Taken at face value, a new JAMA article [2] entitled "Effect of a Single Dose of Oral Opioid and Nonopioid Analgesics on Acute Extremity Pain in the Emergency Department (ED) A Randomized Clinical Trial," makes it seem clear that ibuprofen (Advil), when combined with acetaminophen (Tylenol), works as well as opioid drugs such as Vicodin or Percocet for relief of severe pain in emergency room patients.

Can that be true? Have we been so misled over the years that we are operating under assumptions that are not really valid?

The answer is yes, we have been misled - by the article. All is not what it seems. This is because of dose. Let's take a look.

Andrew K. Chang and colleagues from the Department of Emergency Medicine at Albany (NY) Medical College compared the efficacy of four different drug combinations in four groups each consisting of 104 patients who visited emergency departments in two different urban hospitals over the course of 13 months. We will examine the doses used in the study below. Their conclusions (emphasis mine):

“For adult ED patients with acute extremity pain, there were no clinically important differences in pain reduction at 2 hours with ibuprofen and acetaminophen or 3 different opioid and acetaminophen combination
analgesics."
Andrew K. Chang, et al. JAMA November 7, 2017 Volume 318, Number 17

This matter seems to be rather cut and dry. The paper's conclusion is straightforward and obvious - ibuprofen and acetaminophen work as well as opioid drugs and acetaminophen. But it's really not because there is more going on here than meets the eye. This becomes evident when factoring in the doses of all the drugs that were used. Then the playing field is not so level.

Drugs.com is an especially useful website for getting information about dosing information for drugs, especially the recommended dose or dose range, the interval between doses, and the daily maximum dose. Below are prescribing information for ibuprofen, acetaminophen, hydrocodone, and oxycodone.

COMPARISON OF THE FOUR TREATMENTS GROUPS (ALL SINGLE DOES)

Group 1 received 400 mg of ibuprofen plus 1000 mg of acetaminophen. Figure 1 gives the dosing information on both drugs.

**Figure 1 - The therapeutic and daily maximum dose of ibuprofen and acetaminophen. Sources (both from Drugs.com): Ibuprofen [3], Acetaminophen [4]**

Group 2 received 5 mg of hydrocodone and 300 mg of acetaminophen. Figure 2 gives dosing information for hydrocodone.

**Figure 2 - Dosing information for hydrocodone. Source: Drugs.com [5]**

Group 3 received 5 mg of oxycodone plus 325 mg of acetaminophen. Figure 3 gives dosing information for oxycodone.
Group 4 received 30 mg of codeine and 325 mg of acetaminophen. Figure 4 gives dosing information for codeine.

One thing that becomes immediately obvious is that the comparison of the four different drug combinations is skewed. In Group 1, patients received the maximum single dose of both ibuprofen and acetaminophen. But in the three other groups, they received the minimum therapeutic dose of the opioid and a small dose of acetaminophen (1).

This is where the study leaves me cold. If the researchers gave the patients 10 mg of oxycodone or hydrocodone, a much more realistic dose for treatment of severe pain, you can bet that the results of this study would be very different. Is this odd? Misleading? I would have to ask the authors why the study was set up this way.

Finally, consider whether any of the patients in the study got an appropriate dose of any medicine:

Findings: "In this randomized clinical trial of 411 ED patients with acute extremity pain (mean score, 8.7 on the 11-point numerical rating scale), there was no significant difference in pain reduction at 2 hours. Mean pain scores decreased by 4.3 with ibuprofen and acetaminophen (paracetamol); 4.4 with oxycodone and acetaminophen; 3.5 with hydrocodone and acetaminophen; and 3.9 with codeine and acetaminophen."
Pain that is rated above 8 is excruciating. At 9 or 10 it is unbearable. This means that the 416 patients who visited the ER were in very bad shape. This may be a personal preference but if I have a kidney stone (3) or herniated disc with nerve pain I’m not going to be so happy to have my excruciating pain reduced to "merely" moderate after two hours.

This study, intentionally or otherwise, provides just a bit more of an assault on pain patients, who have already suffered mightily through no fault of their own. In concluding Advil/Tylenol is just fine for relieving severe acute pain, it is really saying that the rest of us should be able to do so. On top of the heinous 2016 CDC "guidance" on prescribing practices, mostly thanks to the equally heinous Physicians for Responsible Opioid Prescribing (PROP), we now have "voluntary suggestions" (4), law enforcement, and burgeoning state laws that place artificial (and scientifically bogus) laws, which will do absolutely nothing to address addiction (See: "No, Vicodin Is Not The Real Killer In The Opioid Crisis [9]") but will certainly hurt pain patients, the victims of the collateral damage from the ridiculous "War on Drugs." Perhaps when Chris Christie gets rushed to an emergency room for a kidney stone and gets Advil he'll change his tune (5,6).

NOTES:

(1) Note that I did not use the term "lowest therapeutic dose" because since acetaminophen is a very poor analgesic and it is unclear what such as dose would be. Although there is evidence that acetaminophen potentiates the action of the opiate. On its own, acetaminophen is fairly close to useless. (See: "Tylenol Isn't So Safe, But At Least It Works, Right?" [10])

(2) However well acetaminophen works for pain relief when combined with the opiate, it works even "less well" than it used to. This is because the FDA required that by 2014 that the maximum dose of acetaminophen in any opiate combination pill cannot exceed 325 mg. It had been as high as 750 mg. The change was made to protect patients from the acetaminophen. (See: "Is Tylenol ‘By Far The Most Dangerous Drug Ever Made?" [11])

(3) I did. Once. That was one time too many. Horrible.

(4) Voluntary? My ass.
(5) No, he won't. Our political leaders enjoy a level of medical care that the rest of us cannot imagine. Christie is more likely to get a Tootsie Pop than Advil when his limousine pulls up the "VIP ward" in the hospital. You know it, I know it. He knows it.

(6) It is fair to question why any emergency room would give the bare minimum (less, really) of a pain drug during a pain emergency. Five mg of hydrocodone for a kidney stone?? Are they kidding? It could be argued that this is malpractice. Most people wouldn't notice the difference whether they got the pill or not. Does anyone really believe that one 10 mg dose of oxycodone is going to addict anyone? Because it's not.

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