CURE: Copenhagen Unit for Respiratory Epidemiology

COP:TRIN (**www.coptrin.eu**)

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Calcium supplement for COPD patients – Cardiovascular risk- KALKOL

Protocol

A study from The Copenhagen Unit for Respiratory Epidemiology (CURE) under COPD: Trial Network – COP:TRIN

Background:

Chronic Obstructive Pulmonary Disease is one of the leading chronic diseases worldwide. Many patients with moderate to severe COPD are hospitalized repeatedly every year. Most of the patients are treated with prednisolone for five days during their exacerbation (1). Due to repeated prednisolone treatments, some patients receive calcium supplements to prevent osteoporosis. (2-4) However, what do we really know about the risk of developing cardiovascular disease in COPD patients receiving calcium supplement? The literature is reviewed and there are very sparse data about it.

In 2011, a large randomized placebo controlled trial was published. It included 36,282 post-menopausal women (5). Some women received calcium supplements, while the rest were given a placebo tablet. It was found that the women receiving calcium supplement had an increased risk of cardiovascular disease, especially myocardial infarction (relative risk 1.21, P = 0.04).

In 2010, a meta-analysis was published on the risk of cardiovascular disease in all patients receiving calcium supplements. The following studies were included in the analysis:

- Randomized studies
- Double blinded placebo controlled studies with calcium supplements
- Studies with at least 100 patients
- Studies where the average age was at least 40 years
- Studies where patients were followed for at least 1 year (6).

There were 15 studies in total. The result of this meta-analysis was similar to the last study from 2011. The result was that 296 patients had myocardial infarction (166 receiving calcium and 130

who received placebo) and an increased incidence for myocardial infarction for those who received a calcium supplement (relative risk 1.27, 95% confidence interval 1 , 01 to 1.59, P = 0.038)

It is not known if this applies equally to COPD patients and, if calcium supplements effectively protect against osteoporotic fractures in COPD patients.

Hypothesis:

Patients with chronic obstructive pulmonary disease, who receive calcium supplement, have significantly increased risk for cardiovascular events compared to similar patients, who do not receive this treatment.

Methods:

It is an epidemiological study, where we look at patients with chronic obstructive pulmonary disease that are followed in the secondary sector in Denmark.

Data is obtained by looking at patient register for COPD patients (DrKOL). The prescription register is also used to obtain data about the prescriptions for calcium supplements. Data is also retrieved from the patients' records.
We are looking at cardiovascular events that occur after patients start to take calcium supplements. We will also investigate the accumulated dose of it before the cardiovascular event occurs.

One of the challenges, has been that calcium tablets are not prescribed. You can buy it at the pharmacy (without prescription) and in other stores. The current price at the pharmacy is 0,62 dkk per tablet (Unikalk Mega), whereas in other stores it costs 0,73 dkk per tablet. As there is no price difference between regular stores and the pharmacy, we suppose that patients will buy their calcium tablets at the pharmacy. We have investigated this presumption with a sample of 100 patients. The patients were called up and asked if they took calcium supplements, where they bought it, how long they had taken it and if we could look at their prescribed online medicine.

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Statistics:

1. Descriptive analysis - baseline and demographics
2. Follow-up data
3. Primary endpoint is analyzed with time-updated Cox proportional hazards model and as a "total exposure model" where total exposure is applied

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