INPLASY PROTOCOL

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Oxidative and Anti-oxidative stress-linked biomarkers in Ankylosing Spondylitis: a systematic review and meta-analysis

Li, J[1]; Liu, S[2]; Cui, Y[3].

Review question / Objective: **How does the level of oxidative and/or anti-oxidative stress-linked biomarkers change in patients with Ankylosing Spondylitis?**
Condition being studied: **Ankylosing Spondylitis is the major subtype of spondyloarthritis that affects the axial skeleton, causing inflammatory back pain, which can lead to impairments in structure and function and a decrease in quality of life. The main pathological manifestation in the early stage of Ankylosing Spondylitis is inflammatory response at joints. Many studies support that oxidative stress and inflammation are interdependent and interconnected. A number of reactive oxygen species(ROS) accumulating at the site of inflammation can lead to exaggerated oxidative damage, which can generate by-products such as malondialdehyde. In addition, a number of ROS and oxidative stress products enhance pro-inflammatory responses. Current studies of the level of oxidative and anti-oxidative stress biomarkers in Ankylosing Spondylitis show inconsistent findings. Thus, exploring the changes of oxidative and anti-oxidative stress biomarkers in Ankylosing Spondylitis is of great significance and may help identify the pathogenesis of Ankylosing Spondylitis.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 May 2020 and was last updated on 15 May 2020 (registration number INPLASY202050066).

INTRODUCTION

Review question / Objective: **How does the level of oxidative and/or anti-oxidative stress-linked biomarkers change in patients with Ankylosing Spondylitis?**

Condition being studied: **Ankylosing Spondylitis is the major subtype of spondyloarthritis that affects the axial skeleton, causing inflammatory back pain, which can lead to impairments in structure**

and function and a decrease in quality of life. The main pathological manifestation in the early stage of Ankylosing Spondylitis is inflammatory response at joints. Many studies support that oxidative stress and inflammation are interdependent and interconnected. A number of reactive oxygen species(ROS) accumulating at the site of inflammation can lead to exaggerated oxidative damage, which can generate by-products such as malondialdehyde. In addition, a number of ROS and oxidative stress products enhance pro-inflammatory responses. Current studies of the level of oxidative and anti-oxidative stress biomarkers in Ankylosing Spondylitis show inconsistent findings. Thus, exploring the changes of oxidative and anti-oxidative stress biomarkers in Ankylosing Spondylitis is of great significance and may help identify the pathogenesis of Ankylosing Spondylitis.

METHODS

Search strategy: PubMed, Web of Science and Cochrane Library databases from inception to April 2020 will be used to collect all relevant published articles. We will used the following terms: ("oxidative", "oxidation", "oxidant", "oxidat*", "antioxidant", "antioxidative", "antioxidat*" "redox") and ("spondylitis, ankylosing", "spondyloarthritis ankylopoietica", "ankylosing spondylarthritis", "ankylosing spondylarthritides", "spondylarthritides, ankylosing", "spondylarthritis, ankylosing", "ankylosing spondylitis", "spondylarthritis ankylopoietica", "bechterew disease", "bechterew's disease", "bechterew s disease", "marie strumpell disease", "marie strumpell disease", "rheumatoid spondylitis", "spondylitis, rheumatoid", "spondylitis ankylopoietica", "ankylosing spondyloarthritis", "ankylosing spondylarthritides", "spondylarthritides, ankylosing", "spondyloarthritis, ankylosing" "axial spondyloarthritis", "peripheral spondyloarthritis", "radiographic axial spondyloarthritis"), and the combinations of these keywords.

Participant or population: Patients with Ankylosing Spondylitis.

Intervention: no.

Comparator: Control group - people without Ankylosing Spondylitis.

Study designs to be included: Case-control study, Cohort study.

Eligibility criteria: To be included, studies should meet the following eligibility criteria: assessment of oxidative or anti-oxidative stress biomarkers in any type of samples from AS patients; case-control or cohort study; English language full-text publication.

Information sources: PubMed, Web of Science and Cochrane Library databases from inception to April 2020 will be used to collect all relevant published articles. We will used the following terms: ("oxidative", "oxidation", "oxidant", "oxidat*", "antioxidant", "antioxidative", "antioxidat*" "redox") and ("spondylitis, ankylosing", "spondyloarthritis ankylopoietica", "ankylosing spondylarthritis", "ankylosing spondylarthritides", "spondylarthritides, ankylosing", "spondylarthritis, ankylosing", "ankylosing spondylitis", "spondylarthritis ankylopoietica", "bechterew disease", "bechterew's disease", "bechterew s disease", "marie strumpell disease", "marie strumpell disease", "rheumatoid spondylitis", "spondylitis, rheumatoid", "spondylitis ankylopoietica", "ankylosing spondyloarthritis", "ankylosing spondylarthritides", "spondylarthritides, ankylosing", "spondyloarthritis, ankylosing" "axial spondyloarthritis", "peripheral spondyloarthritis", "radiographic axial spondyloarthritis"), and the combinations of these keywords.

Main outcome(s): The concentration of oxidative or anti-oxidative stress biomarkers.

Additional outcome(s): The concentration of oxidative or anti-oxidative stress biomarkers in active patients; the concentration of oxidative or anti-oxidative stress biomarkers in inactive patients.

Data management: Stata 15.1.

Quality assessment / Risk of bias analysis: We will use the Newcastle-Ottawa scale to assess the quality of the studies.

Strategy of data synthesis: We will extract the following data from included studies: mean oxidative and anti-oxidative stress marker concentrations, sample size, publication year, disease activity, diagnostic criteria, age, gender. Two reviewers will extract the data, and the disagreement between two reviewers will be resolved by the third author. The continuous variable will be recorded as mean and standard deviation, and then analyzed by Stata software to derive standardized mean difference and 95% confidence intervals. I^2test will be used to examined the study heterogeneity. I^2>50% is considered as significant heterogeneity, a random-effect model will be used. A fixed-effects model will be employed when $I^2 \leq 50\%$.

Subgroup analysis: If the data are sufficient, we will perform the subgroup analysis according to the type of biomarkers and sample source.

Sensibility analysis: Sensibility analysis will be conducted if the included studies are sufficient.

Language: English.

Country(ies) involved: China.

Keywords: Ankylosing Spondylitis; oxidative stress; anti-oxidative.

Contributions of each author:
Author 1 - Jiaxiao Li - search strategy; study selection; data analysis; quality assessment of studies; writing of the article.
Author 2 - Suling Liu - search strategy; study selection; data analysis; quality assessment of studies; writing of the article.
Author 3 - Yang Cui - search strategy; study selection; data analysis; quality assessment of studies; writing of the article.