Antidepressants

When you first hear the name antidepressant you may think of a medicine used to treat depression. Did you know that antidepressants are also effective in treating symptoms of IC?

Antidepressants are a standard treatment for many chronic pain conditions, including IC. Some antidepressants also reduce symptoms of urinary urgency and frequency. In addition to treating your IC, your healthcare provider may prescribe an antidepressant for other health problems such as fibromyalgia, irritable bowel syndrome, depression and anxiety, or attention deficit/hyperactivity disorder (ADHD). Some doctors also prescribe antidepressants to help cigarette smokers quit.

Types of Antidepressants

There are several main types, or classes, of antidepressants. Researchers also continue to study and create new antidepressants and variations of existing antidepressants that do not fit into any of these classes. Antidepressant classes include, but are not limited to:

- Tricyclic antidepressants (TCAs)
- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin and norepinephrine reuptake inhibitors (SNRIs)
- Noradrenaline reuptake inhibitors (NRIs)
- Monoamine oxidase inhibitors (MAOIs) and reversible inhibitors of monoamine oxidase type-A (RIMAs)

Tricyclic antidepressants (TCAs) are a proven treatment for IC. The pain-relieving effects of TCAs are distinct from any effect on mood. The dosage is much lower than when treating depression and the speed of onset is much faster.

Newer types of antidepressants (SSRIs, SNRIs, and NRIs) selectively work on specific brain chemicals — messengers in the central nervous system (serotonin, norepinephrine, acetylcholine, and/or dopamine, for instance). They selectively block the reuptake of these brain chemicals (more so than the TCAs) so that your body has access to more of the specific chemical(s).

They do not make your body actually produce more of these brain chemicals.

Reversible inhibitors of monoamine oxidase type-A (RIMAs) are a newer subtype of one of the oldest antidepressant classes, monoamine oxidase inhibitors (MAOIs). RIMAs, not yet available in the United States, appear to be a safer choice than the older MAOIs, as they require fewer dietary restrictions and have fewer significant interactions with other medicines.

Tricyclic antidepressants

TCAs block the reuptake, or reabsorption, of serotonin and norepinephrine. In doing so, they help to treat IC by blocking pain and reducing urinary urgency. However, we do not know the exact reason they work. When used to treat IC, helpful effects of TCAs include:

- **Anticholinergic effects**, meaning TCAs relax the bladder and decrease the intensity of bladder contractions. This effect diminishes urinary frequency by delaying the desire to urinate.
- **Antihistamine effects** or blocking of the response that occurs during an allergic inflammatory reaction and calming IC pain.
- **Blockage or re-absorption of certain neurotransmitters** (such as serotonin and noradrenaline) prompting the brain to ignore pain impulses.
- **Sedative properties**. TCAs also make you sleepy and if taken in the evening can help decrease sleep problems.
Selective serotonin reuptake inhibitors

SSRIs block the reuptake of serotonin. SSRIs are the most widely prescribed new class of antidepressants, and fluoxetine (Prozac) was the first in this new class on the market in the United States. But do the SSRIs or any of the other new antidepressants work to treat IC? The jury is still out. One reason for the development of newer antidepressants was to reduce the negative side effects (constipation, dry mouth, and weight gain, for example) of the TCAs. In doing so, some of the side effects that actually help to treat IC were lost (anticholinergic, antihistamine, and sedative properties, for instance).

While the results of studies using SSRIs for various medical conditions besides depression are encouraging, very little data is available regarding their use in treating IC.

Serotonin and norepinephrine reuptake inhibitors

SNRIs block the reuptake of both serotonin and norepinephrine. This class of newer antidepressants is receiving high marks for pain management, and doctors are using some medicines in this class effectively to treat many different types of pain, including fibromyalgia. However, thus far, only one study investigated SNRI as a treatment for IC.

Noradrenaline reuptake inhibitors

NRIs specifically block the reuptake of noradrenaline (norepinephrine) and possibly dopamine, while having very little effect on serotonin. Norepinephrine is a brain chemical that plays an important role in attention regulation and blood pressure. NRIs tend to have a stimulating effect and healthcare providers use these medicines to treat conditions like chronic fatigue syndrome, narcolepsy, and ADHD.

Reversible inhibitors of monoamine oxidase type-A

Similar to monoamine oxidase inhibitors (MAOIs), RIMAs reduce the activity of monoamine oxidase. Monoamine oxidase breaks down noradrenaline, serotonin and other brain chemicals. RIMAs increase the amount of noradrenaline and serotonin in the brain, with fewer risks, side effects, and dietary restrictions than MAOIs.

Studies Testing Antidepressants to Treat IC

With the exception of the TCA called amitriptyline (Elavil), there are limited studies evaluating the use of antidepressants in IC. While it is general knowledge that TCAs can help with the symptoms of IC and that they are a first-line therapy for IC, it was not until 2004 that researchers put amitriptyline to the test for use in IC in a placebo-controlled study.

Researchers tested amitriptyline, the TCA most commonly used to treat IC, in a randomized, prospective, placebo-controlled trial for IC.

If your doctor prescribes you an antidepressant, be sure to ask the following questions:

- What is the name of the antidepressant?
- What class is it in?
- How does it work to treat IC (and/or any of your other conditions it is being used for)?
- Why are you prescribing this specific antidepressant?
- What are the side effects?

The researchers found that symptom scores dropped, and that pain and urinary urgency improved significantly in the amitriptyline group compared with the placebo group. Urinary frequency and functional bladder capacity improved more in the amitriptyline group, but the difference was not statistically significant. In a follow-up study, the drug proved to be effective for long-term management of IC.

In 2009, the National Institutes of Health (NIH) released its Interstitial Cystitis Clinical Research Network (ICCRN) amitriptyline trial results. The ICCRN trial aimed to discover whether early treatment with amitriptyline could give patients a better chance at getting IC under control and to see if it might be the best first treatment. Patients who recently developed IC started with 10 mg of amitriptyline (or placebo) per day and took higher doses as they could tolerate them up to 75 mg per day.

After 12 weeks, there was no significant difference between the groups on their overall rating of how they were feeling. There were bigger differences based on other measures, however, especially for patients who were taking higher doses. Those who were able to take at
least 25 mg per day did much better than others did, with 73 percent responding compared with 53 percent of those taking placebo. Dropout rates because of side effects, such as fatigue, dry mouth, constipation, dizziness, and sleepiness, were high in this study, making it difficult to draw firm conclusions.

Researchers out of the Albert Einstein College of Medicine presented a study on another TCA called desipramine at the 2012 American Urological Association (AUA) meeting. The study found that desipramine was effective in treating both overactive bladder (OAB) and OAB with bladder pain. The researchers concluded patients treated with amitriptyline should consider desipramine if they experienced side effects linked to amitriptyline, like memory problems.

Researchers investigated the SNRI Duloxetine (Cymbalta) in a small study (48 females with IC) in 2007 and found it not to be a very effective treatment for IC. The study also had a high dropout rate because of the main side effect of nausea in the IC patients in the study.

Some physicians are prescribing these newer antidepressants to treat IC and related conditions, and some IC patients find that symptoms improve when using these medicines, some find that their symptoms are not affected, and some find that their symptoms worsen. We need more research in this area. It is best to take a “trial and error” approach when trying out a non-TCA for our IC (or for treating other chronic conditions when you have IC).

Antidepressants Used to Treat IC
Some of the current antidepressants your physician may prescribe you to treat your IC and/or other chronic conditions include:

Tricyclic antidepressants (TCAs)
- amitriptyline (Elavil)
- desipramine (Norpramin) — also an NRI
- doxepin (Sinequan)
- imipramine (Tofranil)
- nortriptyline (Pamelor) — also an NRI

Selective serotonin reuptake inhibitors (SSRIs)
- citalopram (Celexa)
- escitalopram (Lexapro)
- fluoxetine (Prozac)
- fluvoxamine (Luvox)
- paroxetine (Paxil)
- sertraline (Zoloft)

Serotonin and norepinephrine reuptake inhibitors
- duloxetine (Cymbalta)
- milnacipran (Savella)
- venlafaxine (Effexor)

Noradrenaline Reuptake Inhibitors (NRIs)
- atomoxetine (Strattera), approved only for attention deficit/hyperactivity disorder
- reboxetine (Edronax)

Other antidepressants include:
- bupropion (Wellbutrin), which inhibits the reuptake of norepinephrine and dopamine
- trazodone (Desyrel), which inhibits the reuptake of serotonin
- moclobemide (Aurorix), which is a RIMA that reduces the activity of monoamine oxidase
- tianeptine (Stablon), which enhances the reuptake of serotonin

Dosage & Treatment Plan
Dosages for TCAs range from 10 - 100 mgs usually taken in the evening or at bedtime. It is typical to start out with a very low dose (10 mgs) and then
gradually increase the dosage every week until you find that your symptoms are improving.

Dosages for other types of antidepressants vary, depending on specific medicine.

**Potential Side Effects**

Give yourself time to adjust when starting any type of antidepressant medicine. Unwanted side effects may tend to decrease after a few weeks.

The effects of TCAs may vary depending on the specific medicine, the dosage, and your individual reaction. For example, if you cannot tolerate amitriptyline, ask your doctor about switching to imipramine or doxepin.

A word of caution: If urinary retention is a predominant feature of your IC, monitor your reaction to your prescribed medicine to be sure that it does not make your urinary retention worse. Some antidepressants are more anticholinergic than others are.

To minimize unwanted side effects of antidepressants:

- Start out at the lowest dosage possible and work your way up to the dosage that seems to alleviate your symptoms with the fewest side effects. This may take several weeks.
- If your physician prescribes you a TCA, take it in the early evening to eliminate unwanted morning drowsiness.
- For constipation, increase the amount of fiber in your diet. Consider taking Metamucil or a stool softener such as Colace.

**Pregnancy & Warnings**

None of the antidepressants in any of the classes should be used during pregnancy and while nursing unless warranted by a physician. In 2004, the US FDA mandated a “black box warning” regarding the potential for suicide and suicidal thinking in children and adolescents taking antidepressants. This warning is now included on virtually all antidepressant materials. Patients with narrow-angle glaucoma should not use TCAs.