

Is there an association between hepatitis C infection and fibromyalgia syndrome?

SYSTEMATIC REVIEW PROTOCOL

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1. Background

1.1 Rationale for the review

This proposed review is an update and expansion of work carried out as part of a larger study examining depression, anxiety, pain and quality of life in people living with chronic hepatitis C (Brunton et al 2015).

Fibromyalgia syndrome (FS), a disorder characterized by widespread muscular pain and tenderness at various anatomical sites called tender points (Wolfe et al 2011), is present in almost 3% of the general population and over 4% of females (Queiroz 2013). Fibromyalgia has been identified as a frequently occurring co-morbid condition in those with chronic HCV infection. The cause of fibromyalgia has not yet been identified (Rahman et al 2014), but a higher prevalence of FS and chronic pain in patients with viral infections has been commented upon (Buchwald et al 1996, Cassisi et al 2001, Ribeiro and Proietti 2005, Buskila et al 2008). Several studies examining the association between FS and HCV infection have now accumulated.

Research investigating the relationship between chronic HCV infection and FS may help to elucidate the aetiology of FS and raise awareness of potential comorbidity (Palazzi et al 2005). Recognition and management of FS in chronic HCV patients provides an opportunity to enhance quality of life.

1.2 Aims of review

The systematic review is being carried out in order to clarify the nature of the relationship between HCV infection and FS in adults. The following research questions will be addressed:

1. What is the prevalence of FS in those who are, or who have been infected with HCV?
2. Is HCV infection associated with an increased risk of FS?
3. Is a diagnosis of FS associated with an increased risk of HCV infection?
4. Does the available evidence suggest a causal role for HCV in the pathogenesis of FS?

2 Methods

2.1 Searching

Potentially relevant citations will be located through three sources: key informants, bibliographic database searches, and reference lists of included studies.

2.1.1 Key informants

Authors of included journal articles will be asked for any further relevant studies.

2.1.2 Bibliographic database searches

Bibliographic database sources of economic and sexual health literature will be searched, including:

- Pubmed
- EMBASE
- CINAHL Plus
- Psycinfo
- HMIC
- LILACs
- WHOLIS
- WHO-EVIPNET
- OpenGrey
- Zetoc

Database searches will not be limited by publication date. Search strings based on a combination of free-text and database-specific terms will be developed in collaboration with an information scientist. The concepts to be combined will include: (fibromyalgia) AND (hepatitis C). An example showing the PubMed search string is provided below. Located citations will be uploaded into EPPI-Reviewer software, for management of retrieval, coding and synthesis (Thomas et al 2010).

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((("Hepatitis C"[tiab] OR CHC[tiab] OR HCV[tiab] OR "hep C"[tiab] OR "Hepatitis C"[mh] OR "Hepatitis C, chronic"[mh]))) AND (fibromyalgia[tiab] OR "Fibromyalgia"[mh])
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Grey literature will be sourced via Google Scholar and the OpenGrey and Zetoc databases.

2.1.3 Citation searching

Reference lists of all included studies will be searched for potentially relevant research.

2.2 Screening for study inclusion/exclusion

2.2.1 Eligibility criteria

Citations will be assessed first on the basis of title and abstract. The full publication of studies meeting inclusion criteria will be retrieved and assessed again for inclusion. Two reviewers will select studies independently and then meet to resolve any disagreements. To be included studies must:

- be empirical epidemiological research (other than case reports or case series)
- concern HCV infection
- concern fibromyalgia syndrome or symptoms

2.5 Coding

Data extraction will be carried out using a standardised form. Two reviewers will code studies independently and then meet to resolve any disagreements. Studies will be coded according to characteristics of interest including:

- study design
- year of publication
- country of study
- sample size
- participant characteristics
- measure of HCV status
- diagnostic criteria for fibromyalgia

2.6 Quality appraisal

Risk-of-bias and methodological quality of primary studies will be assessed using an appropriate criteria (e.g. Munn et al (2014) for prevalence studies, von Elm et al (2007) for observational studies). Two reviewers will appraise studies independently and then meet to resolve any disagreements.

2.7 Synthesis

Odds ratios will be pooled across studies through meta-analysis, using either fixed effects or random effects models. Two sets of models will be constructed to examine: (i) the odds of Hepatitis-C among patients with Fibromyalgia Syndrome; and (ii) the odds of Fibromyalgia Syndrome among patients with Hepatitis-C. Heterogeneity will be assessed

using Higgins' I^2 and we will explore potential sources of heterogeneity using study-level characteristics as appropriate. Publication bias will be assessed through examining funnel plots and tested using Egger's test (Egger et al 1997) and Begg's test (Begg and Mazumdar 1994).

3 References

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