Pharmacology of the Buprenorphine/Naloxone Combination [1]

**Description:** Buprenorphine/naloxone combination formulations are designed to minimize the potential for abuse of buprenorphine. When taken as indicated (sublingually), the naloxone component has virtually no effect on the patient; however, when injected, the naloxone component attenuates buprenorphine's reinforcing effects and possibly will induce withdrawal (Johnson et al., 2003).

In addition to buprenorphine monotherapy tablets, film and tablets combining 4 parts buprenorphine and 1 part naloxone (a mu opioid antagonist) are also being used in maintenance treatment for opioid dependence (Chiang and Hawks, 2003). (The original manufacturer of the combination tablets stopped supplying them but generic versions and new brand, Zubsolv®, are now available.) In fact, the buprenorphine/naloxone combination is preferred over buprenorphine monotherapy in almost all situations because the combination tablets are less liable to be abused (Johnson et al., 2003.) Combination buprenorphine/naloxone sublingual film is also available, marketed under the brand name Suboxone®.

The reason why the combination formulation is unlikely to be abused stems from 2 facts:

1. Patients who are using buprenorphine as indicated will take the medication sublingually. People who abuse buprenorphine will usually inject it, since injecting produces a more immediate effect than taking the drug sublingually.

2. Naloxone has very poor bioavailability when it is taken sublingually or orally. However, it has excellent bioavailability when it is taken by injection.

As a result, patients who take combination buprenorphine as indicated experience virtually none of naloxone's antagonistic effects. However, if the medication is dissolved and injected, the injector experiences naloxone's full antagonistic effects (Fudala et al., 1998; Mendelson et al., 1996; Mendelson et al., 1997; Mendelson et al., 1999).

<table>
<thead>
<tr>
<th>Bioavailability of Buprenorphine/Naloxone</th>
<th>Sublingual</th>
<th>Parenteral</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bioavailability</strong></td>
<td>Buprenorphine: Good</td>
<td>Buprenorphine: Excellent</td>
</tr>
<tr>
<td><strong>Predominant Effect</strong></td>
<td>Naloxone: Poor</td>
<td>Naloxone: Excellent</td>
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The exact consequences of injecting the combination formulation will vary depending on how opioid-dependent the injector is.
Individuals dependent on illicit opioids or on most medically used opioid agonists are very likely to go into opioid withdrawal.

Individuals maintained on buprenorphine/naloxone are unlikely to go into withdrawal because buprenorphine has a very high affinity for mu opioid receptors and is unlikely to be displaced by naloxone. However, the agonist effects of buprenorphine will be attenuated by the naloxone, which should decrease the desirability of injecting (Lewis and Walter, 1992).

Individuals who are not dependent on opioids will not be affected by naloxone, although the agonistic effects of buprenorphine will be attenuated. According to Strain et al. (2000), this group is the most likely to abuse buprenorphine/naloxone combination medication.

*We are using brand names since there is a difference in the product that is not reflected in the generic name. We are not advocating one brand or the other.

Links:
[1] https://www.buppractice.com/PharmacologyoftheBuprenorphine/NaloxoneCombination