

Management of substance
dependence review series

Systematic review of
treatment for
amphetamine-related
disorders



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and Substance Dependence

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ABSTRACT

The ease of synthesis from inexpensive and readily available chemicals makes possible the wide spread of amphetamine dependence and abuse. During the phase of chronic, high-dose consumption of amphetamines, many amphetamine users may have the experience of paranoia and hallucination. In addition, amphetamine withdrawal has been less studied although it is a common problem with a prevalent rate of 87% among amphetamine users. The objective of this review is to search and determine risks, benefits and costs of a variety of treatments for amphetamine dependence or abuse, psychosis and withdrawal. Electronic searches of MEDLINE (1966 - December 2000), EMBASE (1980 - February 2001), CINAHL (1982 - January 2001) and Cochrane Controlled Trials Register (Cochrane Library 2000 issue 4) were undertaken. References to the articles obtained by any means were searched. All relevant randomised controlled trials (RCTs) and clinical controlled trials (CCTs) were included. Participants were people with amphetamine dependence or abuse, amphetamine psychosis and amphetamine withdrawal diagnosed by any set of criteria. Any kinds of biological and psychological treatment both alone and combined were examined. A variety of outcomes, for example, number of treatment responders, score changes, were considered. Two reviewers evaluated and extracted the data independently. The dichotomous data were extracted on an intention-to-treat basis in which the dropouts were assigned as participants with the worst outcomes. For amphetamine dependence or abuse, short-term treatment of fluoxetine significantly decreased craving. Medium-term treatment of imipramine significantly increased the duration of adherence to treatment. No treatment for amphetamine dependence or abuse had benefits on a variety of outcomes, including amphetamine use. The comprehensive searches found no controlled trials of treatment for amphetamine psychosis meeting the criteria for considering studies. For amphetamine withdrawal, amineptine had some benefits in the respects of discontinuation rate and global state. However, no direct benefit of amineptine on amphetamine withdrawal symptoms or craving was shown. The evidence about the treatment for amphetamine dependence and abuse, amphetamine psychosis and amphetamine withdrawal is very limited. At present, no available treatment has been demonstrated to be effective in the treatment of amphetamine dependence or abuse, psychosis and withdrawal.

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INTRODUCTION

Rationale for this series of systematic reviews on the treatment of amphetamine-related disorders.

Healthcare providers, consumers, researchers, and policy makers are inundated with unmanageable amounts of information. We need systematic reviews to efficiently integrate valid information and provide a basis for rational decision making. Systematic reviews establish where the effects of healthcare are consistent and research results can be applied across populations, settings, and differences in treatment (e.g. dose); and where effects may vary significantly. The use of explicit, systematic methods in reviews limits bias (systematic errors) and reduces chance effects, thus providing more reliable results upon which to draw conclusions and make decisions. Meta-analysis, the use of statistical methods to summarise the results of independent studies, can provide more precise estimates of the effects of healthcare than those derived from the individual studies included in a review.

Wider recognition of the key role of reviews in synthesising and disseminating the results of research has prompted people to consider the validity of reviews. In the 1970s and early 1980s, psychologists and social scientists drew attention to the systematic steps needed to minimise bias and random errors in reviews of research. It was not until the late 1980s that people drew attention to the poor scientific quality of healthcare review articles. However, recognition of the need for systematic reviews of healthcare has grown rapidly and continues to grow, as reflected by the number of articles about review methods and empirical studies of the methods used in reviews the number of systematic reviews published in healthcare journals, and the rapid growth of the Cochrane Collaboration.

The ease of synthesis from inexpensive and readily available chemicals makes possible the wide spread of amphetamine dependence and abuse. During the phase of chronic, high-dose consumption of amphetamines, many amphetamine users may have the experience of paranoia and hallucination. In addition, amphetamine withdrawal has been less studied although it is a common problem with a prevalent rate of 87% among amphetamine users. A systematic review relevant to the treatment of amphetamine dependence or abuse, psychosis and withdrawal, therefore, would be helpful in providing evidence-based medical services for people with amphetamine-related disorders.

This review was conducted using the Cochrane Collaboration standards for preparing systematic reviews. An electronic version of this report will be published as a Cochrane Review, and will be updated to include new evidence as it emerges.

BACKGROUND

The evidence from both in vivo and in vitro studies has shown that amphetamine administration increases concentration of monoamines in the synapse by inducing their release, blocking their uptake, or both (Seiden et al, 1993). They are toxic to dopamine and/or 5-hydroxytryptamine neurons (Seiden & Sabol, 1996). The duration and magnitude of these effects are dose dependent and are accompanied by different degrees of recovery. The results of a recent study show that methamphetamine users have dopamine transporters reduction in the striatum associated with motor slowing and memory impairment (Volkow et al, 2001).

Although amphetamines are classified as stimulants, their pharmacological actions appear to be different from those of other stimulants, including cocaine. While dopamine re uptake blockade, in particular in the nucleus accumbens, is generally believed to be the most important action of cocaine, it is generally agreed that enhancing the release of dopamine in the nucleus accumbens is of major importance in mediating amphetamines reinforcing and psychomotor stimulant effects (Altman et al, 1996). While other types of stimulants such as cocaine, which act through storage pools of catecholamines, amphetamines increase the release of newly synthesized norepinephrine and dopamine (Ellinwood & Petrie, 1977). The pharmacological effects of amphetamines also last longer than cocaine.

Because amphetamine dependence or abuse, psychosis and withdrawal are prevalent amphetamine-related disorders, only the treatment for these conditions are included in this review. Although there are a variety of amphetamines and amphetamine derivatives, the word "amphetamines" in this review stands for amphetamine, dextroamphetamine and methamphetamine only.

AMPHETAMINE DEPENDENCE OR ABUSE

Amphetamines produce feelings of euphoria and relief from fatigue, may improve performance on some simple tasks, increase activity levels, and produce anorexia. The abuse liability of the amphetamines is thought to be primarily related to their euphorogenic effects (King & Ellinwood, 1997). However, their dependence and abuse are viewed as resulting from a process in which multiple interacting factors (social, psychological, cultural, and biological) influence drug-using behaviour (Jaffe, 2000).

Amphetamines have been abused almost since their introduction. Taken intravenously, the abuse potential of amphetamines is comparable to that of heroin or cocaine (Kramer et al, 1967). The ease of synthesis from inexpensive and readily available chemicals makes possible the wide spread of amphetamine dependence and abuse. Two major epidemics of amphetamine dependence and abuse were widely recognized in 1960s and 1990s. These epidemics, in particular the recent one, affect many developed and developing countries around the world, in particular North America, Europe, Far East Asia, and Australia. Of 180 million people worldwide consuming drugs in the late 1990s, 29 million people of them were taking amphetamine-type stimulants (United Nations Office for Drug Control and Crime Prevention, 2000). This figure was larger than the number of people consuming cocaine and opiates combined.

Routes of amphetamine administration and patterns of amphetamine use are complex, not stable and various among different individuals or cultural groups. While smoking, injecting and oral taking are prevalent routes of administration, there have been some reports of amphetamine sniffing or snorting. The patterns of amphetamine use may be classified as follows (World Health Organization 1997):

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