Ed) GERD: the last word? (Gastric pathobiology research group, 1998). — 2. SONNEBER A, EL-SERAG A, Epidemiology of gastroesophageal reflux disease. In: MODLIN I (Ed) GERD: the last word? (Gastric pathobiology research group, 1998). — 3. MACDOUGAL N, JOHANSTON B, KEE F, COLLINS J, MCFARLAND R, LOVE A, Gut, 38 (1996) 481. — 4. HIRSCHOWITZ B, Pepsin and the oesophagus. In: MODLIN I (Ed) GERD: the last word? (Gastric pathobiology research group, 1998). — 5. PULJAK L, Gastroezofagealna refluksan bolest, accessed 18.04.2010. Available from: URL: http://www.medicina.hr/clanci/gastroezofagealna_refluksna_bolest.htm. — 6. KOOP H, Endoscopy, 36 (2004) 103. — 7. SAMPLINER A, Ann Int Med, 130 (1999) 67. — 8. RICHTER JE, Gastroenterol Clin North Am, 25 (1996) 75. — 9. NAPIERKOWSKI J, WONG RK, Am J Med Sci, 326 (2003) 285. — 10. MALAGELADA JR, Aliment Pharmacol Ther, 19 Suppl 1 (2004) 43. — 11.VAEZI MF, HICKS DM, ABELSON TI, RICHTER JE, Clin Gastroenterol Hepatol, 1 (2003) 333. — 12. SPECHLER SJ, Am J Med Sci, 326 (2003) 279. — 13. THAKKAR K, BOATRIGHT RO, GILGER MA, EL-SERAG HB, Paediatrics, 125 (2010) 925. — 14. ORLANDO RC, Am J Med Sci, 326 (2003) 274. — 15. O'MALLEY P, Clin Nurse Spec, 17 (2003) 286. — 16. ŽIVKOVIĆ R, Praktična gastroenterologija (Školska knjiga, Zagreb, 1993). — 17. SHAHEEN N, PROVENZALE D, Am J Med Sci, 326 (2003) 264. — 18. LEPOGLAVEC Ž, Gastroezofagealna refluksne bolest, accessed 18.04.2010. Available from: URL: http://www.plivazdravlje.hr/aktualno/clanak/16054/Gastroezofagealna-refluksna-bolest-GERB.html. — 19. JEREB B, TODOROVIĆ J (Eds) Gastroenterologija (Školska knjiga, Zagreb, 1987). — 20. KINOSHITA Y, FURUTA K, Nippon Shokakibyo Gakkai Zashi, 107 (2010) 531. — 21. SPRINGER F, SCHWARTZ M, MACHANN J, FRITSCHE A, CLAUSSEN CD, SCHICK F, SCHNEIDER JH, Obes Surg, 20 (2010) 749. — 22. HEALY LA, RYAN AM, PIDGEON G, RAVI N, REYNOLDS JV, Dis Esophagus, 23 (2010) 386. — 23. BASSERI B, LEVY M, WANG HL, SHAYE OA, PIMENTEL M, SOFFER EE, CONKLIN JL, Dis Esophagus, 23 (2010) 368. — 24. TEITELBAUM JE, SINHA P, MICALE M, YEUNG S, JAEGER J, J Pediatr, 154 (2009) 444. — 25. WIJK MP, BENNINGA MA, DAVIDSON GP, HASLAM R, OMARI TI, J Pediatr, 156 (2010) 744. — 26. PENAGINI R, MANGANO M, BIANCKI P, Gut, 42 (1998) 330-333. — 27. PANAGINI R, BARTESAGHI B, CONTE D, BIANCKI P, Eur J Gastroenterol Hepatol, 4 (1992) 35. — 28. MISSONI S, Coll Antropol, 30 (2006) 673. — 29. PARZIKOVA J, Coll. Antropol, 11 (1987) 45. — 30. KERN J, JUREŠA V, VULETIĆ S, IVANKOVIĆ D, Coll. Antropol, 10 (1986) 21. — 31. ZHANG Z, PATCHETT S, PERRET D, DOMIZIO P, FARTHING M, Eur J Gastroenterol and Hepatol, 12 (2000) 497. — 32. JI B, CHOW W, ZANG G, MCLAUGHLIN J, Int J Cancer, 76 (1998) 659. — 33. TERRY P, LAGERGREN J, YE W, NYREN O, WOLK A, Int J Cancer, 87 (2000) 750. — 34. DRAPER HH, Coll Antropol, 10 (1986) 221. — 35. ZELJKO H, ŠKARIĆ-JURIĆ T, SMOLEJ-NARANČIĆ N, PERIČIĆ-SALIHOVIĆ M, MARTINOVIĆ-KLARIĆ I, BARBALIĆ M, BARAĆ-LAUC L, JANIĆIJEVIĆ B, Coll Antropol, 32 (2008) 315.

M. Lukić

Department of Nutrition, Osijek University Hospital Centre, J. Hüttlera 4, 31000 Osijek, Croatia
e-mail: lukic.marko@kbo.hr

ULOGA PREHRANE U PATOGENEZI GASTROEZOFAGEALNE REFLUKSNE BOLESTI, BARRETTOVOGA EZOFAGUSA I EZOFAGEALNOGA ADENOCARCINOMA

SAŽETAK

Cilj rada je evaluirati ulogu nepravilne prehrane u patogenezi gastroezofagealne refluksne bolesti (GERB), Barrettovoga ezofagusa (BE) i ezofagealnoga adenokarcinoma (EADC). Nadalje nastoji se istražiti utjecaj konzumacije alkohola, nikotina i kave na nastanak spomenutih boesti. Studija je obuhvatila 180 sudionika, 109 muških i 71 ženskih, koji su bili podijeljeni u četiri skupine (70 pacijenata s GERB-om, 20 pacijenata s BE-om, 20 s EADC-om, te 70 zdravih ispitanika iz kontrolne skupine). Rezulti su pokazali da su brzo jedenje i nedovoljno žvakanje zastupljeni u 64,3–85% bolesnika s GERB-om, BE-om i EADC-om nasuprot samo 15% zdravih ispitanika iz kontrolne skupine. Nadalje, vrlo topla hrana je preferirana od 25,0–42,9% spomenutih bolesnika u usporedbi sa samo 12,9% zdravih ispitanika. U skladu s time, 60,0–75,0% spomenutih bolesnika preferiralo je jako začinjenu hranu nasuprot 17,1% zdravih ispitanika. Nadalje, žestoka alkoholna pića su konzumirana tri ili više puta tjedno od 55,0–75,0% spomenutih bolesnika u usporedbi sa samo 15,7% zdravih ispitanika. Konačno, 15,7–55,0% bolesnika s GERB-om, BE-om i EADC-om su bili okorjeli pušači nasuprot 1,4% iz kontrolne skupine.