Examining the effectiveness of naloxone on opioid related overdose: A structured review
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Abstract
Opioids are a psychotomimetic group of drugs that are used by approximately 35 million people worldwide, and account for majority of the 190 000 drug related deaths that occur annually. Globally, there has been an increase in the usage of both synthetic and natural opioids, resulting in a higher number of deaths due to opioid overdose. Naloxone, however, is an opioid antagonist that can be used to stop or reverse the effects of these potentially fatal drugs by increasing respiration, thus aiding in the avoidance of death. This review, therefore, aims to assess the relationship between the usage of Naloxone and mortality rates due to opioid overdose among opioid users. PubMed and Scopus databases were used to gather literature using the following key words: (“Naloxone” AND “overdose” AND “mortality rate”). Articles were then included if they met the following criteria: written in English, published within the past 15 years, including humans only, and cohort studies, case-controls or prospective reviews. The reference lists were also included, and taken into consideration for the selection process. Titles and abstracts of articles that met the inclusion criteria were then examined to determine relevance with regards to the scientific question. Finally, each article was read in full to obtain the total number of articles to be included in the structured review. A total of 7 articles met the criteria and were used in the final structured review. These studies indicate a positive association between the usage of Naloxone and decreased mortality rates due to opioid overdose, demonstrating that Naloxone is effective in reversing the effects of opioid overdose. Future research should compare mortality rates before and after the greater implementation of Naloxone treatments to determine if there has been a significant decrease in the number of deaths.

Background
- Global increase in the usage of both synthetic and natural opioids, resulting in a higher number of opioid related deaths (ORDs), with men being the primary victims.
- Opioid related overdose (ORO) leads to respiratory depression (decreased oxygen levels in the body) which may lead to death if untreated.
- Naloxone acts as an opioid antagonist that can stop or reverse the effects of these potentially fatal drugs by increasing respiration.
- Naloxone’s high-affinity for opioid receptors leads to the displacement of bound opioids and inhibits additional binding of opioids for 20 to 90 minutes.
- Standard dosage: 2mg of naloxone intravenously or intramuscularly or 4mg via an endotracheal tube – repeat if necessary.
- As of March 2016, naloxone (both nasal spray and injection) has been readily available to Canadians.

Methods

Table 1: Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Study Subject</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humans only</td>
<td>Overdose</td>
<td>Non-human animals</td>
</tr>
<tr>
<td>Non-human animals</td>
<td>Cancer</td>
<td>Tissue cultures, etc.</td>
</tr>
</tbody>
</table>

Figure 1: Naloxone injection kit

Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Population</th>
<th>Key Findings</th>
<th>CASP</th>
</tr>
</thead>
<tbody>
<tr>
<td>McAuley, Aucott &amp; Matheson (2015)</td>
<td>Systematic Review</td>
<td>n = 9 studies</td>
<td>35 000 – 183 000 ORDs can be avoided every 3 months</td>
<td>81%</td>
</tr>
<tr>
<td>Clark, Wilder, Winstaney (2014)</td>
<td>Systematic Review</td>
<td>n = 19 studies</td>
<td>Significant relationship between number of cities that implement naloxone treatment and number of lives saved</td>
<td>94%</td>
</tr>
<tr>
<td>Albert, Brason, Sanford, Dsagupta, Graham, Lovette (2011)</td>
<td>Community-based prevention program (Wilkes County, NC)</td>
<td>ORDs decreased from 43 to 29 per 100 000 persons within a span of 2 years after program implementation</td>
<td>68%</td>
<td></td>
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<tr>
<td>Vike, Sloane, Smith, Chan (2003)</td>
<td>Cohort</td>
<td>n = 556 427 (emergency medical responses)</td>
<td>No deaths or poisoning attributed to naloxone administration</td>
<td>68%</td>
</tr>
<tr>
<td>Bird, McAuley, Perry &amp; Hunter (2015)</td>
<td>Cohort</td>
<td>n = 12 000 kits provided</td>
<td>Use of naloxone prevented 42 ORDs (95% CI)</td>
<td>89%</td>
</tr>
<tr>
<td>Sherman, Gann, Scott, Carleberg, Bigg, Heimer (2008)</td>
<td>Cohort</td>
<td>n = 31 persons (Chicago Recovery Alliance)</td>
<td>Increased QALY by 6.1 years per person</td>
<td>84%</td>
</tr>
<tr>
<td>Schumann, Erickson, Thompson, Zautke, Scott (2008)</td>
<td>Cohort</td>
<td>n = 55 ER visits</td>
<td>Mortality rates call for greater implementation of out-patient naloxone programs</td>
<td>82%</td>
</tr>
</tbody>
</table>

Discussion
Summary of Findings
- No reported deaths due to Naloxone administration
- Doses for 20x the estimated number of users need to be made available.
- ORD and ORD rates have not increased since the implementation of naloxone programs.
- Naloxone does not need to be administered by an HCP or in a medical setting.
- More effective than the current practices.

Limitations
- ORO is subjective
- Examined different populations
- Lack of statistical analysis
- No comparison to gold-standard
- Confounders: sex, age, socioeconomic status
- New intervention

Strengths
- Consistent results
- Examined different populations
- Used multiple methods to retrieve articles

Conclusion
- Naloxone treatment decreases mortality rates due to ORDs among non-medical opioid users.
- Future directions: Focus on Canadian population, More statistical analysis comparing naloxone with current gold-standard treatment, Compare mortality rates before and after implementation of intervention.
- Implement laws/policies that facilitate access to naloxone.

Acknowledgments
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References