INTERNATIONAL MULTIDISCIPLINARY JOURNAL FOR RESEARCH & DEVELOPMENT
SJIF 2019: 5.222 2020: 5.552 2021: 5.637 2022:5.479 2023:6.563
eISSN 2394-6334 https://www.ijmrd.in/index.php/imjrd Volume 10, issue 12 (2023)

POSITIVE AND NEGATIVE CONSEQUENCES OF THE DRUG ASPIRIN

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Annotation: You can walk into any pharmacy, grocery or convenience store and buy aspirin without a prescription. The *Drug Facts* label on medication products, will help you choose aspirin for relieving headache, pain, swelling, or fever. The *Drug Facts* label also gives directions that will help you use the aspirin so that it is safe and effective.

Key words: Drug, aspirine, heard, blood.

But what about using aspirin for a different use, time period, or in a manner that is not listed on the label? For example, using aspirin to lower the risk of heart attack and clot-related strokes. In these cases, the labeling information is not there to help you with how to choose and how to use the medicine safely. Since you don't have the labeling directions to help you, you need the medical knowledge of your doctor, nurse practitioner or other health professional.

You can increase the chance of getting the good effects and decrease the chance of getting the bad effects of any medicine by choosing and using it wisely. When it comes to using aspirin to lower the risk of heart attack and stroke, choosing and using wisely means: Know the facts and work with your health professional.

Aspirin has been shown to be helpful when used daily to lower the risk of heart attack, clot-related strokes and other blood flow problems in patients who have cardiovascular disease or who have already had a heart attack or stroke. Many medical professionals prescribe aspirin for these uses. There may be a benefit to daily aspirin use for you if you have some kind of heart or blood vessel disease, or if you have evidence of poor blood flow to the brain. However, the risks of long-term aspirin use may be greater than the benefits if there are no signs of, or risk factors for heart or blood vessel disease.

Every prescription and over-the-counter medicine has benefits and risks — even such a common and familiar medicine as aspirin. Aspirin use can result in serious side effects, such as stomach bleeding, bleeding in the brain, and kidney failure. No medicine is completely safe. By carefully reviewing many different factors, your health professional can help you make the best choice for you.

Before deciding if daily aspirin use is right for you, your health professional will need to consider:

- Your medical history and the history of your family members
- Your use of other medicines, including prescription and over-the-counter
- Your use of other products, such as dietary supplements, including vitamins and herbals
- Your allergies or sensitivities, and anything that affects your ability to use the medicine
- What you have to gain, or the benefits, from the use of the medicine
- Other options and their risks and benefits

- What side effects you may experience
- What dose, and what directions for use are best for you
- How to know when the medicine is working or not working for this use

If you are at risk for heart attack or stroke your doctor may prescribe aspirin to increase blood flow to the heart and brain. But any drug — including aspirin — can have harmful side effects, especially when mixed with other products. In fact, the chance of side effects increases with each new product you use.

New products include prescription and other over-the-counter medicines, dietary supplements (including vitamins and herbals), and sometimes foods and beverages. For instance, people who already use a prescribed medication to thin the blood should not use aspirin unless recommended by a health professional. There are also dietary supplements known to thin the blood. Using aspirin with alcohol or with another product that also contains aspirin, such as a cough-sinus drug, can increase the chance of side effects.

Your health professional will consider your current state of health. Some medical conditions, such as pregnancy, uncontrolled high blood pressure, bleeding disorders, asthma, peptic (stomach) ulcers, liver and kidney disease, could make aspirin a bad choice for you.

There are no directions on the label for using aspirin to reduce the risk of heart attack or clot-related stroke. You may rely on your health professional to provide the correct information on dose and directions for use. Using aspirin correctly gives you the best chance of getting the greatest benefits with the fewest unwanted side effects. Discuss with your health professional the different forms of aspirin products that might be best suited for you.

Aspirin has been shown to lower the risk of heart attack and stroke in patients who have cardiovascular disease or who have already had a heart attack or stroke, but not all over-the-counter pain and fever reducers do that. Even though the directions on the aspirin label do not apply to this use of aspirin, you still need to read the label to confirm that the product you buy and use contains aspirin at the correct dose. Check the *Drug Facts* label for "active ingredients: aspirin" or "acetylsalicylic acid" at the dose that your health professional has prescribed.

Remember, if you are using aspirin everyday for weeks, months or years to prevent a heart attack, stroke, or for any use not listed on the label — without the guidance from your health professional — you could be doing your body more harm than good.

Aspirin’s second-best known effect is its ability to protect the heart. In people with heart disease who have already had a heart attack, it has been shown to lower the risk of having another. Studies consistently show that people who have had heart attacks or strokes and who take a low-dose aspirin (also known as baby aspirin, which at 81 mg is about a quarter of the dose of regular-strength aspirin) a day can significantly reduce their risk of having another event.

Its protective benefits come from aspirin’s ability to lower inflammation, a condition that can attract clot-building factors within blood vessel walls. These can rupture, plugging up tiny vessels in the heart and blocking blood flow.

Doctors now believe that taking a daily low-dose aspirin is also a cheap and easy way for people who do not yet have heart disease — but who have certain risk factors for it, including high cholesterol and obesity — to avoid first heart attacks. The U.S. Preventive Services Task Force (USPSTF), a government-appointed group of independent experts, recommends the regimen for people ages 50 to 59 who fall into this category. For them, the group concludes, the benefits of aspirin outweigh the potential risks of the drug, which include gastrointestinal bleeding.

In older people, however, that risk-benefit balance tips the other way. In a recent study published in the *New England Journal of Medicine*, scientists found that in a group of more than 19,000 people ages 65 years and older, taking daily aspirin for nearly five years did not significantly lower their risk of having heart problems, but did increase their chances of having bleeding issues by 38% compared to people who did not take a low-dose aspirin daily. For this group, the over-the-counter pill seems to come with more risks and little benefit when it comes to the heart. For years, doctors have been enthused about aspirin's potential to lower the risk of certain cancers. Researchers noticed that people in heart studies who took daily aspirin not only had a lower risk of heart problems, but also had fewer cases of colon cancer compared to people who didn't take aspirin. In 2016, after reviewing the available evidence, the USPSTF also recommended that most people ages 50 to 59 years take low-dose aspirin daily to lower their risk of developing colon cancer. As with heart disease, aspirin seems to produce this benefit by lowering inflammation, which can contribute to tumors in the colon.

This year, two separate studies, both published in *JAMA Oncology*, found that people who popped aspirin regularly tended to have lower rates of ovarian and liver cancers. It's not yet clear what dose is best or how frequently people should be taking the drug to expect a cancer-lowering effect, but these results expand the list of potential cancers that aspirin may affect.

Researchers are actively exploring why aspirin might work on a range of cancers. "As we learn about inflammatory-related diseases that impact aging — including cancer and heart disease — we are increasingly finding that aspirin can impact those processes on a much more global level on many, many parts of the body," says Dr. Tracey Simon, clinical research fellow in gastroenterology at Massachusetts General Hospital, and an author of the liver cancer study. "The important part is to find out why. The full potential of aspirin won't be realized until we understand those mechanisms that are driving risk reduction in other tissues outside of the colon and the heart."

They have some ideas. Like cancer in the colon, liver cancer is driven in large part by inflammation, which can be triggered by changes in the DNA. Aspirin controls inflammatory reactions by tamping down the activity of certain enzymes, called COX1 and COX2. In Simon's study, which involved more than 170,000 people in the Nurses' Health Study and the Health Professionals Follow-Up Study, people who said they took the equivalent of two or more regular-strength aspirin (325 mg) a week for five years lowered their risk of developing liver cancer by 59% compared to people who did not take aspirin. The effect waned if people stopped taking the drug after about eight

years. But other painkillers, such as acetaminophen and nonsteroidal anti-inflammatory drugs like ibuprofen, which work in slightly different ways than aspirin does, did not impact the risk of liver cancer.

In the ovarian cancer study, Shelley Tworoger, associate director of population science at Moffitt Cancer Center, and her colleagues also analyzed data from the Nurses' Health Study. Among more than 205,000 women who were followed from the 1980s to the 2010s, they found that women who took low-dose aspirin lowered their risk of developing ovarian cancer by 23%, compared to women who did not use the drugs. But standard-dose aspirin did not have an effect on ovarian cancer risk, and neither did longer term use of low-dose aspirin.

It's not entirely clear why the two doses have differing effects on the two cancers. But in the case of ovarian cancer, the difference can likely be explained by how the two doses work, says Tworoger. Higher dose aspirin tends to suppress the effects of both COX-1 and COX-2 enzymes that contribute to inflammation, while low-dose aspirin tends to inhibit mainly COX-1. It's also possible that people taking low-dose aspirin, who usually do so to prevent heart problems, take the drug more regularly than those who take the occasional full dose pills or tablets. "It may be that consistent reduction of inflammation is most important," she says.

In the case of liver cancer, the data suggest that the consistent anti-inflammatory effect may also be contributing to a lower risk of cancer; most of the people in the study, says Simon, took low-dose aspirin daily, which equals about two full dose tablets a week. "It does seem like just taking 81 mg a day would be sufficient to give people a risk reduction," she says.

Other data suggest that aspirin may be working in many different ways to lower liver cancer risk. In addition to suppressing inflammation, it could also be reducing the amount of fibrosis that can contribute to out-of-control growth, says Simon. And aspirin might also be affecting the formation of micro-clots that can affect liver disease as well.

But with liver cancer in particular, there is a fine line between enough aspirin for its anti-inflammatory benefit, and the side effect of stomach and gastrointestinal bleeding. People with liver disease are already at high risk of bleeding, and taking too much aspirin could elevate that risk. "We tried to find the lowest acceptable dose that would potentially offer meaningful benefit," Simon says.

For that reason, it's too early to advise people who might be at risk of developing liver cancer, or people with cirrhosis, who are at higher risk of the cancer, to start popping baby aspirin. But the results raise hope that with more research, aspirin could become a part of a liver cancer prevention program, says Simon.

If her results are confirmed, researchers could start exploring ways that aspirin may be used early in the disease to slow or even prevent liver tumors from forming.

How aspirin affects diabetes

People with type-1 and type-2 diabetes are two to three times more likely to have a vascular event like stroke or heart problems than those without the disease. Because of the close relationship between heart disease and diabetes, doctors have studied whether people with diabetes should consider taking aspirin to lower their risk of heart events. The American Diabetes Association recommends that among people with type-1 or type-2 diabetes, only those who also have other risk factors that make them more vulnerable to developing heart problems — such as people who are 50 and older and who have high blood pressure, high cholesterol or are smokers — should consider taking a low-dose aspirin every day to lower their risk of heart problems. Younger people with diabetes, or those who don't have additional risk factors for heart events, may not benefit from aspirin, since the risk of bleeding may outweigh benefits.

That finding was supported by a recent study published in the *New England Journal of Medicine*, which analyzed more than 15,000 people over nearly eight years and found that those taking 100 mg of aspirin a day lowered their risk of having a vascular event by 12% — but increased their risk of gastrointestinal bleeding by 29% — compared to people taking the placebo.

How aspirin affects the brain

Inflammation drives many chronic diseases — especially those associated with aging, such as arthritis, heart disease and even degenerative brain conditions like dementia and Alzheimer's. Researchers have been investigating whether aspirin's anti-inflammatory effects can slow down cognitive decline as well.

The results have been mixed. In one study, women with type-2 diabetes and dementia who took low-dose aspirin every day for nearly 10 years lowered their risk of dementia by 60% compared to those who didn't take aspirin, but men did not have the same benefit. And in a review of existing studies of aspirin and cognitive decline, scientists in Italy found no evidence that the over-the-counter drug provides any benefit.

Because inflammation contributes to so many aging-related diseases, and because aspirin can lower inflammation, scientists have also been studying whether people who take aspirin tend to live longer overall. They might be spared some of the chronic diseases that claim so many lives, the thinking goes.

But according to two studies published in the *New England Journal of Medicine*, that may not be the case. Using a large data set of people in Australia and the U.S. of people aged 65 years or older, the researchers found that people taking 100 mg of aspirin every

day did not have lower rates of disability than people who were taking placebo. But they did have higher rates of gastrointestinal bleeding; in fact, the aspirin group was more likely to die during the study's nearly five years than people who did not take aspirin. Another study analyzing the same data set found that people assigned to take 100 mg of aspirin a day for nearly four years were more likely to die of a variety of causes during the trial than those taking a placebo.

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