Methadone vs. L-alpha-acetylmethadol (LAAM) in the treatment of opiate addiction: a meta-analysis of the randomized, controlled trials

Glanz M, Klawansky S, McAuliffe W, Chalmers T

Authors' objectives
To assess the overall efficacy of L-alpha-acetylmethadol (LAAM) therapy, compared with methadone, in heroin addiction.

Searching
MEDLINE was searched from 1966 to 1996 using the keywords 'heroin addiction', 'methadone' and 'levo-alpha-acetylmethadol'. The bibliographies of the retrieved articles and other pertinent review articles were also examined for additional studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) comparing methadone with LAAM therapy in the management of heroin addiction. The median study duration was 26 weeks (range: 3 to 52). The studies varied in their design in terms of the following: open versus closed design; the presence or absence of a stabilisation period on methadone for both treatment arms; the option of dosage variability; and differences in the dosing schedule.

Specific interventions included in the review
LAAM (30 to 80 mg dosages on a 1, 2 or 3 day, or weekly schedule) versus methadone. The duration of treatment ranged from 3 to 52 weeks.

Participants included in the review
Out-patients receiving treatment for opiate addiction. Most of the patients were men from lower socioeconomic strata.

Outcomes assessed in the review
The study outcomes were:
- illicit drug use, as determined by urine testing;
- retention in the treatment programme, as defined by the proportion of patients remaining in the assigned treatment arm of the study until its completion; and
- the discontinuation of treatment because of side-effects, as defined by the proportion of patients discontinuing the study specifically because of side-effects.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
Quality scoring was performed using the method of Chalmers et al. (see Other Publications of Related Interest) to assess blinding and randomisation. The descriptive and analytic data display in each study was also assessed. The scores were expressed as a ratio of the total number of points over the total possible points. The authors do not state how the papers were assessed for quality, or how many of the authors performed the quality assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

**Methods of synthesis**

How were the studies combined?
Both fixed-effect and random-effects models were used to pool the data. The pooled data was expressed in the form of the risk difference with 95% confidence intervals (CIs) and p-values.

How were differences between studies investigated?
Heterogeneity was assessed by calculating the Q statistic for each of the three end points of the review: illicit drug use (11 studies), retention in the treatment programme (10 studies), and the discontinuation of treatment because of side-effects (4 studies).

To investigate the effects of heterogeneity, a sensitivity analysis was carried out on the three studies that had two different datasets available (2 with different dosages of methadone, and 1 with different treatment schedules).

**Results of the review**

Twelve RCTs (7 double-blind, 1 single-blind, and 4 open), with 954 participants taking methadone treatment and 834 participants taking the LAAM therapy, were included.

The individual quality scores ranged from 0.30 to 0.73 (mean: 0.50 plus or minus 0.14).

For compliance, the fixed-effect method was reported since the Q statistic for heterogeneity was 1.34, which was not significant. The initial and adjusted pooled results for compliance favoured the methadone treatment and were significant (both were 0.04, 95% CI: 0.02, 0.05; p<0.0001).

For retention in the programme, the random-effects method was reported since the Q statistic for heterogeneity was 27.20, which was significant. The initial and adjusted pooled results for retention in programme favoured the methadone treatment and were significant: -0.13 (95% CI: -0.21, -0.04) and -0.11 (95% CI: -0.19, -0.03), respectively (p<0.003).

For illicit drug use, the random-effects method was reported since the Q statistic for heterogeneity was 10.74, which was significant. The initial and adjusted pooled results for illicit drug use favoured the LAAM treatment, but these results were not significant: -0.01 (95% CI: -0.07, -0.04) and -0.02 (95% CI: -0.08, -0.03), respectively (p less than or equal to 0.36).

The number-needed-to-treat with methadone over LAAM, to prevent one patient from dropping out, was 8.

**Authors’ conclusions**

It would seem reasonable at this point to support and encourage LAAM therapy as an important alternative to methadone, given the potential practical and operational benefits of LAAM therapy over methadone in certain situations. However, in terms of treatment retention, methadone does appear to have a statistically-significant advantage.

**CRD commentary**

This was a relatively well-conducted systematic review with a clear objective. In addition, the quality assessment was comprehensive, there was adequate provision of study details, and the statistical pooling was appropriate.

The search was restricted to English language studies identified in MEDLINE and so relevant studies could have been missed. No attempt was made to identify unpublished articles or to contact researchers in this field.

The authors stated their inclusion criteria and conducted a quality review of the included studies. They addressed
heterogeneity in the studies by conducting additional sensitivity analyses.

There is a discrepancy in the numbers of participants reported for three of the individual studies: the numbers of participants listed in the table of original data (table 1) do not match those listed in the table of extracted data (table 2). The authors do not explain this inconsistency between the original and extracted data.

Despite the sensitivity analysis performed by the authors, the results of the review should be viewed with caution because of the limitations of the literature search, and the lack of clear results on the benefits of LAAM therapy over methadone treatment. The authors' conclusion, that the results of this review support and encourage the use of LAAM therapy as an alternative treatment, are a reasoned opinion and are only partially supported by the results.

Implications of the review for practice and research
The authors do not state any further research implications. Further research may be required to evaluate LAAM therapy as an alternative to methadone treatment.

Bibliographic details

PubMedID
9398932

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Female; Humans; Male; Methadone /adverse effects /therapeutic use; Methadyl Acetate /adverse effects /therapeutic use; Middle Aged; Narcotics /adverse effects /therapeutic use; Opioid-Related Disorders /rehabilitation; Randomized Controlled Trials as Topic; Treatment Outcome

AccessionNumber
11998003193

Date bibliographic record published
31/08/1999

Date abstract record published
31/08/1999

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.