The “Brisighella Terme” Project: effectiveness of preventive medicine in thermal ambient.
Hematochemical parameters


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Abbreviations:
CK: Creatine-Kinase;
CT: Total Cholesterol;
GPT: Alanine Amino Tranferase;
GOT: Aspartato Amino Transferase;
HDL-C: High Density Lipoproteins Cholesterol;
LDL-C: Low Density Lipoproteins Cholesterol;
TG: Triglycerides.

Abstract. – Background: The main aims of the Brisighella Terme Project are: 1. evaluation of feasibility and effectiveness of preventive medicine intervention in thermal ambient; 2. identification of subjects with cardiovascular risk factors; 3. to give patients informations on risk factor correction.

The data of this work concern the hematochemical parameters: CT, HDL-CT, LDL-CT, TG, ApoA1, ApoB, fibrinogen, GOT, GPT, CPK, glucose, uric acid.

Methods: CT, HDL-CT (after precipitation of the non-HDL fractions), TG, glucose, uric acid are evaluated by enzymatic-colorimetric reactions; GOT, GPT, CK by enzymatic method. ApoA1, ApoB, fibrinogen by immunoturbidimetric methods. LDL-CT is calculated by the Friedewald formula.

Results: 390 subjects spontaneously adhered to the Brisighella Terme Project. Of these subjects 38% requested laboratory service and we observed a 47% increment, from 1995 to 1996, with regard to this request. Females showed higher mean values than males of these parameters: CT, LDL-CT, ApoA1, ApoB, fibrinogen, CPK. 55% of females had LDL-CT >159 mg/dl, values considered high risk for cardiovascular diseases. 55% of males showed LDL-CT <159 mg/dl, with 2 cases < 25 mg/dl. TG values >399 mg/dl were found only in males (2%). We identified new cases of hypertriglyceridaemia, hypercholesterolaemia and hypoHD Laemia; these metabolic pathologies had not yet been diagnosed, whereas the subjects already knew they were affected by hyperglycaemia or hyperuricaemia.

Conclusions: People’s interest in the Brisighella Terme Project, new case identification, the possibility of providing correct information about risk factors and healthy life style confirm the feasibility and effectiveness of preventive medicine in a thermal ambient.

Key-Words:
Preventive medicine, Hypo-HD Laemia, Hypercholesterolaemia, Hypertriglyceridaemia, Thermal plant.

Introduction

In recent years preventive medicine has assumed a significant role in physician-patient relationships and in people’s awareness concerning some of the most widespread pathologies, among these cardiovascular diseases1-5. The effectiveness of prevention is indisputed, nevertheless new strategies to increase people’s attention are necessary.

The Atherosclerosis Center of Bologna University, in collaboration with Cervia and Brisighella Spa and Brisighella Town (Emilia-Romagna Region), organized a preventive medicine project which was carried out in the Brisighella thermal plant. This program, called “The Brisighella Terme Project”, started in 1994 and it is still going on; its purpose is to avail citizens with a greater number of results of the “Brisighella Heart Study” which represents a valid example of primary and secondary prevention, regarding atherosclerosis and cardiovascular diseases in our Region.

The “Brisighella Study” started in 1972; at first it was a longitudinal observational study
to monitor the spontaneous trend in risk factors for atherosclerosis and to assess the incidence of coronary heart disease (CHD) in the population. Every 4 years a control of the whole population (3663 subjects) was performed, without any intervention until 1984. Subsequently, for the general deterioration in personal habits and the trend towards increasing CHD risk factors in the citizens observed, an Intervention Study, named “Brisighella Heart Study”, began in 19867. The programme included: A) a population strategy comprising nutritional intervention, by informative campaigns about correct nutrition and life style, and B) a high risk strategy comprising nutritional and/or pharmacological intervention. The results, obtained by a low cost/benefit ratio, were nutrition habit improvement, a principal risk factor decrease and a reduction of cardiovascular disease incidence.

The “Brisighella Terme Project” has essentially 3 aims:

1. to value the feasibility and the effectiveness of a preventive medicine intervention in thermal ambient. The choice of this location was suggested by the assumption that a “Spa” client was particularly receptive to the problems concerning his own health;

2. to identify new subjects with cardiovascular risk factors (hypercholesterolaemia, hypertension ecc.) by medical examination, electrocardiogram, carotid echotomography, dietary consultation, blood pressure and hematocentral parameter evaluation;

3. to give the patients clear information about cardiovascular risk factor correction.

The hematocentral parameter evaluation results, in particular values concerning lipid metabolism, of the subjects who spontaneously adhered to this preventive programme during the 1996 thermal season, are the specific topics of this present work.

Methods

Every 15 days the preventive protocol was explained to the “Spa” clients during public meetings by physicians, biologists and dietitians. A n informative Centre was opened in the “Spa” and posters and informative brochures were prepared and given out. The study was carried out on 390 patients (mean age 59.0 years, 200 males and 190 females). Participant evaluation included behavioural, nutritional habits, alcohol intake, smoking habit, clinical and familiar history, electrocardiographic assessment, carotid echotomography, dietary consultation, measurement of blood pressure and anthropometric parameters5, determination of clinical chemistry variables.

Venous blood was drawn after 12 hours fasting and the hematocentral parameters determined were:

- total cholesterol (CT)8, triglycerides (TG)9, uric acid, glucose10 by enzymatic-colorimetric methods;
- HDL cholesterol (HDL-C), after selective precipitation of non-HDL fractions by dextran sulfate-magnesium chloride, by enzymatic-colorimetric method;11
- LDL cholesterol (LDL-C) calculated by the Friedewald formula: CT - (TG/5 + HDL-CT) for triglycerides <400 mg/dl;
- apolipoproteins A1 and B (ApoA1, ApoB) and fibrinogen by immunoturbidimetric methods12;
- aspartate and alanine aminotransferases (GOT, GPT), creatine kinase (CK) by enzymatic methods.

The measurement of serum lipids was subjected to quality control by the World Health Organization Lipid Reference Center in Prague, Czech Republic.

Statistical analyses were performed with SPSS (Windows release 6.1). A descriptive statistics of the population was used: data are expressed as mean ± standard deviation and 95% Confidence Interval (CI); the statistical significance of all parametric data was estimated by Student t test for unpaired data. P values <0.05 were considered significant. To evaluate significance between percentage, chi-square test ($\chi^2$) was applied.

Results

Thirty-eight percent of the subjects (52.21% males and 47.79% females) requested labora-
tory services; from 1995 to 1996 a 47% increase in analyses request was observed.

Table I shows the main characteristics of the subjects examined in the 1996 thermal period: age, height, weight, body mass index (BMI = kg/m²), blood pressure mean values. The patients checked are middle-aged, overweight with normal blood pressure.

Subjects were subdivided into 3 age classes: <40; 40-59; >59 years. The lipid profile was requested mostly by the two lower male age classes; the opposite was observed in the females. The distribution into these age classes between males and females is not statistically significant (Table II).

Hematochemical parameter mean values and the 95% confidence interval (CI) in males and females are shown in Table III. The females, with respect to males, show higher mean values of CT, LDL-CT, HDL-CT (p <0.0001) and fibrinogen (p <0.01); also ApoA1 and ApoB and CK mean levels are higher, but the difference is not significant. The males show higher mean values of uric acid, glucose (p <0.0001 and p<0.05 respectively), GOT and GPT (not significantly different).

The subjects were subdivided into three cholesterol value classes:

- **Class I**: <200 mg/dl - cardiovascular disease low risk values (LR);
- **Class II**: 200-239 mg/dl - medium risk values (MR);
- **Class III**: >240 mg/dl high risk values (HR).

By statistical analysis ($\chi^2$ test) of the data, a difference between the sexes (p <0.001) was found. Fifty-six percent of females has CT values >240 mg/dl and only 11% show cholesterolemia <200 mg/dl; 30% of males present a cholesterolemia <200 mg/dl, while 46% of males show values between 200 mg/dl and 240 mg/dl. In both sexes there are a significant differences (p <0.005 and p <0.05 respectively) between cholesterol classes I and III and between classes II and III; no statistical differences between classes I and II was found.

Three classes of LDL-CT values were also evaluated:

- LDL-CT <130 mg/dl (LR values);
- LDL-CT 130-159 mg/dl (MR values);
- LDL-CT >159 mg/dl (HR values).

The results are similar to those found in the total cholesterol classes (Figure 1): 55% of the females display LDL-CT values >159 mg/dl versus 27% of the males; 42% of the males are in the LDL-C range 130-159 mg/dl and 31% show values <130 mg/dl.

Only 17% of females exhibit desirable values for this hematochemical parameter. The same statistical differences between sexes and between classes found with regard to total cholesterol were found also in LDL-C.

A subdivision into two arbitrary classes of HDL-cholesterolemia was made: HDL-CT <40 mg/dl and HDL-CT >39 mg/dl. M ost of the population (91% females; 64% males) present recommended values of HDL-CT (>40 mg/dl); 36% of males shows low HDL-CT values; in these subjects we found 2 cases of HDL-CT <25 mg/dl.

We considered 3 classes of triglyceridaemia: values <200 mg/dl (recommended); values be-

### Table I. Brisighella Terme 1996 - characteristic of subjects who requested laboratory services (mean values and CI 95%).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.9</td>
<td>60.6</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>173.0</td>
<td>159.0</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.9</td>
<td>64.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.9</td>
<td>25.7</td>
</tr>
<tr>
<td>PAS (mm/Hg)</td>
<td>138.2</td>
<td>135.4</td>
</tr>
<tr>
<td>PAM (mm/Hg)</td>
<td>89.9</td>
<td>87.0</td>
</tr>
</tbody>
</table>

### Table II. Brisighella Terme 1996 - subjects (% who requested laboratory services: age classes ($\chi^2 = 2.34, gdf = 2; p = 0.31$)).

<table>
<thead>
<tr>
<th>Age classes</th>
<th>Males %</th>
<th>Females %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>42</td>
<td>30</td>
</tr>
<tr>
<td>40-59</td>
<td>45</td>
<td>38</td>
</tr>
<tr>
<td>&gt;59</td>
<td>35</td>
<td>41</td>
</tr>
</tbody>
</table>
between 200 mg/dl and 399 mg/dl; values >399 mg/dl (Figure 2). No female displayed TG values >399 mg/dl, while we found these values only in 2% of the males (one case presented TG >700 mg/dl). The number of subjects (91% females and 80% males) with desirable TG values (<200 mg/dl) is significantly (p <0.0001) higher than that of the hypertriglyceridaemic patients.

Finally we evaluated whether the subjects found to be affected by hyperlipoproteinaemia knew of their lipid metabolism alterations:

- 4% of subjects with TG >200 mg/dl were unaware of the hypertrygliceridaemia;
- 51% of subjects with CT between 200 mg/dl and 239 mg/dl did not know this;
- 11% of hypercholesterolemic subjects did not know they had CT >240 mg/dl.
- 8% of hypercholesterolemic subjects showed CT values >280 mg/dl; 2% of these cases were unaware they were affected by severe hypercholesterolaemia;
- none of the subjects with high LDL-CT was aware of this;

Table III. Brisighella Terme 1996 - hematochemical parameters values (mean and CI 95%).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>222.2 (211.5-232.8)</td>
<td>252.8 (238.8-266.89)</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>44.1 (41.2-46.9)</td>
<td>52.7 (49.6-55.8)</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dl)</td>
<td>147.1 (138.5-157.0)</td>
<td>176.6 (163.7-189.4)</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>152.0 (125.8-178.0)</td>
<td>117.6 (103.1-132.2)</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>91.9 (87.3-96.3)</td>
<td>86.3 (83.5-89.1)</td>
</tr>
<tr>
<td>Uric acid (mg/dl)</td>
<td>6.0 (5.6-6.3)</td>
<td>4.5 (4.0-4.9)</td>
</tr>
<tr>
<td>APO A 1 (mg/dl)</td>
<td>122.8 (102.1-143.4)</td>
<td>131.3 (110.5-152.2)</td>
</tr>
<tr>
<td>APO B (mg/dl)</td>
<td>115.2 (101.8-128.7)</td>
<td>123.9 (93.4-154.4)</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>119.4 (152-246.9)</td>
<td>284.9 (239.9-329.9)</td>
</tr>
<tr>
<td>GOT (U/l)</td>
<td>17.4 (7.8-27.1)</td>
<td>12.0 (10.0-14.0)</td>
</tr>
<tr>
<td>GPT (U/l)</td>
<td>27.4 (8.8-46.1)</td>
<td>12.8 (10.4-15.1)</td>
</tr>
<tr>
<td>CK (U/l)</td>
<td>55.9 (39.7-72.6)</td>
<td>83.2 (46.4-120.1)</td>
</tr>
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Figure 1. Subdivision in to LDL cholesterol classes (<130 mg/dl; 130-159 mg/dl; >159 mg/dl) of subjects who adhered to the Brisighella Terme Project and requested laboratory services.
- 50% of subjects characterized by low values of HDL-CT (<40 mg/dl) were unaware of their metabolic alteration;
- all subjects with glucose or uric acid high values knew of their pathologies.

**Conclusions**

The present study started with the aim of transferring the preventive medicine experience made during the Brisighella Heart Project to a thermal ambient, hoping to obtain positive results with regard to CHD prevention. In the Brisighella citizens during the observational phase, from 1972 to 1986, an increase of total serum cholesterol and triglycerides was observed and it was demonstrated that cholesterol values are predictive for CHD mortality, also in the elderly\(^{14}\). After the preventive phase, which included many subprojects (intervention on high risk subjects (HR), nutritional education program, special project for school-boys\(^ {15} \), media utilization, therapeutic guidelines etc...), positive results were obtained. Marked reduction in LDL-C and TG was found in HR, in Hyperlipidaemic patients and at present CHD mortality is decreasing in the Brisighella population\(^ {16} \).

This means that nonguided therapies and life style spontaneous changes have no effects, while correct nutritional information and application of therapeutic guidelines seem to achieve evident results.

For this reason we attempted a synthesis of the previous experiences, regarding prevention, to be performed over a short period: in fact a thermal cycle care lasts only about 15 days.

Just two years after the beginning of the "Brisighella Terme Project", we are able to give some encouraging results about the feasibility of this study. Concerning the request for laboratory services, in 1996 we had a 47% increment with respect to 1995, confirming that the procedure used for patient awareness was right.

The identification of subjects with cardiovascular risk factors was one of the first and most important aims of this project. The new case identification of hypercholesterolaemia and hypoHDLaemia (subjects who do not know they were affected), a condition tightly related to cardiovascular disease, is therefore a good result. Hypertriglyceridaemia was less unknown: only 4% of hypertriglyceridaemic subjects were unaware of this. We identified very

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**Figure 2.** Subdivision into triglyceride classes (<200 mg/dl; 200-399 mg/dl; >399 mg/dl) of subjects who adhered to the Brisighella Terme Project and requested laboratory services.
few cases of hyperuricaemia (data not shown), but all cases had already been diagnosed. A ll hyperglycaemic or diabetic subjects knew of their pathology.

In conclusion, at least in our sample of population, people pay less attention to metabolic lipid disorders with respect to other hematochemical parameters (e.g. glycaemia, uricaemia), although informative campaigns, especially via mass media, versus cholesterol control and lipid metabolism alterations, are now numerous and repeated.

The effectiveness of a preventive medicine project consists not only of the identification of subjects at high risk for a particular pathology; the essential aim is giving the identified new cases clear information about cardiovascular risk factor correction and about the improvement of life style.

Concerning the laboratory parameters we enclosed, with the hematochemical parameter report, a diagnostic orientation (proposed according to the results of the lipid values) and a considerable amount of nutritional advice. We suggested to patients that they submit our reports to their own doctor, so that the preventive medicine programme could last for a long time and would not just be limited to the short period of thermal Spa permanence.

References

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