Humoral and cellular immune response after influenza vaccination in patients with postcancer fatigue and in patients with the chronic fatigue syndrome.

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By means of this study we would like to answer the following questions:- Differs the humoral or cellular immune response after influenza vaccination between fatigued patients (with PCF or CFS) and non-fatigued patients?- Differs the humoral or...

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

Summary

ID

NL-OMON35062

Source
ToetsingOnline

Brief title
Influenza study PCF and CFS

Condition

- Other condition
- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Fatigue, tiredness

Health condition

Chronisch vermoeidheidssyndroom

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Nederlandse Kankerbestrijding (KWF)

Intervention

Keyword: Chronic fatigue syndrome, Immune response, Influenza vaccination, Postcancer fatigue

Outcome measures

Primary outcome

With every blood collection, hemoglobin level, trombocytes, and the amount and differentiation of leukocytes will be checked. This assessment will take place in the UMC St. Radboud in Nijmegen.

The remaining blood will be analyzed by the TIL (Tumor Immunologisch Laboratorium, associated with the UMC St. Radboud) and by the department of Virology of the UMC St. Radboud in Nijmegen. This analysis will concern the actual immune response to the vaccin. Humoral (antibodies) and cellular (T-cell mediated) reactions to the influenza vaccin will be measured.

The first time blood will be collected, an additional 20 ml of blood will be collected (2,5 ml for BSE, 3 ml for alkaline phosphatase, ALAT, creatine kinase, sodium, potassium, calcium, UK, CRP and iron, 3 ml for bicarbonate, 3 ml for ferritin, 2 ml for glucose, 3.5 ml for TSH and T4V and 3 ml for albumin) to screen for possible alterations in the blood, which could explain the

fatigue complaints, like anemia or hyperthyreoidie.

Secondary outcome

N.v.t.

Study description

Background summary

Fatigue during -but also after- curative cancer treatment is a severe and invalidating problem. The prevalence of fatigue in cancer patients, undergoing chemo- and/or radiotherapy, has been estimated to range from 70-96%. About 20 to 40% of the disease-free cancer patients remain fatigued (at least 1 year). These patients mention fatigue as a frequent complaint, impairing quality of life. Previous disease and treatment characteristics seemed to be unrelated to postcancer fatigue (PCF). However, there is some evidence that patients who are treated with surgery only are less at risk for PCF and survivors who are treated with more aggressive treatments are more at risk for PCF. The existing evidence suggests that cognitive behavior therapy, especially designed for PCF, and a home-based physical activity intervention, are effective treatment options for PCF.
However, although it is possible to effectively treat PCF, the nature of the underlying (neuro)physiology of PCF remains unclear. Several hypotheses about mechanisms explaining cancer-related fatigue have already been described, including dysregulation of brain serotonin, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis responsiveness, disruption of the circadian rhythm, alterations in muscle and ATP metabolism and activation of the vagal afferent nerve. Another possible explanation for PCF is that patients suffering from PCF have a (subtle) disturbance in the cellular and/or humoral immune system. Activation of the immune system, as a response to the tumor or its treatment, leads to the release of cytokines and other immune factors. Cytokines are critical to both the innate and adaptive immune response, but also mediate neural symptoms such as fatigue. Most of these changes in immune parameters resolve following completion of cancer treatment, but it is possible that (subtle) differences in the immune response remain, which could (partly) explain the symptoms of fatigue. In 2007, Schubert et al reviewed the association between cancer-related fatigue and inflammatory marker levels in a quantitative way and a significantly positive correlation between cancer-related fatigue and the levels of inflammatory markers in the circulation was shown. Next to (subtle) differences in cytokines levels between fatigued and non-fatigued cancer survivors, there is also evidence that there are also variations in the prevalence of cytokine producer cells between those two groups.

Another group of patients suffering from severe fatigue symptoms are patients with the chronic fatigue syndrome (CFS). The estimated worldwide prevalence of CFS is 0.4-1%. In the Netherlands, about 100.000 patients are suffering from chronic fatigue, of which 30.000 to 40.000 suffer from CFS. In contrast to fatigue in patients with PCF, in patients with CFS no clear precipitating factor could be identified. CFS is present when patients suffer from severe, persistent or continuously returning complaints of fatigue, which do not improve noteworthy after rest and which are not the consequence of continuous exertion, the fatigue resulted into a substantial decrease in former levels of professional, social and/or personal functioning, the complaints cannot be explained by a physical cause, and the complaints persist for at least 6 months. Also for patients with CFS, a cognitive behaviour therapy is designed, which is proven to be effective, but the pathophysiological mechanism of CFS is unclear. Hypotheses explaining CFS include morphological and metabolic abnormalities in the brain, diminished central activation failure of muscles, a neuroendocrine disturbance, or cognitive impairment caused by response to specific stimuli. Another possible explanation for CFS is altered central nervous system functioning resulting from an abnormal immune response. Studies have sought evidence for a disturbance in immunity in people with CFS: an alteration in cytokine profile, a decreased function of inflammatory markers, a presence of autoantibodies, and a reduced T-cell response to specific antigens have been reported. It is possible that in patients with CFS, (subtle) differences in immune response could (partly) explain the symptoms of fatigue.

There seem to be similarities between patiente suffering from PCF and patients suffering from CFS, but also differences are present between both groups. In comparison to patients with PCF, CFS patients score more problematic with regard to the level of fatigue, functional impairment, physical activity, pain and self-efficacy.
The question is whether PCF and CFS could be explained by the same immunologic pathofysiological mechanism. What have never been done before, is to compare the immune response of patients with PCF and patients with CFS with each other directly. By means of this proposed explorative study, we would like to improve the understanding of the humoral and cellular immune response in patients suffering from PCF and CFS. The most ideal situation to study the immune system is in an activated state, like after vaccination. In this study, the influenza vaccination will be used to activate the immune system.

Study objective

By means of this study we would like to answer the following questions:
- Differs the humoral or cellular immune response after influenza vaccination between fatigued patients (with PCF or CFS) and non-fatigued patients?
- Differs the humoral or cellular immune response after influenza vaccination between patients with PCF and patients with CFS?

Study design

The immune response is the highest after the first vaccination. That's why this study will focus on patients receiving the influenza vaccination in this study for the first time. Patients and controls, who participate in this study and who have no or now for the first time an indication for the influenzavaccination because of their age. Ofcourse, the patients and controls decide by themselves whether they would like to participate in this study or not, and with that also whether they would receive the influenzavaccination or not.

The effect of influenza vaccination on the immune response will be assessed in 20 patients with PCF and in 20 patients with CFS. As a control group for patients with PCF, 20 patients without PCF (but with a cancer history) will participate in the study. Additionally, 20 healthy controls will be asked to participate in the study as a control group without a cancer history and without fatigue symptoms. These four groups will be age- and sex-matched as good as possible.

The study will take place in the UMC St. Radboud in Nijmegen. All patients have been treated in this hospital for cancer (patients with PCF and patients without PCF) or have been referred to the Nijmegen Expert Centre Chronic Fatigue (NKCV; patients with CFS). The healthy controls will be approached by their general practioner. A minimum age of 18 years and a maximum age of 60 years will be maintained. From 2008 on, all people who are at least 60 years of age will be offered influenza vaccination.

Healthy controls who are suitable for this study will be approached by their general practioner, who will explain the study and who will ask whether they would like to receive influenza vaccination or not if they would participate in the study.

Patients who are suitable for this study will be approached by their treatment officer, who will explain the study and who will ask whether they would like to receive the influenza vaccination or not and if they would participate in the study.

In case of approval to participate in the study by the patient and/or the healthy control, an appointment will be made at the policlinic Medical Oncology with the research assistent. Additionally, the general practioner will be informed about the study.

The first appointment (day 1) will take place between the second half of October and the first half of November, because this is the period the national influenza vaccination takes place. Where possible, the appointments will be compared with the routine control apppointments in the UMC St. Radboud. The

patient/healthy control will be ask to bring a list of current used medicines and of the medicines used the former two weeks.

At the policlinic will, after informed consent is signed, 103 ml blood be collected and will the patient/healthy control complete a questionnaire about the current use of medicines and formed vaccinations. Subsequently, the patient/healthy control will receive the influenza vaccination by the research assistent. The patient/healthy control will be asked to contact the research assistent in case of influenza symptoms, in order that the severity and the duration of the complaints can be registered.

Subsequently, on day 8 and day 22 of the study, the patient will visit the policlinic again for blood collection, 83 ml a time, by the research assistent.

The blood collections will be combined as much as possible with the regular blood collections. Further controls of the patients will go by the normal route scheme at the own oncologist.

In april the research assistent will contact the patient/healthy control one more time by phone to check whether a possible infection by influenza had taken place or not the former 6 months.

Patients will receive, if desired, travel expenses.

Study burden and risks

The burden consists mainly out of the time investment in the visits of the UMC. St. Radboud and the collection of blood and the influenza vaccination. At the first day, the vaccination can cause some pain, redness or a light swelling at the place of injection (upper arm). These symptoms will disappear spontaneously after one or two days. The influenza vaccination cannot cause influenza. Complaints like listlessness, headache and fever are infrequent, but can occur the day after injection. When the exclusion criteria will be taken into consideration, no other risks will be associated with participation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

No indication for influenza vaccination

Exclusion criteria

An immune deficiency or an chicken protein allergy

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2010
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Date:	20-08-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL31631.091.10