The New York Times | https://nyti.ms/1mLxa6o

SundayReview | OPINION

A Placebo Treatment for Pain

By JO MARCHANT JAN. 9, 2016

THE crisis of painkiller addiction is becoming increasingly personal: Sixteen percent of Americans know someone who has died from a prescription painkiller overdose, according to a recent Kaiser Family Foundation survey; 9 percent have seen a family member or close friend die.

Addictive opioid painkillers were once reserved for extreme situations like terminal cancer. But opioids like Vicodin and OxyContin are now widely prescribed for common conditions like arthritis and lower back pain. The consequences have been catastrophic: In 2013, prescription painkillers caused nearly 7,000 emergency room visits and 44 deaths every day.

How do we tackle this crisis? We often hear about efforts to clamp down on abuse, for example by regulating pain clinics and monitoring prescription patterns. But these won't dent the demand for opioids unless we can find better ways to treat the hundred million Americans said to suffer from chronic pain. Simply switching to other drugs isn't the answer. Few new painkillers are being approved, and existing ones, like Motrin and Tylenol, come with their own risks when used long-term, and some appear to be less effective than we once thought.

Help might instead come from an unexpected corner: the placebo effect.

This phenomenon — in which someone feels better after receiving fake treatment — was once dismissed as an illusion. People who are ill often improve

regardless of the treatment they receive. But neuroscientists are discovering that in some conditions, including pain, placebos create biological effects similar to those caused by drugs.

Taking a placebo painkiller dampens activity in pain-related areas of the brain and spinal cord, and triggers the release of endorphins, the natural pain-relieving chemicals that opioid drugs are designed to mimic. Even when we take a real painkiller, a big chunk of its effect is delivered not by any direct chemical action, but by our expectation that the drug will work. Studies show that widely used painkillers like morphine, buprenorphine and tramadol are markedly less effective if we don't know we're taking them.

Placebo effects in pain are so large, in fact, that drug manufacturers are finding it hard to beat them. Finding ways to minimize placebo effects in trials, for example by screening out those who are most susceptible, is now a big focus for research. But what if instead we seek to harness these effects? Placebos might ruin drug trials, but they also show us a new approach to treating pain.

It is unethical to deceive patients by prescribing fake treatments, of course. But there is evidence that people with some conditions benefit even if they *know* they are taking placebos. In a 2014 study that followed 459 migraine attacks in 66 patients, honestly labeled placebos provided significantly more pain relief than no treatment, and were nearly half as effective as the painkiller Maxalt. (The study also found that a placebo labeled "placebo" was 60 percent as effective as Maxalt if it was labeled "placebo." If the placebo was labeled "Maxalt," it was again 60 percent as effective as the real drug under its real label.)

With placebo responses in pain so high — and the risks of drugs so severe — why not prescribe a course of "honest" placebos for those who wish to try it, before proceeding, if necessary, to an active drug?

Another option is to employ alternative therapies, which through placebo responses can benefit patients even when there is no physical mode of action. A series of large trials in Germany published between 2005 and 2009 compared real

and sham acupuncture (in which needles are placed at nonacupuncture points) with either no treatment or routine clinical care, for chronic pain conditions including migraine, tension headaches, lower back pain and osteoarthritis. Patients who received the acupuncture, real or sham, reported a similar amount of pain relief — and more than those who received no treatment or routine care that included pain medication.

Rather than relying on dummy pills and treatments, however, a broader hope is that teasing out why and when placebos work — and for whom — will help to maximize the effectiveness of drugs, and in some cases allow us to do without them.

The available funding for such research is minuscule compared with the efforts poured into developing new drugs. But a key ingredient is expectation: The greater our belief that a treatment will work, the better we'll respond.

Individual attitudes and experiences are important, as are cultural factors. Placebo effects are getting stronger in the United States, for example, though not elsewhere. Researchers reported last year that in trials published in 1996, drugs for chronic pain produced on average 27 percent more pain relief than placebos. By 2013, that advantage had slipped to just 9 percent. Likely explanations include a growing cultural belief in the effectiveness of painkillers — a result of direct-to-consumer advertising (illegal in most other countries) and perhaps the fact that so many Americans have taken these drugs in the past.

These findings have implications for deciding which patients are likely to benefit from drugs — someone who has strong faith in painkillers' effectiveness is more likely to benefit than someone who is suspicious of conventional medicine — as well as how physicians explain the benefits and side effects of treatments they prescribe. Trials show, for example, that strengthening patients' positive expectations and reducing their anxiety during a variety of procedures, including minimally invasive surgery, while still being honest, can reduce the dose of painkillers required and cut complications.

Placebo studies also reveal the value of social interaction as a treatment for pain. Harvard researchers studied patients in pain from irritable bowel syndrome and found that 44 percent of those given sham acupuncture had adequate relief from their symptoms. If the person who performed the acupuncture was extra supportive and empathetic, however, that figure jumped to 62 percent.

Placebos tell us that pain is a complex mix of biological, psychological and social factors. We need to develop better drugs to treat it, but let's also take more seriously the idea of relieving pain without them. With dozens of Americans dying every day from prescription painkillers, we need all the help we can get.

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A version of this op-ed appears in print on January 10, 2016, on Page SR5 of the New York edition with the headline: A Placebo Treatment for Pain.
