Non-alcoholic beer and respiratory tract health: incidence and inflammation reduction

7th European Beer and Health Symposium

Ass. Prof. Johannes Scherr, MD
Topics

- Effects of prolonged & strenuous exercise (as a model for inflammation-associated illnesses)
  - Inflammation & infection
  - Cardiovascular system

- Effects of the polyphenols in (non-alcoholic) beer
  - Inflammation & infection of the respiratory tract system
  - Cardiovascular & rheological effects
Background inflammation / infection

Prolonged and strenuous exercise results in
a) an increase in biomarkers representing pro-inflammatory activity

- IL-6 concentration [ng/L]
  - n = 102 healthy male marathon runners
  - Age = 42 ± 9 J.

- hs-CRP concentration [mg/L]

# p < 0.001
Prolonged and strenuous exercise results in
a) an increase in biomarkers representing pro-inflammatory activity
b) an immune dysfunction and an elevated incidence/susceptibility of infections (especially upper respiratory tract infections (URTI))
Background cardiovascular alterations

- Prolonged and strenuous exercise results in
  a) an increase in biomarkers representing pro-inflammatory activity
  b) an immune dysfunction and an elevated incidence/susceptibility of infections (especially upper respiratory tract infections (URTI))
  c) an increase in biomarkers representing myocardial damage/injury

Background cardiovascular alterations

- Prolonged and strenuous exercise results in
  a) an increase in biomarkers representing pro-inflammatory activity
  b) an immune dysfunction and an elevated incidence/susceptibility of infections (especially upper respiratory tract infections (URTI))
  c) an increase in biomarkers representing myocardial damage/injury
  d) discussed underlying mechanisms resulting in an increase in elevated myocardial biomarkers:
    1. oxidative stress or inflammation (in the meaning of inflammatory cardiomyopathy)
    2. Injury of myocytes caused by ischemia
      I. reversible
      II. Irreversible (leading to necrosis)
    3. Impaired renal clearance
    4. Stretch-mediated liberation (due to enhanced wall stress)
Background cardiovascular alterations

- Prolonged and strenuous exercise results in
  a) an increase in biomarkers representing pro-inflammatory activity
  b) an immune dysfunction and an elevated incidence/susceptibility of infections (especially upper respiratory tract infections (URTI))
  c) an increase in biomarkers representing myocardial damage/injury
  d) discussed underlying mechanisms resulting in an increase in elevated myocardial biomarkers:
    1. oxidative stress or inflammation (in the meaning of inflammatory cardiomyopathy)
    2. Injury of myocytes caused by ischemia
       I. reversible
       II. Irreversible (leading to necrosis)
    3. Impaired renal clearance
    4. Stretch-mediated liberation (due to enhanced wall stress)
Prolonged and strenuous exercise results in:

a) an increase in biomarkers representing pro-inflammatory activity

b) an immune dysfunction and an elevated incidence/susceptibility of infections (especially upper respiratory tract infections (URTI))

c) an increase in biomarkers representing myocardial damage/injury
d) discussed underlying mechanisms resulting in an increase in elevated myocardial biomarkers:

1. oxidative stress or inflammation (in the meaning of inflammatory cardiomyopathy)
2. Injury of myocytes caused by ischemia
   I. reversible
   II. irreversible (leading to necrosis)
3. Impaired renal clearance
4. Stretch-mediated liberation (due to enhanced wall stress)

Background cardiovascular alterations

- 3-4 weeks pre-race
- One week pre-race
- Immediately post-race
- 24 hrs post-race
- 72 hrs post-race

Spontaneous Aggregation (Multiplate)
**Daily total polyphenol intake**

- Measured in gallic acid equivalent (GAE)
- 48.3mg GAE/d in Brazil \(^1\) (??)
- 783.9 ± 31.7 mg GAE/d in Portugal \(^2\)
- 1 g GAE/d \(^3\)
- → ~ 800-900 mg GAE/d

- Total phenol content in beer of 500-1000 mg GAE/L \(^4\)

<table>
<thead>
<tr>
<th>Foodstuff</th>
<th>Total phenols (^5)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Foodstuff</strong></td>
<td><strong>Folin-Ciocalteu assay (GAE [mg])</strong></td>
</tr>
<tr>
<td>Vegetables</td>
<td></td>
</tr>
<tr>
<td>Potato, 200 g</td>
<td>57</td>
</tr>
<tr>
<td>Tomato, 100 g</td>
<td>37</td>
</tr>
<tr>
<td>Onion, 20 g</td>
<td>18</td>
</tr>
<tr>
<td>Fruits</td>
<td></td>
</tr>
<tr>
<td>Apple, 200 g</td>
<td>440</td>
</tr>
<tr>
<td>Cherry, 50 g</td>
<td>276</td>
</tr>
<tr>
<td>Other foods</td>
<td></td>
</tr>
<tr>
<td>Dark chocolate, 20g</td>
<td>168</td>
</tr>
<tr>
<td>Beverages</td>
<td></td>
</tr>
<tr>
<td>Red wine, 125 ml</td>
<td>225</td>
</tr>
<tr>
<td>Coffee, 200ml</td>
<td>179</td>
</tr>
<tr>
<td>Black tea, 200 ml</td>
<td>200</td>
</tr>
</tbody>
</table>

\(^1\) Faller et al, Rev Saúde Pública 2009
\(^3\) Kuhnau J. World Rev Nutr Diet. 1976:117–91
\(^4\) Leupold, G., Brauwissenschaft 1981: 205–210
Aim:
Investigation of the influence of two quercetin doses (500 and 1000 mg/day) compared to placebo on upper respiratory tract infection (URTI) rates in a community group (N= 1002) of subjects varying widely in age (18–85 years)
Polyphenols & infections (URTIs)

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N = 317)</th>
<th>Q-500 (N = 315)</th>
<th>Q-1000 (N = 315)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>URTI, # days</td>
<td>8,4 ± 0,5</td>
<td>8,5 ± 0,5</td>
<td>8,5 ± 0,5</td>
</tr>
<tr>
<td>URTI severity</td>
<td>19,3 ± 1,3</td>
<td>18,3 ± 1,3</td>
<td>19,8 ± 1,3</td>
</tr>
<tr>
<td>URTI symptom</td>
<td>108 ± 8,0</td>
<td>108 ± 8,3</td>
<td>111 ± 8,0</td>
</tr>
</tbody>
</table>

1-Way ANOVA F-value:

- URTI, # days: 0,982
- URTI severity: 0,67
- URTI symptom: 0,946

Subjects ≥ 40 years of age & self-assessment: top half of the group for fitness.

In summary, for all subjects combined, quercetin supplementation over 12 weeks had **no** significant influence on URTI rates or symptomatology compared to placebo.

A reduction in URTI total sick days and severity was noted in **middle aged and older subjects** ingesting 1000mg quercetin/day for 12 weeks who rated themselves as **physically fit**.

*P < 0.05 compared to placebo
Be-MaGIC: Beer, Marathon, Genetics, Inflammation and the Cardiovascular System

Be-MaGIC-Trial: Material & Methods

- n = 277 marathon (MT) runners (♂, age 42±9J., BMI 23.7±2.1kg/m², finishing time 3h 51min ± 30min)
- supplementation with a mixture of polyphenols (= non-alcoholic beer= verum (V), 32.6±0.1 mg Gallic acid equivalents (GAE)/100 g)) compared to placebo (except for polyphenols identical composition; also taste, color and foaming)
  - Composition of the polyphenol: catechin (4.7 mg GAE/100g), epicatechin (0.8 mg GAE/100g), procyanidin B-3 (3.3 mg GAE/100g), other proanthocyanidins acid (0.5 mg GAE/100g), vanillic acid (1.5 mg GAE/100g), syringa acid (4.2 mg GAE/100g), p-cumaracid (1.5 mg GAE/100g), ferulic acid (5.2 mg GAE/100g), sinapinic acid (0.4 mg GAE/100g), other hydroxycinnamic acids (0.9 mg GAE/100g), isoxanthohumol (3.9 mg GAE/100g), and other flavonols (5.4 mg GAE/100g)

Screening examination (n = 374) → 1:1 randomisation (n = 277)

Intervention group (V)
(1-1.5l polyphenol-containing beverage
[≥ 326mg GAE/l]/ day)

Control group
(1-1.5l placebo beverage/ day)

Double-blinded
n = 277 marathon (MT) runners (♀, age 42±9J., BMI 23.7±2.1kg/m², finishing time 3h 51min ± 30min)

Statistical analysis of a Full-Analysis-Set (FAS; participants, who finished the marathon successfully) & Per-Protocol (PP)-Gruppe (FAS criteria & ingestion of ≥ 1L study beverage /d (≧ at least 326 mg GAE)).
Flow chart participants Be-MaGiC trial

Flow Diagram of Be-MaGiC participants

- Assessed for eligibility (n = 374)
- Excluded:
  - Meeting exclusion criteria (n = 3)
    - e.g., former alcohol addiction
  - Refused to participate (n = 94)
    - e.g., personal timing constraints or lack of adequate training
- Randomized (n = 277)
  - Allocated to Intervention Group (Polyphenols containing beverage) (n = 142)
    - Lost to follow-up:
      - Did not start the marathon race (n = 16)
        - Respiratory tract infection (n = 8)
        - Orthopedic injury (n = 4)
        - Personal time constraints (n = 4)
    - Did not finish the marathon race (n = 11)
      - Discontinued intervention (n = 6)
        - Gastrointestinal problems due to beverage (n = 0)
      - Discontinued examinations (n = 2)
        - Unexpected personal timing constraints at V4 and/or V5 (n = 2)
- Analyzed full analysis set (FAS_{a.d}) (n = 113)
- Excluded from FAS for per protocol analysis (n = 55)
  - Intake of NSAR (n = 21)
  - Incomplete questionnaire concerning NSAI (n = 23)
  - Beverage intake < 1 L/day or incomplete beverage diary (n = 19)
  - Interaction is possible due to multi-referencing

- Allocated to Control Group (Non-polyphenols containing beverage) (n = 135)
  - Lost to follow-up:
    - Did not start the marathon race (n = 12)
      - Respiratory tract infection (n = 4)
      - Orthopedic injury (n = 4)
      - Lyme disease (n = 1)
      - Extreme orthostatic dysregulation during blood drawing (n = 1)
      - Allergic reaction after mosquito bite (n = 1)
      - Initial diagnosis of a Crohn's disease (n = 1)
    - Did not finish the marathon race (n = 6)
      - Discontinued intervention (n = 3)
        - Gastrointestinal problems due to beverage (n = 3)
      - Discontinued examinations (n = 7)
        - Unexpected personal timing constraints at V4 and/or V5 (n = 7)
  - Analyzed full analysis set (FAS_{a.d}) (n = 109)
  - Excluded from FAS for per protocol analysis (n = 46)
    - Intake of NSAR (n = 15)
    - Incomplete questionnaire concerning NSAI (n = 22)
    - Beverage intake < 1 L/day or incomplete beverage diary (n = 13)
  - Analyzed per protocol (PP_{a.d}) (n = 63)
### Study cohort – baseline (PP)

<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><strong>Intervention Group (n = 58)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fluid intake</strong></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><strong>Anthropometry</strong></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><strong>Marathon run</strong></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>2:53:50/4:42:34</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>HRₘᵢ/calculated HRₘᵢ (%)</td>
<td>89.1 ± 4.5</td>
<td>89.6 ± 4.7</td>
<td>0.41</td>
</tr>
<tr>
<td><strong>Training history</strong></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><strong>Cardiovascular risk factors (%)</strong></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>Smoker/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). HRₘᵢ, mean HR during marathon race; RRdia, diastolic blood pressure; RRsys, systolic blood pressure.

**Polyphenols & Inflammation (PP)**

GEE analysis: difference in leukocyte levels at V3 (immediately post-race) and V4 (24-hrs post-race): overall comparison:
mean difference ± SE = 1.2 ± 0.65 × 10⁹/L, p = 0.02

n = 277
Age = 42 ± 9 yrs.
Polyphenols & URTI

PP group
OR: 3.3-fold (95% CI: 1.38 to 7.66)
p=0.007

Percentage of participants with clinical relevant URTI

Days after marathon race

Race day
Cardiovascular effects of NAB

Reduction 4.7±2.5–fold

Reduction 3.8±2.0–fold

p=0.02

p=0.04
Rheologic effects of NAB

Within the group with upper quartile intake of study beverage (>1.28 L/d)
Polyphenols (in non-alcoholic beer) seems to

- have anti-inflammatory effects
- reduce strain-induced incidence of upper respiratory tract infections
- be linked to enhanced cardiomyocyte recovery after prolonged and strenuous exercise
- have possible rheological effects with respect to exercise-induced thrombocyte aggregation
Bier ist gut ... sagt der Arzt!

Überarbeitet? Bier hilft entspannen!
Nervös? Bier beruhigt die Nerven!
Verkrampft? Bier lockert die Glieder!

Mit dem Bier im Bunde - Natur und Gesundheit!
Contact

- Ass. Prof. Johannes Scherr, MD
  Department of Prevention, Rehabilitation and Sports Medicine
  Klinikum rechts der Isar
  Technische Universität München, Germany
  Georg-Brauchle-Ring 56-58 (Campus C)
  80992 München

- scherr@sport.med.tum.de
  www.sport.med.tum.de