Revista de Gastroenterología de México. 2014;79(2):135–144

REVISTA DE GASTROENTEROLOGÍA DE MÉXICO

www.elsevier.es/rgmx

REVIEW ARTICLE

The role of oxidative stress in the development of alcoholic liver disease☆

M. Galicia-Moreno[a], **G. Gutiérrez-Reyes**[b,*]

[a] *Adscrita al laboratorio de Hígado, Páncreas y Motilidad (HIPAM), Unidad de Investigación en Medicina Experimental, Facultad de Medicina, UNAM, México D.F., México*
[b] *Jefa del laboratorio de Hígado, Páncreas y Motilidad (HIPAM), Unidad de Investigación en Medicina Experimental, Facultad de Medicina, UNAM, México D.F., México*

Received 13 December 2013; accepted 26 March 2014
Available online 14 July 2014

KEYWORDS
Oxidative stress;
Cirrhosis;
Alcoholism;
Antioxidants;
Mexico

Abstract
Background: Alcohol is the most accepted addictive substance worldwide and its consumption is related to multiple health, economic, and social problems. The liver is the organ in charge of ethanol metabolism and it is susceptible to alcohol's toxic effects.
Objetivos: To provide a detailed review of the role of oxidative stress in alcoholic liver disease and the mechanisms of damage involved, along with current information on the hepatoprotective effectiveness of the molecules that have been studied.
Materials and methods: A search of the PubMed database was conducted using the following keywords oxidative stress, alcoholic liver damage, alcoholic cirrhosis, and antioxidants. There was no time limit for gathering all available information on the subject at hand.
Results: According to the literature reviewed, oxidative stress plays an important role in the pathogenesis of alcoholic liver damage. Molecules such as reactive oxygen species (ROS) and reactive nitrogen species (RNS), formed during ethanol metabolism, structurally and functionally modify organic molecules. Consequently, biologic processes are altered and hepatocytes are sensitized to the action of cytokines like tumor necrosis factor-α, as well as to the action of endotoxins, activating signaling pathways such as those controlled by nuclear factor kappa B, extracellular signal regulated kinases, and mitogen activated protein kinase.
Conclusions: Oxidative stress plays an important role in the development of liver damage resulting from alcohol consumption. The molecules that have currently displayed a hepatoprotective

☆ Please cite this article as: Galicia-Moreno M, Gutiérrez-Reyes G. Papel del estrés oxidativo en el desarrollo de la enfermedad hepática alcohólica. Revista de Gastroenterología de México. 2014;79:135–144.

* Corresponding author.
E-mail address: gabgurey@yahoo.com.mx (G. Gutiérrez-Reyes).

effect in preclinical and clinical trials must be studied further so that their effectiveness can be confirmed and they can possibly be used as adjuvant treatments for this disease.

PALABRAS CLAVE
Estrés oxidativo;
Cirrosis;
Alcoholismo;
Antioxidantes;
México

Papel del estrés oxidativo en el desarrollo de la enfermedad hepática alcohólica

Resumen
Antecedentes: El alcohol es la sustancia adictiva más aceptada mundialmente y su consumo está relacionado con múltiples problemas de salud, económicos y sociales. El hígado es el órgano encargado del metabolismo del etanol y es susceptible de sufrir los efectos tóxicos generados por este.
Objetivo: Proveer una revisión detallada del papel del estrés oxidativo en la enfermedad hepática alcohólica, los mecanismos de daño involucrados, así como información actual de moléculas cuya eficacia hepatoprotectora ha sido investigada.
Materiales y métodos: Se consultó la base de datos PUBMED utilizando como palabras clave: estrés oxidativo, daño hepático por alcohol, cirrosis alcohólica y antioxidantes, sin límite de tiempo para recabar toda la información disponible acerca de este tema.
Resultados: Conforme a la literatura consultada, el estrés oxidativo desempeña un papel importante en la génesis del daño hepático por alcohol. Moléculas como las *especies reactivas de oxígeno (ERO) y las especies reactivas de nitrógeno (ERN)*, formadas durante el metabolismo del etanol, modifican estructural y funcionalmente moléculas orgánicas alterando procesos biológicos y sensibilizando a los hepatocitos a la acción de citocinas como el factor de necrosis tumoral-α, así como a la acción de endotoxinas, activando rutas de señalización como las controladas por el factor nuclear kappa-B, las cinasas reguladas por la señalización extracelular 1/2 ERK1/2 y las proteína cinasa activada por mitógenos.
Conclusiones: El estrés oxidativo tiene un papel importante en el desarrollo del daño hepático por alcohol y las moléculas que actualmente han mostrado un efecto hepatoprotector en ensayos preclínicos y clínicos necesitan someterse a más estudios que demuestren su eficacia para considerarlos como tratamientos adyuvantes de esta enfermedad.

Introduction

The most socially accepted addictive substance worldwide is alcohol. The consumption of alcoholic beverages is a hallmark of social gatherings. However, in many societies the consumption of these beverages in excess represents serious health and economic problems.[1,2] Despite this fact, drinking in moderation is not considered a health risk.[3–6] Chronic or excessive alcohol consumption can put physical and mental health at risk, damaging different organs such as the brain, liver, heart, lungs, skeletal musculature, and bones. Its abuse is also associated with social problems, including traffic accidents, social violence, divorce, low productivity, child abuse, and other crimes.[7,8]

The liver is the main site of ethanol metabolism and the principal target organ of alcohol-induced damage. The susceptibility of the liver to alcohol-induced toxicity is due to the high concentrations of alcohol present in the portal blood, as well as to the metabolic consequences of ethanol metabolism. Alcoholic liver disease covers a spectrum of stages that includes steatosis (fatty liver), steatohepatitis, and in severe cases, fibrosis and/or cirrhosis.[9]

Hepatic fibrosis can be regarded as an integrated and highly dynamic cellular response to chronic liver damage.[10] Its progression is characterized by the perpetuation of necrosis of the parenchyma, chronic hepatitis, and qualitative and quantitative alterations in the composition of the extracellular matrix (ECM), while the activation of hepatic stellate cells (HSC) and the participation of macrophages and Kupffer cells predominate at the cellular level.[10–12] At the molecular level, growth factors, cytokines, chemokines, changes in ECM organization and composition, as well as oxidative stress-related molecules, are seen to play an important pathologic role.[10–12] The participation of oxidative stress in almost all clinical and experimental conditions of chronic liver disease of different etiologies, including alcohol consumption, has been demonstrated.[13–15]

Methods

The PubMed database was searched using the following keywords oxidative stress, liver damage from alcohol, alcoholic cirrhosis, antioxidants. There was no time limit and the