Effect of hyperglycemia on the ventilatory response to hypoxia

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25005

Source
NTR

Brief title
N/A

Health condition

Control of breathing/physiology

Sponsors and support

Primary sponsor: LUMC
Source(s) of monetary or material Support: -

Intervention

Outcome measures

Primary outcome

The ventilatory response to hypoxia in terms of delta(ventilation)/delta(lopPaO2)

Secondary outcome

N/A

Study description

Background summary

The carotid bodies, strategically located at the bifurcation of the carotid arteries, are the metabolic sensors of the human body. They contain specific chemosensors which do detect variations in the chemical composition of the arterial blood. They are sensitive to changes in arterial oxygen concentration (PaO2), arterial carbon dioxide concentration (PaCO2), and arterial pH. Recent studies indicate that the carotid bodies are further sensitive to glucose, temperature and osmolality of the blood. For example, hypoxia (the reduction in arterial blood Hb-oxygen saturation) will cause an immediate response from the carotid bodies causing a hyperventilatory response aimed at the restoration of the oxygen content of the blood; changes in body temperature will affect breathing via the carotid bodies.

Recent studies indicate that the carotid body response to changes in blood gas composition are influenced by changes in blood glucose concentration. For example, hyperglycemia will blunt the ventilatory response to hypoxia, resulting in little to no hyperventilatory response despite a sharp reduction in arterial Hb-oxygen saturation (SpO2). The mechanism of the interaction between glucose and hypoxia at the carotid bodies is unknown, but it may be argued that the production of reactive oxygen species during the process of glucose metabolism may be the major cause of the blunting of the ventilatory response to hypoxia. Important evidence for this hypothesis comes from studies from our laboratory. We recently examined the effect of the removal of reactive oxygen species (ROS) on anesthesia-induced blunting of the ventilatory response to acute hypoxia. Administration of antioxidants (2 gram of ascorbic acid and 200 mg of á-tocopherol) was able to fully reverse or prevent the large depression of the carotid body-mediated ventilatory response to hypoxia, normally seen after just 0.1 % halothane or isoflurane (about 1/10th of the dose required for anesthesia). Earlier work from our laboratory show that there is a clear relationship between the magnitude of depression of the ventilatory response to hypoxia by all volatile anesthetics and the magnitude of their metabolism (during hypoxia these agents show reductive metabolism creating ROS). Agents with greater metabolism (producing more ROS), such as halothane will have more depression of the ventilatory response to hypoxia, while the reverse is true for agents with little to no metabolism, such as desflurane. These data indicate that ROS play an import modulatory role in the complex pathway from hypoxic stimulus to the hyperventilatory response, most probably at the site of the carotid bodies.

The aim of the current study is two-fold:

1. What is the influence of hyperglycemia on the ventilatory response to hypoxia (acute hypoxic response or AHR);

2. To test whether antioxidants (ascorbic acid) are able to influence any effect observed

during hyperglycemia.

Study objective

High levels of glucose in the blood will affect the functioning of the carotid bodies and suppress the ventilatory response to isocapnic hypoxia. Our hypothesis is that antioxidant pretreatment will prevent such depression.

Study design

There will be three study sessions at least two weeks apart

Intervention

Our primary outcome is the ventilatory response to hypoxia. To that end, hypoxia will be induced by lowering the inspired oxygen concentration using a computer-controlled dynamic end-tidal forcing system, such that the oxygen saturation will 80 ± 2%. The hypoxic sensitivity will be calculated as delta Ventilation/delta desaturation in L/min per % desaturation. One hypoxic experiment will last about 25 min.

We will assess the effect of hyperglycemia on the hypoxic sensitivity. Hyperglycemia will be induced by infusion of 20% glucose intravenously. Glucose blood concentrations will be measured at regular intervals from an arterial line. After reaching a hyperglycemic level (20 mmol/L) we will perform a next hypoxic experiment.

Next we will infuse intravenously either placebo or antioxidants. Placebo is NaCl 0.9%, antioxidant is ascorbic acid 2 gram iv, followed by a continuous infusion of 1 gram/h.

During the session X the sequence of events is Control hypoxic response, followed by a response during infusion of glucose. Next the antioxidant experiment will be performed. Duration of the whole procedure is approx. 4 h. During session Y the sequence of events is Control –hyperglycemia – placebo, again lasting about 4 h. Sessions X and Y are performed in a double blinc fashion with placebo/antioxidant as blinded treatment.

Contacts

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Eligibility criteria

Inclusion criteria

1. Healthy volunteers in the age group of 18 years - 45 years

Exclusion criteria

1. Obesity (BMI > 30)

2. Presence of medical disease (heart-, lung-, liver-, kidney-, neurologic disease; diabetes m.; pyrosis; diaphragmatic hernia)

3. Presence of psychiatric disease

4. History of chronic alcohol or drug use

5. Allergy to study medications

6. Possibility of pregnancy

7. Lactation

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2008
Enrollment:	12
Type:	Anticipated

Ethics review

Positive opinion

Date:	21-03-2008
Application type:	First submission

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
NTR-new	NL1207
NTR-old	NTR1252
Other	CME LUMC : P04.066
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
N/A