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What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review

DA Fishbain, B Cole, J Lewis, HL Rosomoff, and RS Rosomoff.

Review published: 2008.

CRD summary

The review concluded that chronic opioid analgesic therapy exposure will lead to abuse/addiction in a small percentage of chronic pain patients, but a larger percentage will demonstrate aberrant drug-related behaviours and illicit drug use. The wide variation of drugs, populations and study designs used in the included studies means the authors' conclusions should be interpreted with caution.

Authors' objectives

To determine what percentage of chronic pain patients developed abuse/addiction and/or aberrant drug-related behaviours on exposure to chronic opioid analgesic therapy.

Searching

MEDLINE, Psychological Abstracts, Science Citation Index and National Library of Medicine Physician Data Query databases were searched for studies in any language. Dates spanned 1966 to 2006. Search terms were reported. Several journals and textbooks were handsearched, as were abstracts from numerous meetings.

Study selection

Studies that presented results for patients on chronic opioid analgesic therapy (for over one month and with a reported time interval for exposure) for chronic benign non-malignant pain were eligible for inclusion. Studies of tramadol or of any opioid antagonist were excluded. Studies of the prevalence of addiction/dependence within chronic pain patients were also excluded, as were studies that did not report the number of patients exposed to opioid therapy and studies that recruited patients suspected of opioid misuse. Levels of abuse/addiction, aberrant drug-related behaviours and urine toxicology measurements were the main outcomes of interest. A wide range of opioids/comparators and populations were studied.

The authors stated neither how the studies were selected for inclusion in the review nor how many reviewers performed the selection.

Assessment of study quality

Study quality was assessed independently by two reviewers who used 12 criteria (result was a percentage score) to examine issues such as sample size, allocation concealment, data collection methods, level of attrition and description of the population. Studies that scored less than 65% were not used to form conclusions. Disagreements were resolved by consensus.

Data extraction

Data were extracted by one author and checked by another.

Methods of synthesis

Results were presented by outcome reported. Mean outcome percentages were calculated.

Results of the review

Sixty-seven studies were included in the review. All studies had quality scores greater than 65%.

Addiction (24 studies: 17 retrospective and seven prospective, n=2,507). The mean percentage of addiction was 3.3% overall (range 0 to 45%, mean exposure time was 26 months) and 0.2% in studies that preselected for no previous history of addiction versus 5% in the not-selected group.

Aberrant drug-related behaviours (total number of studies reported as 17, but eight retrospective and 10 prospective were included, n=2,466). The mean rate of aberrant drug-related behaviours was 11.5% (range 0 to 45%, mean exposure time 10.8 months) and 0.59% in studies that preselected for no previous history of aberrant drug-related behaviour versus 11.2% in the not-

selected group.

Urine toxicology (five studies: two retrospective and three prospective, n=1,965). Illicit drugs were found in a mean of 14.5% of patients (range 4% to 57%). Exposure time reported by one study was 36 months.

Further results were reported.

Authors' conclusions

Chronic opioid analgesic therapy exposure will lead to abuse/addiction in a small percentage of chronic pain patients; a larger percentage will demonstrate aberrant drug-related behaviours and illicit drug use. Percentages appeared much less if patients were preselected for an absence of current or past history of alcohol/illicit drug use or abuse/addiction.

CRD commentary

The review addressed a clear question supported by appropriate inclusion criteria. Four databases were searched (handsearches were also undertaken) to identify all relevant studies. It appeared that methods to minimise the risk of reviewer error and bias were used for both the data extraction and quality assessment processes, but no details were reported for the study selection process. Study quality was assessed adequately and the results were used to inform the interpretation of the review findings. Study details were tabulated, but details on participant groups were often not presented (when they were presented, there appeared to be clinical heterogeneity between studies). The authors acknowledged that absence of opioid dose reporting in the studies could confound the results. Several different opioids were studied, and both the addiction and behaviour outcomes had a percentage range of 0 to 45%. The pooling of such heterogeneous data from both prospective and retrospective studies raises questions about the reliability and generalisability of the results. The authors' conclusions should be interpreted with caution.

Implications of the review for practice and research

Practice: The authors stated that clinicians can be relatively certain that opioid exposure will lead to abuse/addiction in a relatively low percentage of chronic pain patients. Chances of abuse/addiction development can be significantly decreased by preselecting patients. Clinicians should routinely use aberrant drug-related behaviour lists and urine toxicology tests to fully assess levels of incidence.

Research: The authors listed a number of conduct/reporting-related recommendations for future prospective studies. The authors suggested that future reviewers should utilise the same inclusion/exclusion criteria as used in the authors' review.

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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.

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CRD has determined that this article meets the DARE scientific quality criteria for a systematic review.

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