

The W-series compounds

Jia Hu, Raymond Li, Roy Pursell, Ashraf Amlani, Jane Buxton

January 8, 2016

What are the W-series compounds?

The “W-series” compounds are a class of opioids discovered at the University of Alberta in 1982. There are 32 compounds, denoted W-1 to W-32. They have never been used clinically. Recently it has emerged that some of these compounds, notably W-18 which is 100x more toxic than fentanyl, are being sold as street drugs in North America. These compounds are not currently regulated under the Controlled Drug and Substances Act and as such can be manufactured and transacted freely.

How are W-series compounds detected?

Special tests allow certain labs to test for the presence of W-series compounds. However, unlike other drugs that are used more commonly, they are not a part of routine drug testing. As a result, the lab must specifically know to look for the W-series compound in question and also have the standard to test against. Thus, detection can be slower than with other drug tests.

What is the effect of W-series compounds on humans?

There have been no reports of any clinical use so our understanding of them is limited. However, it is likely they could be inhaled if aerosolized and could also potentially be absorbed through the skin. W-1 to W-19 are pure opioid receptor agonists; similar to the action of most opioids like morphine or fentanyl they only activate the opioid receptors. On the other hand, W-20 to W-32 are opioid receptor agonist-antagonists; this means they can displace other agonists from the receptor but also have some agonist effects themselves, similar to the action of buprenorphine. There is significant variation in the toxicity of these compounds. The most toxic are W-18 (100x fentanyl), W-19 (10x fentanyl) and W-11 (1.5 x fentanyl) while some are many times less toxic than fentanyl.

Will naloxone reverse the effect of W-series compounds?

The mixed agonist-antagonist effect and varying toxicity makes the administration of naloxone challenging as it is unlikely that the identity of the specific compound will be known. There is little evidence for the use of naloxone in these compounds. Only W-3 was tested for reversibility and then only in mice. Naloxone successfully reversed the analgesic effects of W-3. Reversal of respiratory depression, the means by which opioid overdose causes death, was not assessed. While reversal has never been tested in humans, naloxone should theoretically be effective, with two caveats. First, given the high toxicity of some of the W-compounds, high doses of naloxone may be required. Second, the agonist-antagonist effects of W-20 to W-32 mean that effects of naloxone would be difficult to predict. Thus, it is important that the naloxone dose be titrated to clinical effect (i.e. reversal of respiratory depression).

What should be done in the event of an overdose?

In any suspected overdose, it is important to immediately call 911 for professional guidance. If there are signs of respiratory depression, the following algorithm for giving naloxone can be followed:

1. Administer one dose (0.4 mg) of naloxone from the "Take Home Naloxone" kit and make preparations for the patient to be taken to hospital immediately for assessment
2. Observe for 2-3 minutes for an increase in respiratory rate
3. If there is no change in respiration, administer another 0.4 mg dose of naloxone
4. Repeat the above two steps until the patient can be seen by a healthcare professional
5. Monitor and support the patient's respiratory efforts throughout the overdose