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Review

The course of chronic solvent induced encephalopathy: A systematic review

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ABSTRACT

Background: Worldwide millions of workers are exposed to organic solvents. Long term exposure leads in some workers to the development of Chronic Solvent induced Encephalopathy (CSE). The first reports about CSE came from the European Nordic countries in the 1970s. In spite of decades of experience with this disease, little is known about the course and prognostic factors of CSE.
Objective: To provide an overview of the evidence about the course and prognostic factors of CSE.
Methods: A systematic review was conducted. Databases PubMed, PsycINFO (1970–2008) and EMBASE (1980–2008) were searched with the search strategy: solvent AND follow up AND (encephalopathy OR chronic intoxication). Inclusion criteria were: written in English, study population of CSE patients, follow-up time of at least 1 year. Included articles were assessed on methodological quality.
Results: Sixty unique articles were retrieved of which sixteen met the inclusion criteria. Data extraction provided information about domains of neurology, neuropsychology, physical and mental health perceptions, and social consequences. In a number of studies no significant changes, and in other studies improvement of functioning could be measured. Prognostic factors resulting from included studies were summarized for each domain indicating a potential positive influence of younger age and lower exposure variables.
Discussion: Due to the large heterogeneity of methodology no levels of evidence could be obtained. This review shows that there is a need for future research that addresses a variety of domains of functioning, hopefully resulting in an overall prognostic model for CSE.
Conclusion: Studies in this review are in agreement about CSE being a non-progressive disease in which no severe deterioration of functioning occurs after diagnosis. In a number of studies no significant changes, and in other studies improvement of functioning could be measured. Presumably cessation of exposure might be one of the causal factors for the non-progressive character of the disease as has been found. Future studies are needed to clarify the role of various prognostic factors on the course of CSE.

Contents

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1. Introduction

Worldwide millions of people are occupationally exposed to organic solvents. These are people working for example as spray painter, printer, industrial cleaner, paint or glue manufacturer. After inhalational or dermal uptake the group of organic solvents is capable of affecting neuronal structures in the brain due to their lipophilic and hydrophilic properties; Organic solvents can be absorbed by fatty tissue and in cell membranes. The resulting neurotoxic effects may be experienced as nausea, dizziness, headache, and problems in concentration. When workers are exposed to solvents during many years, some workers develop a syndrome, characterized by complaints that remain chronic (White and Proctor, 1997). Various denominations exist for this syndrome that we refer to as Chronic solvent induced encephalopathy (CSE), for example: 'occupational solvent encephalopathy', 'solvent intoxication', 'toxic solvent syndrome', 'painters disease', 'psycho-organic syndrome', and 'chronic toxic encephalopathy'. Patients with CSE often complain about fatigue, mood changes, memory loss, difficulty in concentration, loss of initiative and headache. Unlike the acute neurotoxic effects, the symptoms do not disappear after cessation of exposure to organic solvents, but often continue to exist.

In the 1970s the first reports about CSE came from the European Nordic countries (Hänninen et al., 1976; Arlien-Søborg et al., 1979). Since then many studies have been published, most focused on exposed workers and far less studies on CSE patients. In 1985 the effects of solvents were discussed in a WHO meeting resulting in a proposal for a classification system (WHO, 1985). A short time later at a meeting in Raleigh a similar classification system was proposed (Baker and Seppäläinen, 1986). Both systems are listed in Table 1. Van der Hoek et al. (2000) showed that in spite of these efforts, only few studies did use either the WHO or Raleigh classification system to diagnose CSE patients.

Although there is still some controversy about the underlying mechanisms of the diffuse brain damage, a general consensus has been reached about the clinical description of the CSE syndrome (White and Proctor, 1997).

The diagnostic process of CSE is a multidisciplinary process, which involves the disciplines of neurology, neuropsychology, industrial hygiene, toxicology, and occupational medicine. Sometimes psychiatry is involved. As CSE is regarded as a diagnosis "per exclusionem", all other possible causes for the syndrome have to be ruled out. Unfortunately, blood tests or brain imaging techniques are not yet available to diagnose CSE, although promising fMRI techniques (Visser et al., 2008) might develop into new diagnostic tools. At present the diagnosis of CSE relies on verification of substantial long term exposure to organic solvents, a relation in time between exposure and onset and course of symptoms and signs, neuropsychological assessment to objectify cognitive impairment associated with the diffuse brain damage due to the chronic exposure to solvents, and exclusion of other etiologies (WHO, 1985; Baker and Seppäläinen, 1986).

Little is known about the course of CSE after diagnosis, especially after exposure has ceased. Knowledge about the course and the role of prognostic factors could improve the understanding of the disease process, and education and advise to patients with CSE and others involved. More knowledge of prognostic factors may also provide key information towards new treatment and rehabilitation strategies. CSE is a relatively mild disease, although with great consequences for functioning in daily life, and with no existing effective treatment other than preventing further deterioration and treating the comorbid (psycho)pathology, prevention of exposure has the highest priority.

The main objectives of this systematic review are to provide an overview of the evidence about the course of CSE after diagnosis and to summarize the available knowledge about prognostic factors. The following questions are addressed:

1. What is the course of the neurological, neuropsychological and psychiatric impairment, the health perceptions and social functioning of CSE patients?
2. Which prognostic variables at time of diagnosis predict the outcome of neurological, neuropsychological and psychiatric impairment, the health perceptions and social functioning of CSE patients at least 1 year later?
3. Are there associations between the course of impairment on neurological functioning, neuropsychological functioning, psychiatric functioning, health perceptions and social functioning of CSE patients?

2. Methods

2.1. Selection of literature

Databases PubMed, PsycINFO (1970–2008) and EMBASE (1980–2008) were searched. Taken the recommendations of Altman (2001) and Schaafsma et al. (2006) into account, the following search strategy was chosen: *solvent AND follow up AND* (*encephalopathy OR chronic intoxication*). Since the terms 'Chronic Solvent Induced Encephalopathy' or related terms are not MeSH terms, the search terms were used as text words in all fields. Two neuropsychologists (EvV and EW) independently extracted studies from the literature search and references of the retrieved articles were checked. Papers were selected if they met the following criteria: they were written in English, the study population consisted of patients with diagnosed CSE, and the follow-up time was at least 1 year. Case studies were excluded.

2.2. Quality assessment

Two neuropsychologists (EvV and EW) independently assessed the methodological quality of the first five selected studies. As the quality assessment of the first five studies did not result in differences, it was decided that EvV continued the quality assessment alone. Eventual doubts on the quality assessment were discussed with EW and solved in consensus.

A standardized checklist was used to assess the quality of the studies. This checklist was a modified version of the checklist used by Kuijpers et al. (2004) for assessing the quality of prognostic cohort studies. The checklist is divided into different subheadings