The effect of a ketogenic diet on the exercise induced immune response

Published: 13-07-2018
Last updated: 11-04-2024

To examine whether a short or longer period on a ketogenic diet leads to an altered immune response after exercise.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON46666

Source
ToetsingOnline

Brief title
KEI-study

Condition

- Other condition

Synonym
Exercise induced immune response

Health condition

Immuun respons na inspanning

Research involving
Human

Sponsors and support

Primary sponsor: Wageningen Universiteit
Source(s) of monetary or material Support: Provincie Gelderland

Intervention

Keyword: exercise, immune response, ketogenic diet

Outcome measures

Primary outcome

Blood sample:

o Serum/plasma: cytokines, CRP, cortisol

o *Homing* estimations: where do the immune cells move to? To upper respiratory tract or to intestines? (*4*1/CCR10/CD62L for upper respiratory tract) (*4*7/ CCR9 for intestines).

o PBMC*s (peripheral blood mononuclear cells): stimulate with LPS and measure IL-1, TNF, IL-6, IL-10 and IL-12

o PBMC*s (peripheral blood mononuclear cells): stimulate with Tetanus Toxoid (TT)

o PBMC*s (peripheral blood mononuclear cells): stimulate with conA (lectine) as positive control

o PBMC*s (peripheral blood mononuclear cells): stimulate with Pokeweed as postive control for B-cells.

o PBMC*s (peripheral blood mononuclear cells): Estimate proliferation by adding K167.

Secondary outcome

- Faeces sample: intestine immunity (with Calprotectin test)

- Saliva sample: IgA and TNF-alpha (with ELISA test)

- Urine sample: Ketone bodies with Ketostix

- Blood sample: stress hormones, glucose, free fatty acids, ketone bodies.

Tertiary:

Blood: lactate, insulin, GI permeability markers

Body composition: weight, length, fat percentage, bone and muscle weight (DEXA)

Diet: food questionnaire app

Physical activity: Physical activity level-questionnaire

Questionnaires: delayed onset muscle soreness (DOMS), upper respiratory tract infection (URTI) questionnaire. Motivational Q and questionnaire on sleep, mental physical and emotional wellbeing

Performance: RER (ratio CO2:O2) during exercise test.

Study description

Background summary

Athletes are much concerned with their diets: good nutrition can*t make a bad athlete good, but poor nutrition can make a good athlete worse. Therefore, sports performance and nutrition are inseparably linked [1]. Recently, more and more athletes are gaining interest in varying the amount of carbohydrates in their diets. Concepts, such as "Train Low * Compete High" and a ketogenic diet are used by both recreational and professional athletes. This concept means training with a low carbohydrate status and competing with a high carbohydrate status [2]. For athletes this means that they start a workout with a low carbohydrate status. The idea is that this improves fat burning [3], and that athletes are able to postpone glycogen use during an extensive exercise bout. Athletes can get a low carbohydrate status by training in the evening, then no dinner or a dinner with hardly any carbohydrates, followed by a training the next morning, without breakfast. Another way to achieve a low carbohydrate status, is to follow a (ketogenic) diet very low in carbohydrates during a number of weeks.
The effect of a low carbohydrate diet on exercise performance is known [4]. A low carbohydrate diet does not result in peak performance at high intensity, compared to a high carbohydrate diet. However, a low carbohydrate diet does not affect moderate intensity exercise performance [5].
Following a low carbohydrate diet could result in temporarily ketogenesis, in other words, the athlete will use ketone bodies (Acetoacetate, acetone and *-hydroxybutyrate) for the production of energy. Adapting to a low carbohydrate,

high fat diet takes 5 days [6], while adapting to a ketogenic diet takes two weeks [7].
There are indications that ketones can have a positive effect on the immune response. For example, *-hydroxybutyrate inhibits the activity of the NLRP3 inflammasome, causing it to release less cytokines [8]. A ketogenic diet is known to have positive effects on persons with certain skin disorders and epileptic attacks [9]. However, the effects of a ketogenic diet on the immune response after exercise are unknown. In sports, a ketogenic diet can possibly suppress the exercise induced immune response.
An immune response occurs during and after exercise in an athletes* body. This immune response results in adaptation of the athletes* body to training, which makes the athlete better and stronger, but it also results in a vulnerable time frame directly after exercise, in which an athlete is more susceptible to infection and diseases [10]. Nutrition could possibly influence this exercise induced immune response.
But whether a low carbohydrate diet really leads to an altered immune response after exercise has never been studied, even though many athletes follow such a diet for shorter or longer periods of time. When athletes follow such a diet for a longer period, they can really switch to ketogeneses, when they follow such a diet for a shorter period/a few days, this diet would probably cause a metabolic stress factor, which can influence the exercise induced immune response as well [11].
Therefore, the aim of this research is to examine the influence of a ketogenic diet on the exercise induced immune response.

1. Jeukendrup, A. and M. Gleeson, Sport nutrition: an introduction to energy production and performance. 2010: Human Kinetics.
2. Burke, L.M., Fueling strategies to optimize performance: training high or training low? Scand J Med Sci Sports, 2010. 20 Suppl 2: p. 48-58.
3. Cox, P.J., et al., Nutritional Ketosis Alters Fuel Preference and Thereby Endurance Performance in Athletes. Cell Metab, 2016. 24(2): p. 256-68.
4. Burke, L.M., Re-Examining High-Fat Diets for Sports Performance: Did We Call the 'Nail in the Coffin' Too Soon? Sports Med, 2015. 45 Suppl 1: p. S33-49.
5. Volek, J.S., T. Noakes, and S.D. Phinney, Rethinking fat as a fuel for endurance exercise. Eur J Sport Sci, 2015. 15(1): p. 13-20.
6. Goedecke, J.H., et al., Metabolic adaptations to a high-fat diet in endurance cyclists. Metabolism, 1999. 48(12): p. 1509-17.
7. Phinney, S.D., Ketogenic diets and physical performance. Nutr Metab (Lond), 2004. 1(1): p. 2.
8. Youm, Y.H., et al., The ketone metabolite beta-hydroxybutyrate blocks NLRP3 inflammasome-mediated inflammatory disease. Nat Med, 2015. 21(3): p. 263-9.
9. McNally, M.A. and A.L. Hartman, Ketone bodies in epilepsy. J Neurochem, 2012. 121(1): p. 28-35.
10. Nieman, D.C., Immune response to heavy exertion. J Appl Physiol (1985), 1997. 82(5): p. 1385-94.
11. Gleeson, M., D.C. Nieman, and B.K. Pedersen, Exercise, nutrition and immune

function. J Sports Sci, 2004. 22(1): p. 115-25.

Study objective

To examine whether a short or longer period on a ketogenic diet leads to an altered immune response after exercise.

Study design

A cross-over intervention study, with a total duration of 6 weeks. An athlete follows a high, or low carbohydrate (ketogenic) diet. After 2 days a test day takes place where the athlete performs an exercise test of 90 minutes, and blood samples are taken at different time points. After that, the athlete still follows the diet for another 12 days, after which he/she comes back again for another identical test day. Then a 2 weeks wash-out period. After that, the athlete follows the same protocol but then with the low (ketogenic), or high carbohydrate diet.

Intervention

The intervention consists of a custom diet that is followed for 2 weeks. After 2 days on the diet, a test day takes place and after 2 weeks on the diet another test day takes place. The diet is low, or high in carbohydrates. With low meaning under 10 En% from carbohydrates, and with high meaning more than 50 En% from carbohydrates. The protein intake will be set at ~15 En% in both diets.

Study burden and risks

Burden: time investment (~31hours), following the prescribed diet (2x two weeks), performing exercise tests (VO2max 1x and 90min exercise test 2x), Blood, saliva, urinary and faeces samples.

Risks: Exercise tests will be intensive, however, athletes are used to that. The diet could cause some discomfort. And blood withdrawals can lead to bruises and discomfort (afterwards).

Contacts

Public
Wageningen Universiteit

Stippeneng 4
Wageningen 6708 WE

NL
Scientific
Wageningen Universiteit

Stippeneng 4
Wageningen 6708 WE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Male
Age: 18 - 45 y
BMI: 18.5 * 25 kg/m2
Hb * 8.5 mmol/L, determined with blood sample from finger tip
Minimal of 3 hours of training per week, and a maximum of 10 hours
DKTP (diphtheria, pertussis, tetanus and polio) vaccinated (for stimulation of isolated cells (PBMC*s) with tatanus toxoid)
No asthma medication and/or anti-inflammatory medication
No use of immunosuppressive medication
No flu and/or travel vaccinations in the 4 months before and during the study
Able to be present and participate at all test days
Willing and able to follow prescribed diet for 2 weeks in a row (2 times 2 weeks)

Exclusion criteria

Chronic illness
Blood donations during study or in 2 months prior to the study
Food allergies (e.g. nuts, gluten, avocado)
Vegetarian diet

Use of immunosuppressive medication
Flu and/or travel vaccination 4 months before and during the study
Hb < 8.5 mmol/L
Working at *Human Nutrition* - Wageningen University
Msc thesis or internship at *Human Nutrition* - Wageningen University
Participating in other scientific research (with the exception of EetMeetWeet)

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-09-2018
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO

Date:	13-07-2018
Application type:	First submission
Review commission:	METC Wageningen Universiteit (Wageningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL65404.081.18