Annals of the Rheumatic Diseases

The EULAR Journal

BMJ

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Vitamin K is involved in osteoarthritis

Vitamin K antagonist anticoagulants increase the risk of osteoarthritis progression by inhibiting the vitamin K pathway

INTRODUCTION

Osteoarthritis is a common condition that makes a person's joints stiff and painful, particularly in the morning. It is caused by damage and destruction of the cartilage within the joints, which allows the bones to rub against each other. Joint swelling and pain are frequent symptoms. It is the most common of all the different types of arthritis, and typically becomes more common as people get older.

Vitamin K is important for healthy functioning of proteins in cartilage and bone, two major tissues in joints that are affected in osteoarthritis. For example, a protein called *matrix Gla protein* (MGP) depends on vitamin K to help prevent cartilage calcification.

Some people may need to take anticoagulant drugs to reduce the chance of blood clots. For example, you may be prescribed an anticoagulant if you have a heart condition called atrial fibrillation. Some anticoagulant medicines work by blocking vitamin K. These are called *vitamin K antagonist anticoagulants* – VKA for short. VKAs limit the availability of vitamin K, and affect the proteins that depend on it, such as MGP. Warfarin and acenocoumarol are two common VKA medicines. In the Netherlands, warfarin is not available, so acenocoumarol is the main prescribed VKA.

WHAT DID THE AUTHORS HOPE TO FIND?

The authors wanted to find out whether taking a VKA increases the risk of osteoarthritis developing or worsening. If it does, this would add extra evidence that vitamin K is involved in osteoarthritis.

WHO WAS STUDIED?

This study looked at over 3400 people who were taking part in a large population-based study in the Netherlands. The Rotterdam study examines thousands of people every 5 years to measure aspects of ageing, including osteoarthritis and medication use.

HOW WAS THE STUDY CONDUCTED?

The Rotterdam Study is a prospective longitudinal study. The people taking part are observed over a period of time and measurements taken, but there is no study intervention or medicine being tested.

The authors used some of the information collected to see if people taking the VKA acenocoumarol had an increased risk of osteoarthritis developing or worsening.

WHAT WERE THE MAIN FINDINGS OF THE STUDY?

The main finding was that people taking acenocoumarol were twice as likely to develop osteoarthritis, or have progression of existing osteoarthritis. The risk of progression was four-times higher for people who had a variant in the gene coding for the MGP protein. This adds to the evidence that there is an association between vitamin K and osteoarthritis.

ARE THESE FINDINGS NEW?

Yes. This is the first study to show that inhibition of vitamin K with acenocoumarol is associated with increased development and progression of osteoarthritis.

An accompanying study by Ballal and colleagues compared people using VKA and non-vitamin K inhibiting anti-coagulants, and they also saw an increased risk for osteoarthritis in people taking VKAs.

WHAT ARE THE LIMITATIONS OF THE STUDY?

One limitation is that everyone taking acenocoumarol did so because they had an underlying health condition. It is therefore possible that the effect seen on osteoarthritis is due to the underlying condition, not the VKA use. However, in the accompanying study this bias was examined, and the authors demonstrated that the effect could not be due to confounding by indication. In addition, the genetic finding indicates that there is a real causal relationship between vitamin K and osteoarthritis.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

The authors want to investigate vitamin K supplementation as a possible treatment for osteoarthritis. They also plan to investigate the role of other proteins that depend on vitamin K.

WHAT DOES THIS MEAN FOR ME?

If you have osteoarthritis – or are at high risk of developing osteoarthritis – you should preferable not be treated with acenocoumarol if you need anticoagulation for another health condition. There are other types of anti-coagulant medicines that do not inhibit vitamin K. These are called new or direct oral anti-coagulants (shortened to NOAC/DOAC). If you have been prescribed a VKA, it is very important that you do not stop taking it without medical advice. Talk to your doctor if you have any concerns about your disease or its treatment. Keep in mind that for some heath conditions you can not switch from VKA to NOAC/DOAC.

The results also suggest vitamin K supplementation might be helpful in people with osteoarthritis. This is yet to be investigated in clinical trials, but you could try including foods with more vitamin K as part of a healthy diet. For example, green leafy vegetables such as broccoli or spinach, or fruits as kiwifruit, blueberry, rhubarb, and cereal grains.

FURTHER READING

Ballal P, *et al*. Warfarin use and risk of knee and hip replacements. *Ann Rheum Dis* 2021;80:605–9. doi:10.1136/annrheumdis-2020-219646

Date prepared: April 2021

Summary based on research article published on: 12 April 2021

From: Boer CG, *et al*. Vitamin K antagonist anticoagulant usage is associated with increased incidence and progression of osteoarthritis. *Ann Rheum Dis* 2021;80:598–604. doi:10.1136/annrheumdis-2020-219483