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Is Hydroxychloroquine Beneficial for Hand Osteoarthritis?

Hand osteoarthritis is characterized by inflammation of the joints of the hand. It is a debilitating disease that causes pain and loss of function. The symptoms of this condition reduce the patient's quality of life because routine daily activities, such as writing, cooking and holding objects, become increasingly difficult to complete.

Treatment of hand osteoarthritis primarily consists of pain management with medications such as acetaminophen, ibuprofen, and capsaicin cream. Hydroxychloroquine is a medication regularly used in treating rheumatoid arthritis (inflammation in the joints caused by the immune system attacking the body). There is, however, insufficient data regarding its use in treating hand osteoarthritis.

A research news article published in the *British Medical Journal* reviewed the results of a study conducted by Sarah Kingsbury and her team in the United Kingdom. The goal of the study was to determine the effectiveness of hydroxychloroquine in managing the pain associated with hand osteoarthritis. There were 248 participants recruited from thirteen primary and secondary care centers in England. The participants were randomly placed in either a hydroxychloroquine group (200mg-400mg) or a placebo group. The outcomes measured include hand pain, grip strength, function, and quality of life.

At six months, the researchers did not find a significant difference in hand pain between the two groups. There was also no significant difference in grip strength, function or quality of life. One of the limitations noted in the article is that the hydroxychloroquine dosing calculation used in the study is less than the starting dose recommended in initiating rheumatoid arthritis therapy. A maximum dose of 6.5mg/kg per

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day, as recommended by the British National Formulary, was administered to the participants and most of the patients received 300mg daily.

The results of the study do not support the use of hydroxychloroquine in the treatment of pain due to hand osteoarthritis. The limitations of the study may be contributing factors to the development of this conclusion. More research in the treatment options of hand osteoarthritis will be valuable in improving the quality of life of patients with this health condition.

References:

(1) Wise, J. Hydroxychloroquine should not be used for hand osteoarthritis, say researchers. *BMJ* 2018;360:k774 doi: 10.1136/bmj.k774

(2) Kingsbury SR, Tharmanathan P, Adamson J, et al. Hydroxychloroquine effectiveness in reducing symptoms of hand osteoarthritis (HERO): study protocol for a randomized controlled trial. *Trials*. 2013;14:64. doi:10.1186/1745-6215-14-64.

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Does Canagliflozin Benefit Heart Disease?

Heart disease is an important co-morbidity in diabetes management. Researchers compared the cardiovascular safety data of canagliflozin with three other antidiabetic drug classes.

A new class of antidiabetic medications called sodium glucose co-transporter 2 inhibitors has shown cardiovascular benefits in patients with type 2 diabetes. This drug class works by blocking the re-absorption of glucose in the kidneys, thereby reducing blood glucose levels. Medications in this class include canagliflozin, dapagliflozin, and empagliflozin. Although maintaining glucose levels within an appropriate range is important in reducing the risk of developing complications, intensive glucose lowering and the use of certain antidiabetics have been associated with negative heart health outcomes.

An American study recently published in *The British Medical Journal* evaluated the cardiovascular safety outcomes of canagliflozin in comparison to DPP-4 inhibitors, GPL-1 agonists, and sulfonylureas. This population-based retrospective cohort study comprised of data collected from a healthcare database in the United States between April 2013 and September 2015. The study participants were adults with a type 2 diabetes diagnosis and had been started on canagliflozin, a DPP-4 inhibitor, GPL-1 agonist, or a sulfonylurea within the 30-month study period. The main outcomes measured were hospital admissions for heart failure and other measures of heart health including hospital admission for acute myocardial infarction, ischemic stroke, or hemorrhagic stroke.

Canagliflozin Lowered the Risk of Heart Failure

The results of the study showed that the participants who were on canagliflozin had a 30% to 49% lower risk of developing heart failure and had fewer hospital admissions for heart failure than the participants on the other antidiabetic medications. There was no significant difference in the risk of hospital admission for acute myocardial infarction, ischemic stroke, or hemorrhagic stroke among the four drug classes.

The study demonstrates the beneficial effects of canagliflozin on hospital admissions due to heart failure. It also notes that the potential benefits of this medication can be observed within the first six

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months of therapy. This study demonstrates the importance of this class of medications in managing cardiovascular outcomes in patients diagnosed with diabetes.

Reference: Patorno, E et al. Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population-based cohort study. *BMJ* 2018;360:k119

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Does Vitamin D Affect Cardiovascular Risk Factors in Young Women?

Researchers reviewed data on the possible relationship between vitamin D levels, cholesterol levels, body composition, and blood pressure in young women.

Vitamin D is an important vitamin known mostly for its work with calcium in maintaining bone health. Vitamin D is also involved in other processes in the body such as immune function, muscle function, and inflammation reduction. It is known as the sunshine vitamin because it is produced in the body when the skin is exposed to the sun. Vitamin D can also be obtained from a few food sources and supplements.

Previous research has shown that high levels of vitamin D in the body is associated with high levels of high-density lipoprotein cholesterol (HDL or "good" cholesterol) and low levels of low-density lipoprotein cholesterol (LDL or "bad" cholesterol). HDL, LDL, and triglycerides are types of cholesterol found in the body. Low levels of LDL, triglycerides and high levels of HDL are necessary for good health and reduce cardiovascular risk.

Body composition includes measurement of abdominal visceral fat, total fat mass and body fat percentage. Visceral fat is found around the internal organs and affects cholesterol and sugar levels in the body.

An Australian study recently published in the *European Journal of Clinical Nutrition* reviewed the association between vitamin D, body composition, cholesterol levels, and blood pressure in young women. There were 557 women included in the study who were between the ages of 16 and 25 years and lived in Victoria, Australia.

The results show that an increase of 10 nmol/L in 25 OHD levels (a measure of Vitamin D in the blood) was associated with a slight increase in HDL (0.65%) and triglyceride (0.92%) levels. This increase in Vitamin D levels was also associated with a reduction in body mass index (0.48%), lower fat percentage (0.5%), and lower visceral fat percentage (0.14%). There was no significant difference observed in blood

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pressure readings. The results of this study cannot be applied to the rest of the population, as only women within a small age range were included in the study.

Due to the small differences observed in the results of the study, more research is required to determine the clinical significance of these findings. The results of the study are not sufficient to conclude on an association between vitamin D levels and cardiovascular risk in young women. Vitamin D continues to play a vital role in the body and it is essential we ensure we meet the recommended daily intake through appropriate sun exposure, food, and supplements.

References:

(1) Tabesh M et al. Associations between 25-hydroxyvitamin D levels, body composition, and metabolic profiles in young women. 2018. European Journal of Clinical Nutrition. doi.org/10.1038/s41430-018-0086-1

(2) National Institutes of Health Office of Dietary Supplements. https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional. Accessed January 31, 2018

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Which Oral Contraceptive is Better: Monthly Cycle or Extended Cycle?

A recent study in the United States compared the benefits experienced by women using two different forms of combined oral contraceptive pills.

The introduction of combined oral contraceptive pills in the sixties provided couples with a new option to consider in family planning and gave women greater flexibility in making life choices. Oral contraceptives supply daily doses of hormones to the body. Some provide a medication-free week to allow bleeding similar to menstruation. Monthly-cycle combined oral contraceptives induce this bleeding every month. Extended-cycle combined oral contraceptives reduce the bleeding to four times a year (every three months) or less. Some studies have shown that women in the United States and Europe would rather have fewer bleeding episodes in a year.

In a study recently published in *BMC Women's Health*, researchers analyzed data from the 2013 National Health and Wellness Survey to compare the benefits of two different forms of combined oral contraceptive pills. This survey is conducted in several countries, but the study focused on participants from the United States.

For the study, they compared women using extended-cycle oral contraceptive pills with women who use monthly-cycle combined oral contraceptive pills. Premenopausal women between the ages of 18 and 50 years, without a hysterectomy and currently on a combined oral contraceptive were chosen for the analysis. Of the 3,876 women surveyed, 260 women used extended-cycle combined oral contraceptive pills while 3,616 women used monthly-cycle combined oral contraceptive pills. The outcomes measured include menstrual-cycle related symptoms such as menstrual pain and heavy bleeding, medication satisfaction, and medication adherence.

The results show that the women on extended-cycle combined oral contraceptive pills were more satisfied with their medication and more adherent to their regimen. These participants also had fewer reports of heavy bleeding. Incidents of bloating, irritability, and tiredness were more common in participants on extended oral contraceptives.

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The analysis performed did not consider the different types of hormones available in different brands of these medications. This could be an important factor in determining if the results obtained are the effect of a drug class. The study supports the use of extended-cycle combined oral contraceptive pills in women of reproductive age. This regimen provides fewer bleeding episodes and is a more convenient and preferred option for a lot of women.

Reference: Nappi R.E et al. Real-world experience of women using extended-cycle vs monthly-cycle combined oral contraception in the United States: the National Health and Wellness Survey. BMC Women's Health (2018) 18:22 DOI 10.1186/s12905-017-0508-6

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Prostate Cancer: Can Metformin Reduce Your Risk?

Researchers conducted a review of 26 studies to determine the possible effects of metformin and ethnicity on the risk of prostate cancer.

Data shows that type 2 diabetes carries an increased risk in the development of some cancers. Diabetes and cancer share some similarities in pathophysiology. Insulin resistance occurs when the body is unable to properly use the insulin produced by the pancreas. This causes the pancreas to increase production, leading to hyperinsulinemia (excess insulin in the blood). Hyperinsulinemia is hypothesized to increase the risk of developing certain cancers.

Metformin is a common medication used in the management of type 2 diabetes. There is significant interest in its potential benefits in cancer risk reduction and treatment. Ethnicity might play a role in the effect of metformin on cancer management, with some studies indicating that the risk of prostate cancer may be reduced only in Asian participants.

Jeffrey Johnson and his team in Alberta, Canada recently published a systematic review in *BMC Cancer* analyzing the association between metformin, ethnicity, and the risk of prostate cancer. They searched several databases and chose 26 studies for the review. There were 23 studies with a Western-based population (Europe and North America) and three studies with an Asian based population (mainly participants from Taiwan). There were 1,171,643 Western-based participants and 400,664 Asian based participants included in the review. The results did not show a significant decrease in the risk of prostate cancer in either the Western- or the Asian based groups.

The review was limited by the absence of individual data for each participant. This is an issue because the studies were classified based on the origin of the database, but the studies potentially included people of different ethnicities. The studies selected for the review had varying definitions for metformin exposure. While some studies defined exposure as presence or absence of metformin in the participant's medication regimen, other studies made a comparison with another medication or diet.

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While this review indicates there is likely no correlation between metformin and the risk of developing prostate cancer, the limitations noted above suggest more research is required in this area.

Reference: Chen, C.B et al. Metformin, Asian ethnicity and risk of prostate cancer in type 2 diabetes: a systematic review and meta-analysis. BMC Cancer (2018) 18:65 DOI 10.1186/s12885-017-3934-9

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