Nonalcoholic Beer Reduces Inflammation and Incidence of Respiratory Tract Illness

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ABSTRACT

SCHERR, J., D. C. NIEMAN, T. SCHUSTER, J. HABERMANN, M. RANK, S. BRAUN, A. PRESSLER, B. WOLFARTH, and M. HALLE. Nonalcoholic Beer Reduces Inflammation and Incidence of Respiratory Tract Illness. Med. Sci. Sports Exerc., Vol. 44, No. 1, pp. 18–26, 2012. Purpose: Strenuous exercise significantly increases the incidence of upper respiratory tract illness (URTI) caused by transient immune dysfunction. Naturally occurring polyphenolic compounds present in food such as nonalcoholic beer (NAB) have strong antioxidant, antipathogenic, and anti-inflammatory properties. The objective of this study was to determine whether ingestion of NAB polyphenols for 3 wk before and 2 wk after a marathon would attenuate postrace inflammation and decrease URTI incidence. Methods: Healthy male runners (N = 277, age = 42 ± 9 yr) were randomly assigned to 1–1.5 L d⁻¹ of NAB or placebo (PL) beverage (double-blind design) for 3 wk before and 2 wk after the Munich Marathon. Blood samples were collected 4 and 1 wk before the race and immediately and 24 and 72 h after the race and analyzed for inflammation measures (interleukin-6 and total blood leukocyte counts). URTI rates, assessed by the Wisconsin Upper Respiratory Symptom Survey, were compared between groups during the 2-wk period after the race. Results: Change in interleukin-6 was significantly reduced in NAB compared with PL immediately after the race (median (interquartile range) = 23.9 (15.9–38.7) vs 31.6 (18.5–53.3) ng L⁻¹, P = 0.03). Total blood leukocyte counts were also reduced in NAB versus PL by approximately 20% immediately and 24 h after the race (P = 0.02). Incidence of URTI was 3.25-fold lower (95% confidence interval = 1.38–7.66) (P = 0.007) in NAB compared with PL during the 2-wk postmarathon period. Conclusions: Consumption of 1–1.5 L d⁻¹ of NAB for 3 wk before and 2 wk after marathon competition reduces postrace inflammation and URTI incidence. Key Words: EXERCISE, INFLAMMATION, UPPER RESPIRATORY TRACT ILLNESS, FLAVONOIDS

In contrast to moderate physical activity, the physiologic stress of prolonged and intensive exercise has been linked in multiple animal and human studies to transient inflammation and immune dysfunction and elevated incidence of upper respiratory tract illness (URTI) (8,10,23,25,28,33,38). Immunonutrition support for endurance athletes, especially during periods of intensive training and race events, is a burgeoning area of scientific endeavor. Long-term consumption of vegetables and fruits has been linked to a decreased incidence of chronic disease such as cancer and cardiovascular disease (4,17,19,42). The disease-preventing effects of these foods are attributed in part to the presence of phenolic compounds, which have strong antioxidant, antipathogenic, and anti-inflammatory properties (16,29,40). Plant phenolics also modulate multiple cell signaling pathways involved in cellular proliferation, differentiation, survival, and apoptosis (40). Therefore, the use of polyphenol-rich supplements might be a promising approach to prevent inflammation-associated diseases such as atherosclerosis, coronary artery disease, sudden cardiac death, cancer, and diabetes mellitus (11,12,15,35).

Alcoholic beverages contain numerous nonalcoholic compounds that have potential health value (14,34). More than 2000 organic and inorganic chemicals have been identified in beer including more than 50 polyphenolic compounds from barley and hops. Beer is a major contributor to dietary phenolic intake and contains 366–875 mg of polyphenols per liter (34). Beer phenolics are rapidly absorbed and increase plasma antioxidant capacity in humans (13). We hypothesized that ingestion of nonalcoholic beer polyphenols
for 3 wk before the Munich Marathon would attenuate post-race inflammation and decrease URTI incidence.

**MATERIALS AND METHODS**

**Study Design**

This prospective, volunteer- and observer-blinded, placebo-controlled trial (the Be-MaGIC Study: Beer, Marathon, Genetics, Inflammation, and the Cardiovascular system) investigated the effects of consuming 1–1.5 L d⁻¹ of nonalcoholic beer on postrace inflammation and URTI incidence in healthy male runners. The study protocol was approved by the ethics committee (approval reference no. 2384/09, University Hospital Klinikum rechts der Isar, Munich, Germany), and the conduct of the study was consistent with the Good Clinical Practice provisions of the Declaration of Helsinki. All participants gave written informed consent before enrollment. Participants were randomly assigned in a 1:1 ratio—stratified by age blocking from 20 to 40 yr and from 40 to 60 yr—either to the intervention group (nonalcoholic beer with polyphenols) or to the control group (beverage with equal composition except for polyphenols). The random allocation sequence was generated by the independent staff at the local Institute for Medical Statistics and Epidemiology.

**Participants**

Participants were recruited by 1) advertisements in local newspapers as well as national running journals in Germany, 2) announcements via the Internet, 3) from athletes who had participated in preparticipation screening in our outpatient clinic, and 4) from track-and-field groups near Munich.

Inclusion criteria were male, age 20–60 yr, history of at least one successfully finished half marathon, intention to participate in the Munich Marathon 2009 (42.195 km), and written informed consent.

Exclusion criteria were known cardiac disease, pharmacological treatment for diabetes mellitus or arterial hypertension, musculoskeletal or psychiatric disease, neoplasia, acute or chronic infection or inflammatory disease, known malabsorption, use of medications or supplements influencing immune function, and history of alcohol and/or drug abuse or addiction.

**Interventions**

After assessing inclusion and exclusion criteria, participants were randomly allocated in a 1:1 ratio to the following interventions for 3 wk before, during, and 2 wk after the Munich Marathon race: 1.0–1.5 L of nonalcoholic beer per day (intervention group) or 1.0–1.5 L of a control beverage, which contained the same ingredients like the nonalcoholic beer except for polyphenols. In addition, taste, color, and foaming of the control beverage were almost identical with the nonalcoholic beer. The overall polyphenol content of the placebo drink was null, whereas that of the nonalcoholic beer, measured by the Folin–Ciocalteu test, was 32.6 ± 0.1 mg of gallic acid equivalents per 100 g (mg GAE/100 g) and consisted predominantly of catechin (4.7 mg GAE/100 g), epicatechin (0.8 mg GAE/100 g), procyanidin B-3 (3.3 mg GAE/100 g), other proanthocyanidin acids (0.5 mg GAE/100 g), vanillic acid (1.5 mg GAE/100 g), syringic acid (4.2 mg GAE/100 g), p-cumar acid (1.5 mg GAE/100 g), ferulic acid (5.2 mg GAE/100 g), sinapinic acid (0.4 mg GAE/100 g), other hydroxycinnamic acids (0.9 mg GAE/100 g), isoxanthohumol (3.9 mg GAE/100 g), and other flavonols (5.4 mg GAE/100 g). The beverage for the intervention group (ERDINGER Alkoholfrei) was manufactured and bottled by the brewing company Erdinger Weissbraeu, Werner Brombach GmbH, Erding, Germany. The beverage for the control group was composed, manufactured, and bottled by Härtsfelder Familienbrauerei Hald, Dischingen, Germany. Both beverages were bottled in identically shaped bottles, differed only in the color of the bottle caps, and were administered in true double-blind fashion.

To ensure compliance of participants, telephone interviews asking for drinking protocols and a training diary were performed on a weekly basis. In addition, all participants kept a diary to document their exact fluid intake, including the study beverage.

**Outcome and End Point Definitions**

The primary outcome parameter was plasma interleukin-6 (IL-6). The related primary end point criterion was the group difference in change of IL-6 (before to after the marathon).

Secondary outcomes included 1) the blood total leukocyte count and 2) incidence of URTI. A clinically relevant URTI was defined if the global severity score of the Wisconsin Upper Respiratory Symptom Survey (WURSS-21) was greater than 7, representing either one severe symptom or impairment or seven mild symptoms/im pairments presented simultaneously (see below) (3).

Secondary outcomes that were recorded as part of the trial protocol not reported here include cardiovascular measurements (diastolic and systolic cardiac function, arteriovenous ratio, and ECG).

**Clinical measurements.** Participants were examined to assess inclusion and exclusion criteria 4 wk before the race (visit V1). Preexisting but yet unknown hepatic disease was excluded by investigating liver enzymes before inclusion in the study. Additional baseline data were collected during the week before the race (visit V2) and included questionnaires that assessed training history (training distance per week during the last 10 wk before the race, previous marathon races finished), history of cardiovascular risk factors (e.g., family history of cardiovascular disease), the WURSS-21, physical examination, anthropometry, clinical chemistry, ECG, and echocardiography.

Collection of blood samples and assessment of blood pressure were performed within 1 h after finishing the race.
Follow-up examinations 24 (visit V4) and 72 h (visit V5) after the marathon race (ECG, echocardiography, blood samples, and blood pressure) were performed in identical settings.

The WURSS-21 is a responsive, reliable, and valid tool for assessing symptoms, functional impairments, and global severity and global change of common cold (1–3). Participants were asked to complete a WURSS-21 questionnaire every evening 1 wk before the race (to get familiar with the questionnaire) and 2 wk after the race. Only complete questionnaires were used for analyses. In case of incomplete questionnaires, participants were contacted up to five times via phone, mail, or face to face.

Participants were requested not to use medications influencing inflammation such as nonsteroidal anti-inflammatory drugs (NSAIDs). Furthermore, subjects were asked to refrain from all polyphenol-containing foods, especially beverages such as wine, beer, and fruit juice, as well as fresh and dried fruits or vegetables. In addition, they were asked to minimize intake of fatty foods and large doses of vitamins (e.g., vitamin C > 500 mg·d⁻¹ or vitamin E > 800 IU·d⁻¹) and to refrain completely from mineral supplementation (e.g., selenium) and probiotic yogurt during the entire study period.

Subjects were instructed in multiple workshops by a nutrition scientist on how to record food intakes using standard nutrition diaries. These workshops took place once a week in the 4 wk before the race, and all participants were asked to take part at least once. In addition, supervised running sessions were offered once per week to ensure compliance and to provide an opportunity to ask questions concerning the trial. Nutritional intake was recorded with a 3-d nutritional record before visit V2 and before the marathon. All participants were asked not to change their dietary habits during the study period.

During the marathon, all participants were asked to use an HR monitor to calculate exercise intensity. %HRmax was calculated as a ratio of mean HR during marathon and HRmax. HRmax was calculated by the following formula:

\[ HR_{\text{max}} = \frac{208 \times \text{age (yr)}}{9} \]

Body mass index was calculated as the ratio of weight and the square of height in meters (kg·m⁻²). Total body fat was assessed by the skinfold caliper technique (6). Hypertension was defined as previously reported (7). An elevated cholesterol level was defined as more than 240 mg·dL⁻¹. Smoking was defined as current smoking or having smoked within the previous year.

**Laboratory Measurements**

**Blood samples.** Fasting blood samples were drawn from an antecubital vein with subjects in supine position at visits V1, V2, V4, and V5. Fasting was defined as abstinence from all food for at least 8 h. Only blood collection directly after the race (V3) was not in a fasted state. Routine complete blood counts were performed by a clinical hematology laboratory to provide hemoglobin and hematocrit for determination of plasma volume change using the method of Dill and Costill (9). IL-6 and all other dehydration-dependent concentrations were corrected for changes in plasma volume in accordance to the method of Dill and Costill.

Other blood samples were centrifuged in sodium heparin or EDTA tubes, and plasma was aliquoted and stored within 1 h at −80°C for further analyses. None of the specimens showed signs of hemolysis.

**IL-6.** IL-6 was measured using a solid-phase two-site chemiluminescent immunometric assay on the IMMULITE® system (Siemens Healthcare, Eschborn, Germany). Expected values in healthy individuals range from nondetectable to 5.9 ng·L⁻¹. The analytical sensitivity is 2 ng·L⁻¹. The measuring range is up to 1000 ng·L⁻¹.

**Leukocytes and differential hemogram.** Complete blood counts and the differential hemogram were performed using a Sysmex SF-3000 Automated Hematology Analyzer (Sysmex Deutschland GmbH, Norderstedt, Germany). Expected values in healthy individuals range from 4 to 10³ L⁻¹. The intermeasure coefficient of variation (CV) under actual routine conditions is 1.5% at a leukocyte count of 6.6 × 10³ L⁻¹. The upper reference limit in healthy volunteers was <5.0 mg·L⁻¹.

**High-sensitivity C-reactive protein (hs-CRP).** Hs-CRP was measured quantitatively with an immune turbidimetric method on an AU2700 analyzer (Olympus Germany, Beckman Coulter, Krefeld, Germany). The measuring range of this assay was 0.7–800 mg·L⁻¹. The interassay CV under actual routine conditions was 1.5% at a concentration of 13 mg·L⁻¹. The intra-assay CV was 0.76% at a concentration of 5.7 mg·L⁻¹. The upper reference limit in healthy volunteers was <5.0 mg·L⁻¹.

**Sample Size Calculation**

Sample size calculation was based on the primary end criterion, the difference in marathon-induced change of IL-6 between the study groups. Because of the expected right-skewed distribution of IL-6, differences in changes of logarithmized IL-6 levels (relative group differences) were considered as the base for inferential statistics. From previous publications, a coefficient of variation of 0.60 for IL-6 changes was expected for the proposed study population (37). With respect to this condition and by assuming a clinically relevant difference of at least 20% for change of IL-6 between the study groups during the marathon race, a sample size of 100 individuals per group had been calculated to be required to achieve an 80% power in the statistical analysis of the primary end point at a two-sided 0.05 level of significance. According to a possible dropout rate of up to 20%, a total of at least 250 individuals had to be included in the study to warrant the specified power requirements.

**Statistical Methods**

Statistical analyses were conducted using the PASW Statistics software (version 18.0.2 for Windows; SPSS, Inc.; Chicago, IL) and R software version 2.11.1 (R Foundation...
FIGURE 1—Study flow diagram. NSAID, nonsteroidal anti-inflammatory drug.
for Statistical Computing, Vienna, Austria). The mean value and SD for normally distributed data or the median and interquartile range (IQR) for nonnormally distributed data were reported for descriptive purposes. Assumption of normal distribution of data was verified by using descriptive methods (skewness, outliers, and distribution plots) and inferential statistics (Shapiro–Wilk test).

The primary end point criterion was statistically evaluated by the use of a Student’s t-test on means of changes in logarithmized IL-6 values (corresponding to a test of group differences in median changes of IL-6). Furthermore, ANCOVA models were used for the analysis of secondary end point criteria. To evaluate differences in the time course of measured parameters (e.g., URTI levels or total blood leukocyte counts), generalized estimation equation models (GEE) were used. The GEE approach adequately reflects the structure of repeated data and allows for simultaneous consideration of within- (time) and between-subject (group) effects. Within the GEE analysis, adjustment of different baseline levels was considered, and smoothing spline functions were applied to approximate functional shape of measurement level course by time. Odds ratios were provided with 95% confidence interval (CI).

All statistical tests were conducted with two sides at a 0.05 level of significance. For the purpose of sensitivity analysis, statistical evaluations of the primary and secondary end points were performed on the full analysis set (FAS) and per-protocol (PP) populations. For the primary end point, the FAS included data of all participants who had IL-6 measurements before and after the marathon. For the secondary end points, the FAS included all individuals who had a complete URTI questionnaire from race day up to day 13 after the race. PP population was defined by all patients who did not take any nonsteroidal anti-inflammatory drug medication during the study period and who ingested an average of at least 1 L of the study beverage per day (Fig. 1). PP data are presented in this article, with FAS data provided in the online supplemental material (see Supplemental Digital Content SDC 1–5; SDC 1 http://links.lww.com/MSS/A99 is a table that shows the baseline characteristics of all randomized study participants. SDC 2 (http://links.lww.com/MSS/A100) is a table that illustrates the incidence of URTI for all groups in the 13 d after the race. SDC 3 (http://links.lww.com/MSS/A101) is a figure that illustrates the IL-6 values for the intervention and control groups at all visits for the FAS. SDC 4 (http://links.lww.com/MSS/A102) is a figure that shows the incidence of clinically relevant URTI after a marathon race in the FAS group. SDC 5 (http://links.lww.com/MSS/A103) is a figure that illustrates the leukocyte counts for the intervention and control groups at all visits for the FAS and PP groups.).

RESULTS

Participants’ Characteristics

We assessed 374 participants for eligibility, 277 of whom were randomly assigned to either the intervention group (nonalcoholic beer beverage) or the control group (Fig. 1).

During the recruitment phase of the trial from June 1, 2009, through September 1, 2009, 277 participants were enrolled in the trial and were followed up to October 25, 2009.

Baseline characteristics for subjects adhering to study requirements are given in Table 1 (see Table, SDC 1, http://links.lww.com/MSS/A99, for baseline characteristics of all subjects).

A poststudy survey was performed and ensured that the participants did not know whether they were consuming nonalcoholic beer with or without polyphenols (data not shown).

**TABLE 1. Baseline characteristics of the study participants completing the study.**

<table>
<thead>
<tr>
<th></th>
<th>Intervention Group (n = 58)</th>
<th>Control Group (n = 63)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study beverage (L·d⁻¹)</td>
<td>1.22 ± 0.16</td>
<td>1.28 ± 0.26</td>
<td>0.18</td>
</tr>
<tr>
<td>Other beverage (L·d⁻¹)</td>
<td>1.49 ± 0.83</td>
<td>1.72 ± 0.93</td>
<td>0.20</td>
</tr>
<tr>
<td>Anthropometry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yr) (median (IQR))</td>
<td>44 (36–51)</td>
<td>42 (35–49)</td>
<td>0.37</td>
</tr>
<tr>
<td>Body mass index (kg·m⁻²)</td>
<td>23.4 ± 2.1</td>
<td>23.8 ± 2.1</td>
<td>0.24</td>
</tr>
<tr>
<td>Total body fat (%)</td>
<td>15.5 ± 4.0</td>
<td>14.6 ± 4.5</td>
<td>0.22</td>
</tr>
<tr>
<td>Mean blood pressure, systolic/diastolic (mm Hg)</td>
<td>126 ± 11/82 ± 7</td>
<td>127 ± 12/83 ± 7</td>
<td>0.91</td>
</tr>
<tr>
<td>Marathon run</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marathon time (h:min)</td>
<td>3:43:19 ± 0:24:20</td>
<td>3:49:18 ± 0:32:24</td>
<td>0.41</td>
</tr>
<tr>
<td>Minimum/maximum race time (h:min:s)</td>
<td>2:52:50/4:22:34</td>
<td>2:51:01/5:25:40</td>
<td></td>
</tr>
<tr>
<td>Mean HR during race (bpm)</td>
<td>156 ± 11</td>
<td>156 ± 11</td>
<td>0.97</td>
</tr>
<tr>
<td>HRj/calculated HRmax (%)</td>
<td>89.1 ± 4.5</td>
<td>89.6 ± 4.7</td>
<td>0.41</td>
</tr>
<tr>
<td>Training history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Training distance per week during the last 10 wk before race (km)</td>
<td>49.7 ± 18.2</td>
<td>53.6 ± 22.4</td>
<td>0.43</td>
</tr>
<tr>
<td>Previous marathon races finished (median (IQR))</td>
<td>4 (1–7)</td>
<td>3 (1–7)</td>
<td>0.69</td>
</tr>
<tr>
<td>Cardiovascular risk factors (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus (type 1 or 2)</td>
<td>0%</td>
<td>0%</td>
<td>1.00</td>
</tr>
<tr>
<td>Family history of cardiovascular disease</td>
<td>57%</td>
<td>46%</td>
<td>0.22</td>
</tr>
<tr>
<td>Hypercholesterolemia (total cholesterol ≥ 240 mg·dL⁻¹)</td>
<td>12%</td>
<td>14%</td>
<td>0.72</td>
</tr>
<tr>
<td>Hypertension (RRsys &gt; 140 mm Hg or RRdia &gt; 90 mm Hg)</td>
<td>9%</td>
<td>16%</td>
<td>0.21</td>
</tr>
<tr>
<td>Smoke/ex-smoker</td>
<td>4%/0%</td>
<td>4%/2%</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or median (IQR).

HRmax = mean HR during marathon race; RRdia, diastolic blood pressure; RRsys, systolic blood pressure.
Primary Outcome

Immediately after the race, the increase in IL-6 was significantly lower in the intervention compared with the control group (median (IQR) = 23.9 (15.9–38.7) vs 31.6 (18.5–53.3) ng·L⁻¹, \( P = 0.03 \)). Groups did not differ in plasma IL-6 levels at all other laboratory visits (Fig. 2).

Secondary Outcome

URTI. The response rate for complete recording of the WURSS-21 questionnaire during the 2-wk period after the Munich Marathon race event was 61% (168 of 277 participants).

Postrace URTI incidence was significantly higher in the control group compared with the intervention group (odds ratio = 3.25 (95% CI = 1.38–7.66), \( P = 0.007 \), Fig. 3). On the basis of these data, the number needed to treat was estimated to be 8.

As shown in Figure 3, percentage of participants with clinically relevant URTI increased in the days after the race, with two peaks especially apparent 1 and 5 d after the race.

Data for the URTI incidence between the groups for each day are given in the table of SDC 2 (http://links.lww.com/MSS/A100).

Blood count and hs-CRP. With measurements at V1 and V2 as adjustment covariates, a significant group difference in total blood leukocyte counts was measured immediately and 24 h after the race (overall comparison: mean difference ± SE = 1.2 × 10⁹ ± 0.65 × 10⁹ L⁻¹, \( P = 0.02 \)) (Fig. 4).

Consistent results were observed for hs-CRP with a lower clinically relevant increase in hs-CRP 24 h after the race in the intervention group compared with the control group (−6.8%, 95% CI = −16.2% to +3.6%, \( P = 0.169 \)).

Adverse Events

Gastrointestinal problems due to the study beverage were only seen in the control group (\( n = 3, ~2\% \)). In the intervention group, no dropouts caused by adverse effects were observed.

DISCUSSION

This study is the first to show that consuming 1–1.5 L·d⁻¹ of nonalcoholic beer with polyphenols for 3 wk before a
In conclusion, consumption of nonalcoholic beer with polyphenols for 3 wk before the Munich Marathon reduced postrace inflammation. Continued ingestion of the

marathon race reduces postrace inflammation and URTI incidence. Subjects in the intervention group ingested about 400 mg of gallic acid equivalents per day of a complex mixture of polyphenols from the nonalcoholic beer beverage.

Numerous food products and supplements have been tested in athletes as countermeasures to exercise-induced inflammation, oxidative stress, immune dysfunction, and URTI, and most have not emerged as efficacious (26). Results from randomized double-blind studies in human athletes with large doses of purified flavonoids such as quercetin have been disappointing, but when mixed with other flavonoids and food components, impressive anti-inflammatory and antioxidative effects have been reported after exercise (29,30).

Polyphenol-rich plant extracts are being tested by an increasing number of investigative teams as performance aids and have surfaced as effective countermeasures to exercise-induced oxidative stress and inflammation (24). Polyphenols and flavonoids vary widely in bioavailability, and most are poorly absorbed, undergo active efflux, and are extensively conjugated and metabolically transformed, all of which can affect their bioactive capacities (22). There is a growing realization that bioactive influences of individual polyphenols are potentiated when ingested in a cocktail or an extract of other polyphenols and nutrients (21). Two or more polyphenols ingested together may increase bioavailability and decrease elimination via competitive inhibition of glucuronide and sulfate conjugation in both the intestine and the liver and by inhibiting efflux transporters. Thus, the anti-inflammatory and antioxidative effects of plant foods are not produced by a single component but rather by complex mixtures of interacting molecules. Our data indicating anti-inflammatory effects in athletes after a marathon race from ingesting a cocktail of polyphenols from beer are consistent with this viewpoint.

Many polyphenols suppress viral replication under in vitro conditions, an effect due in part to modulation of the cellular redox milieu (5,16). Quercetin supplementation during a 5-wk period reduced URTI incidence in exercise-stressed cyclists without altering immune function (29). The beneficial influence of quercetin on URTI incidence in endurance athletes, however, has not been a consistent finding (27,39). The reduction in URTI incidence reported in this study from beer polyphenols is a novel finding and suggests that a complex mixture of plant phenolics exerts antiviral effects during the 2-wk period after marathon competition.

Polyphenol-rich beverages and supplements that exert anti-inflammatory and antipathogenic influences within the context of athletic endeavor may also prove to be efficacious in chronically inflamed groups such as the obese. Inflammation is a key mechanism in the pathogenesis of certain disease states, supporting the proposed strategy of increased polyphenol intake for prevention of cancer, diabetes mellitus, and cardiovascular disease (4,17,19,40,42). Therefore, polyphenol-rich beverages and supplements might be a promising approach to prevent and positively modulate these pathologies associated with increased inflammation (12,15,35).

Besides its origin in immune–active cells, IL-6 is also produced in exercising skeletal muscle during strenuous exercise (32). Therefore, the cause of the lower increase in IL-6 in the intervention group in our study might also be in exercising musculature. Qin et al. (36) were able to show that polyphenols are able to decrease inflammatory markers also at the mRNA level in myocytes.

The current trial has certain limitations. First, although everything possible was done to obtain the completed WURSS-21 questionnaires, 39% of subjects failed to comply. Nevertheless, the response rate was comparable to other studies using paper-and-pencil version questionnaires (18). In addition, we did not measure the amounts of polyphenols absorbed from the intestinal tract and plasma concentrations of the primary beer phenolics including ferulic acid and catechins. Nonetheless, our results are very clear, and the possible mechanisms of interference (e.g., anti-inflammatory medication, food) were minimized so that other possible explanations for the results of our study are unlikely.

Furthermore, we did not measure objective correlates of upper respiratory tract infections like quantitative viral titer or mucus weight. Therefore, we could not determine whether the symptoms reported in the WURSS-21 questionnaire had been caused by local inflammation or infections. Therefore, we used the term “respiratory illness” to cover both inflammatory and infectious entities.

Despite these limitations, the randomized design and the large number of individuals participating in the study ensure reliable conclusions to be drawn from the data.

An aspect that also has to be mentioned is the administration of polyphenols. In our trial, participants were asked to drink 1–1.5 L of study beverage per day. This could be challenging. Therefore, other forms of administration (e.g., tablets) should be used in future studies to simplify the transfer to everyday use regarding period and frequency as well as route of administration. Whether these alternative forms of administration have similar effects as those observed in our study has yet to be determined.

Ingestion of nonalcoholic beer with polyphenols decreased both inflammation and URTI rates in athletes after the race. The linkage between decreased inflammation and URTI is difficult to ascertain within the multiple factors involved in URTI episodes. Heavy exertion impairs expression of Toll-like receptors (TLR), whereas flavonoids may improve toll-interleukin 1 receptor (TIR)-domain-containing adapter-inducing interferon-β (TRIF)-dependent signaling TLR pathways (20,31). Thus, a focus on TLR in future studies may be one of several areas to investigate when evaluating the influence of polyphenols on inflammation and URTI in athletes.

In conclusion, consumption of nonalcoholic beer with polyphenols for 3 wk before the Munich Marathon reduced postrace inflammation. Continued ingestion of the
nonalcoholic beer during the 2-wk period after the race reduced the incidence of clinically relevant URTI. Whether these findings are linked and dependent on each other will have to be confirmed in future studies.

Funding for the study was received from Erdinger Weissbraeu, Werner Brombach GmbH. The funders had no direct role in the study’s design, conduct, analysis, interpretation of data, and reporting beyond approval of the scientific protocol in peer review for funding. No other grants were received.

The authors thank the staff and especially the doctoral students of the Department of Prevention and Sports Medicine, Technische Universität München, for their assistance with this project. Furthermore, the authors would like to thank Jeff Christie for careful proofreading of the article and Erich Elstner for supplying information concerning polyphenols in beer.

The study’s ClinicalTrials.gov ID is NCT00933218. The study followed the guidelines on Good Publication Practice.

The study was primarily designed by J.S. and M.H.; J.S., M.H., and T.S. represent the steering committee of the Be-MaGIC study. All other authors contributed to the design of the study and supervised the trial and statistical analysis plan in collaboration with the staff of the Institute for Medical Statistics and Epidemiology, Klinikum rechts der Isar, Technische Universität München. The first author (J.S.) wrote the first draft of the article, which was next revised in detail by D.C.N. Subsequent drafts were prepared by all authors. Besides things mentioned above, J.S., T.S., and J.H. principally did the statistical analysis of the data. J.H., M.R., and A.P. were responsible for the administrative and technical support. Furthermore, S.B. was responsible for the material support. B.W. additionally contributed preciously to the analysis and interpretation of the data. J.S. has the primary responsibility for the final content of the article. All authors read and approved the final article.

None of the authors had any personal or financial conflicts of interest.

The results of the present study do not constitute endorsement by the American College of Sports Medicine.

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