Opium Trial: a randomized controlled non-inferiority clinical trial comparing opium tincture with methadone for opioid substitution treatment


Background

• In recent years, there has been a growing interest in using opium tincture (OT) for withdrawal management and opioid substitution treatment of opioid dependence in certain parts of the world, particularly Iran.
• A systematic review in 2016 indicated a lack of adequate published evidence supporting its effectiveness and safety for this indication*.
• Opium trial was the first clinical trial to compare OT with methadone for opioid substitution treatment.

Objective: to test if OT was non-inferior to methadone in retaining participants in opioid substitution treatment.

Methods

A phase III multicentre parallel group, non-inferiority randomized double-blind clinical trial with an allocation ratio of 1:1, conducted in Iran between July 2017 – April 2018.

Results

• The average daily dose for OT and methadone were 273.42 (142.57) mg and 79.53 (49.59) mg, respectively.
• A total of 70 participants (68.6% in ITT and 69.3% in PP analyses) in the methadone arm and 61 participants (59.8% in ITT and 60.4% in PP analyses) in the OT arm remained in treatment at the end of the 12-week follow-up period.
• For opioid use outside treatment, 46 out of 152 (30.3%) responses were positive in OT arm and 83 out of 168 (49.4%) responses were positive in methadone arm.
• The proportion of patients with adverse events in the OT (n=9, 8.8%) in the OT and methadone arms (n=2, 2.0 %) were not significantly different (P value = 0.06). There was no serious adverse event in the OT arm and one in the methadone arm.

Conclusion

• Findings of this study support the use of OT for substitution treatment despite inconclusive non-inferiority comparison with methadone.
• OT was a clinically effective medication in retaining participants in treatment and was superior to methadone in reducing self-reported opioid use outside the treatment.
• Number of people with adverse events was not significantly different between the two arms and no major adverse events were observed in the OT arm.
• Further research on the effectiveness and safety of OT in comparison with commonly used substitution treatment medications is needed.

Fig 1. Study design diagram

Fig 2. Relative retention rate of methadone arm compared to opium tincture.

Fig 3. Comparison of self-reported opioid use in follow up visits 22, 26, and 30 in opium trial.