

Side Effects of Over-the-Counter Drugs

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Primum non nocere.

Every doctor has learned the Hippocratic Oath, the most well-known and most important ethical rule in medicine: "Above all, do no harm." This is the physician's first rule: a treatment prescribed to a patient must not harm the patient. It does not say harm should be relative, although that is how the rule is interpreted. It does make the point that the harm, ideally, should be as little as is humanly possible. Paracelsus wrote, *Sola dosis facit venenum*—too much of anything will hurt you. For centuries, this has precipitated the question, How much is too much?

Any discussion of side effects or of toxic reactions without specifying the doses is meaningless, for at zero levels nothing is toxic and at sufficiently high levels everything is toxic, including oxygen and water. Critics of optimum (often high) doses of vitamins generally talk about toxic reactions without any reference to the doses being used. They report that vitamins "may" be toxic. Note they do not write "are" harmful because the word "may" is a very useful term; it has little meaning but can be used to appear to be very scientific. How often have we seen screaming headlines "Vitamin C May be Harmful" or "May Cause Cancer?" One of the well entrenched fictions is that vitamin C "may" cause kidney stones. This is not based on fact. There are no reports in the literature which prove that this is true, yet there are many good studies that show that it is not true. Nevertheless, the statement has developed a life of its own which is not anchored by any observation of facts. Yes, it "may" cause kidney stones if the word "may" is allowable when the odds that this will happen are less than one million to one. Millions of people take vitamin C. So far not one finding has established that vitamin C causes kidney

stones. So in discussing side effects and toxicity we must always use the simplest, most accurate language possible referring to the doses being discussed.

In this review, I will report the side effects of a few very common over-the-counter drugs. They are freely available in drug stores and some in department stores. These compounds are analgesics, anti-histamines, and anti-inflammatory drugs. I will not discuss the efficacy of these compounds. I accept that they have value or they would not be in common use and I also use them occasionally. This discussion focuses on potential side effects and toxicity; it is not about efficacy. The information comes from the medical literature and from the drug companies.

Comparing Side Effects of OTC Drugs and Vitamins

A comparison of the side effects of vitamins to those of over-the-counter drugs will provide the reader with an estimate of the degree of safety associated with vitamins. Vitamins should not be compared against prescription drugs since all drugs have side effects and toxic effects, even within the recommended dose ranges. That is why they are controlled by prescription and drug stores. The Compendiums are huge, larger than telephone books, with hundreds of pages devoted to these reactions, to side effects, to toxic reactions, to contraindications. These long descriptions, usually in small print, scare most patients and many doctors as well. Some of the side effects seem exaggerated since it is seldom indicated how often they occur. On the other hand, the toxic reactions ascribed to placebo are exaggerated because they are listed but not defined. Thus nausea caused by a drug is usually much more severe than nausea caused by a placebo and the placebo reaction is usually

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short lived. If 10% of the placebo group and 12% of the drug group complain of nausea, it does not mean that the drug is not much worse than placebo. It may well be that the drug induced nausea is much more severe and debilitating. The intensity of all the side effects should be, but is not, recorded.

The best protection patients can have is to keep in close touch with the doctor who prescribed the medication. At the first indication of any adverse reaction they should contact their doctor. Xenobiotics (substances foreign to the body) interfere with reactions in the body and often suppress some reactions, but because they are foreign they must be converted to less toxic substances and then excreted. If excretion is too slow the drug and its metabolic products will build up in the body. This is the reason they cause toxic reactions and also why energy is used to eliminate them, energy that might be better used for the normal reactions in the body. Nutrients on the other hand do not interfere. Vitamins enhance reactions that are inhibited. Larger doses force reactions that have been retarded by other factors.

Over-the-counter drugs are considered much safer than prescription drugs. That is why they are more freely available. Some over-the-counter drugs were first issued as prescription items and later were allowed to be sold over-the-counter. Some products such as aspirin and niacin are both prescription and OTC. Folic acid which once was OTC in 25 mg tablets is now available by prescription in 5 mg tablets; the OTC tablets now contain 800 mcg.

I have selected five very popular OTC drugs and will discuss the side effects and toxicity patterns of these five, not because I disapprove of them but to illustrate what is considered acceptable for OTC drugs.

Acetylsalicylic Acid, also called Aspirin

Aspirin is the most popular OTC drug and most often recommended by doctors. It is also available on prescription, which is an advantage for patients who have drug

plans. There is even an Aspirin Foundation, established in 1981, which extols the efficacy of this drug. It is effective in dealing with heart disease, for arthritis, perhaps inhibiting colon cancer, and for headaches. Here are some of the official warnings that are listed for aspirin.¹

Fluid and electrolyte effects: Increased metabolic rate, pyrexia, tachypnea, and vomiting lead to fluid loss and dehydration. Compensation for respiratory alkalosis leads to increased renal excretion of bicarbonate and increased excretion of sodium and potassium. Because of significant water losses, hyponatremia might not be present; however, hypokalemia is prominent.

Central nervous system effects: Toxic effects in the CNS range from mild confusion to coma. The exact mechanism that produces CNS toxicity is not known, but the degree of CNS effects, as well as overall mortality, correlates with the concentration of salicylates in brain tissue. Acidemia increases the non-ionized form of salicylates, allowing for movement across the blood-brain barrier and, therefore, increasing CNS toxicity.

Gastrointestinal effects: Salicylate ingestion can cause nausea, vomiting, and abdominal pain. Emesis is produced by salicylate stimulation of medullary chemoreceptors and by local irritation of the GI tract. Upper GI ulceration and bleeding can occur. Gastrointestinal effects are much more prominent in acute ingestion.

Ototoxicity: Salicylate toxicity results in a reversible ototoxicity characterized by tinnitus, deafness, and dizziness.

Pulmonary effects: Non-cardiogenic pulmonary edema is the most common cause of major morbidity and might be related to an increase in permeability of pulmonary vasculature caused by salicylates. Acute respiratory distress syndrome (ARDS) is more prominent in chronic ingestions than in acute ingestions.

Hematological effects: Salicylates in-

hibit vitamin K-dependent synthesis of factors II, VII, IX, and X, leading to a prolonged prothrombin time (PT). Salicylates prolong bleeding time by inhibiting a prostaglandin-initiated sequence required for platelet aggregation.

Hepatic effects: Dose-dependent hepatotoxicity can occur with salicylate poisoning. A small percentage of patients might develop hepatitis, but the majority will have asymptomatic elevation of transaminases.

Renal effects: Acute renal failure has been reported rarely.

Mortality/Morbidity: Mortality rates vary with chronicity of exposure. Chronic toxicity carries a higher morbidity and mortality rate than acute toxicity and is more difficult to treat.

Acute overdose: Mortality rate of less than 2%

Chronic overdose: Mortality rate as high as 25%

Azer et al.² used more than 11 pages of printed material to describe the toxicity of aspirin including treatment information and medical care. The *British Medical Journal*,³ promotes a new elixir of youth called polypill. One of the six ingredients is aspirin.

Ranitidine, also called Zantac

Its use is described as follows: "Zantac is prescribed for the short-term treatment (4 to 8 weeks) of active duodenal ulcer and active benign gastric ulcer, and as maintenance therapy for gastric or duodenal ulcer, at a reduced dosage, after the ulcer has healed. It is also used for the treatment of conditions in which the stomach produces too much acid, such as Zollinger-Ellison syndrome and systemic mastocytosis, for gastroesophageal reflux disease (backflow of acid stomach contents) and for healing- and maintaining healing of-erosive esophagitis (severe inflammation of the esophagus)." As I have written earlier, close contact with one's doctor is the best safeguard. More common side effects include: headache, sometimes severe. Less common

and rare side effects include: abdominal discomfort and pain, agitation, changes in blood count (anemia), changes in liver function, constipation, depression, diarrhea, difficulty sleeping, dizziness, hair loss, hallucinations, heart block, hepatitis, hypersensitivity reactions, inflamed blood vessels, inflammation of the pancreas, involuntary movements, irregular heartbeat, jaundice (yellowing of eyes and skin), joint pain, muscle pain, nausea and vomiting, rapid heartbeat, rash, reduced white blood cells, reversible mental confusion, severe allergic reactions, sleepiness, slow heartbeat, swollen face and throat, vague feeling of bodily discomfort, vertigo.

The following special warnings are listed: a stomach malignancy could be present, even if your symptoms have been relieved by Zantac. If you have kidney or liver disease, this drug should be used with caution. If you have phenylketonuria, you should be aware that the "Efferdose" tablets and granules contain phenylalanine.

Here are more possible food and drug interactions when taking this medication: If Zantac is taken with certain other drugs, the effects of either could be increased, decreased, or altered. It is especially important to check with your doctor before combining Zantac with the following: Alcohol, Blood-thinning drugs such as Coumadin, Diazepam (Valium), Diltiazem (Cardizem), Glyburide (DiaBeta, Micronase), Ketoconazole (Nizoral), Metformin (Glucophage), Nifedipine (Procardia), Phenytoin (Dilantin), Theophylline (Theo-Dur), Triazolam (Halcion) and several others I have omitted.

Ibuprofen, also called Motrin

Ibuprofen is another very popular OTC drug. Here is how it is described: It is a non-steroidal, anti-inflammatory drug available in both prescription and nonprescription forms. Prescription Motrin is used in adults for relief of the symptoms of rheumatoid arthritis and osteoarthritis, treatment of

menstrual pain, and relief of mild to moderate pain. In children aged 6 months and older it can be given to reduce fever and relieve mild to moderate pain. It is also used to relieve the symptoms of juvenile arthritis.

Common side effects may include: Abdominal cramps or pain, abdominal discomfort, bloating and gas, constipation, diarrhea, dizziness, fluid retention and swelling, headache, heartburn, indigestion, itching, loss of appetite, nausea, nervousness, rash, ringing in ears, stomach pain, vomiting. Less common or rare side effects may include: Abdominal bleeding, anemia, black stool, blood in urine, blurred vision, changes in heart beat, chills, confusion, congestive heart failure, depression, dry eyes and mouth, emotional volatility, fever, hair loss, hearing loss, hepatitis, high or low blood pressure, hives, inability to sleep, inflammation of nose, inflammation of the pancreas or stomach, kidney or liver failure, severe allergic reactions, shortness of breath, skin eruptions or peeling, sleepiness, stomach or upper intestinal ulcer, ulcer of gums, vision loss, vomiting blood, wheezing, yellow eyes and skin.

Special warnings about this medication: Peptic ulcers and bleeding can occur without warning. Tell your doctor if you have bleeding or any other problems. This drug should be used with caution if you have kidney or liver disease, or are severely dehydrated; it can cause liver or kidney inflammation or other problems in some people.

Do not take aspirin or any other anti-inflammatory medications while taking Motrin unless your doctor tells you to do so. If you have a severe allergic reaction, seek medical help immediately. Motrin may cause vision problems. If you experience any changes in your vision, inform your doctor. Motrin may prolong bleeding time. If you are taking blood-thinning medication, this drug should be taken with caution. This drug can cause water retention. It should be used with caution if you have

high blood pressure or poor heart function. Avoid the use of alcohol while taking this medication.

Motrin may mask the usual signs of infection or other diseases. Use with care in the presence of an existing infection.

Advice about taking it (and indeed any other OTC analgesic) should always be sought from a pharmacist. Individuals who should be especially cautious are:

- Pregnant women
- Nursing mothers
- The elderly
- Those suffering from asthma
- Individuals who have suffered from gastric ulcers or gastric bleeds in the past
- Those with bleeding disorders
- Those who suffer from allergies

As with all painkillers, if symptoms persist for more than three days, you should consult your doctor.

Acetaminophen, also called Tylenol

Acetaminophen is primarily metabolized by the liver. Too much acetaminophen can overwhelm the way the liver normally functions.⁴ If the liver is already damaged because of infection, alcohol abuse, or other illness, you may be more susceptible to damage from acetaminophen overdose. For this reason, people with liver illnesses or who chronically consume large amounts of alcohol should be particularly careful when taking acetaminophen and should consult their doctor prior to taking acetaminophen compounds.

Long-term use of acetaminophen in recommended doses has not been shown to be harmful to the liver, even when combined with moderate alcohol consumption.

There are no immediate symptoms from taking a toxic amount. You may remain symptom free for up to 24 hours after taking a toxic overdose of acetaminophen. After this initial period, the following symptoms are common: Nausea, vomiting, not feeling well, not able to eat or poor appetite, abdominal pain.

Tylenol can cause kidney damage,

which can be lethal if there is underlying kidney damage. Dosages exceeding 10-15 g daily are toxic and 25 g can be immediately fatal. Symptoms include jaundice and pain in upper abdomen, hypoglycemia, encephalopathy, kidney failure and analgesic rebound.

Loratadine, also called Claritin

This popular anti-histamine is used to relieve hay fever and allergy symptoms such as sneezing, runny nose, red, itchy, tearing eyes. It causes less drowsiness than other anti-histamines. Generally anti-histamines are among the safest OTC compounds but even with this good safety record, some of the side effects and warnings include: headache, dry mouth, nose and throat, drowsiness, rapid heartbeat, difficulty urinating, vision problems, dizziness and muscle weakness. If these occur you are warned to call your doctor immediately.

Before you take it tell your doctor and pharmacist what else you are taking, if you have ever had kidney or liver disease, if you are pregnant or breast feeding, if you plan to have surgery, and avoid prolonged exposure to sunlight.

Summary

These are the side effects, toxic reactions, contraindications and warnings that have to be studied before taking any of these five very popular OTC drugs. None of the vitamins have side effects and toxic reactions remotely similar to this. It is clear that drugs allowed to be sold over-the-counter have to be used with caution because they are xenobiotic and within the recommended dose range can be, and often are, harmful. This cannot be said about the vitamins. Within the recommended doses vitamins are safe. The fat soluble vitamins can accumulate in the body but the effects are reversible.

A survey in the United States showed that in one year 106,000 patients died from the proper use of medication in hospital.

Over the past three decades there have been no deaths from the proper use of vitamins.

References

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