



THE COMPLEMENTARY VIEW OF CHEMICAL INDUCED HEPATOTOXICITY AND MANAGEMENT: A NARRATIVE REVIEW

Ayurveda

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ABSTRACT

The concept of chemical induced toxicity could be found even in hunting age. Though the concept is older, its significance is more remarkable in the current era. Present world is mixture of toxins, all of the living beings are part of it in actively or passively. The classical definition of the chemical toxicity is related to one chemical compound but, these days chemical compounds are common and hepatotoxicity is critical health issue. Hence the discussion of chemical induce toxicity is important, and trying to find successful detoxification strategy is crucial. Though having remarkable capabilities, the liver has limitation in advance damage and can worsen without proper management. Consequently, abstention from causative factors and symptomatic management is not enough to reverse the liver damage. Ayurveda, the practice of Indian system of medicine is a science addressed life from micro level to macro level, including all the concept that discuss in modern. In Ayurveda concept of visha (poison) is broad and informative and liver disease are comprehensively elaborated. Hence notion of contemporary science is crucial in the Chemical induced hepatotoxicity.

KEYWORDS

Liver, Hepatotoxicity, Detoxification, Ayurveda

INTRODUCTION

The liver is the largest internal organ within the body, making up approximately 2% of an adult's bodyweight (Molina, 2012) and is involving in number of functions in human body. This vital organ is responsible for carrying out metabolic function, detoxification process, production of bile, lipid and cholesterol homeostasis and processing xenobiotic compounds (Trefts, 2017) Parenchymal cells of the liver (eg hepatocytes) that make up about 70 percent of the liver mass and express very high levels of catalase, an enzyme that inhabits peroxisomes. Although hepatocytes comprise most of the liver mass, nonparenchymal cells, including Kupffer cells, sinusoidal endothelial cells, hepatic stellate cells, and liver-associated lymphocytes make up the remaining 15 to 30 percent of the liver mass. These nonparenchymal cells interact with hepatocytes and with each other via soluble mediators and by direct cell-to-cell contact. Each liver cell type plays a specific role in hepatic physiology (Natalia A. Osna, Donohue, & Kharbanda, 2007).

Ayurveda, the practice of Indian system of medicine days backed to more than 3500 years and is based on strong unique philosophical origin and scientific method that exceptional in itself. Basically, this science addressed life from micro level to macro level, including all the concept that discuss in modern science. Apart from that many natural and herbal base strategies are include in the system and practicing up to date. In the classical text of Ayurveda there is a separate chapter for toxicology known as the AgadaTantra. In this chapter all the theories related to the poison, toxin and toxic compounds, pathological changes, clinical manifestation, features and treatments for toxic condition were explained in detail.

Contemporary view of Chemical Induced Hepatotoxicity

A significant part in the digestion and expulsion of medications is undertaken by the liver. Detoxification of medications and xenobiotic in the liver by drug utilizing chemicals is a vital function in securing of homeostasis of the body (Singh, 2011). In case where the primary site of the drugs, chemical compounds and xenobiotic metabolism it is more vulnerable to damage. Liver injury caused by various toxic chemicals or their reactive metabolites is known as hepatotoxicity. Alcohol, drug overdose, industrial chemicals, natural chemicals like microcystins, herbal remedies and dietary supplements are hepatotoxicants (MohanH., .2002). Hepatotoxicity due to chemical is mostly connected with drugs and intoxication of alcohol in present. Antituberculosis drugs, paracetamol, carbon tetrachloride, erythromycin and its derivatives and methotrexate are known hepatotoxic chemicals (Singh A. B., 2011; Lee KJ, 2002) Though the frequent cause for acute liver failure in developed countries is pharmacological intoxication followed by acute hepatitis B is proven fact (David, 2014) but successful management is still pending.

Chemical induced toxicity occurs when particular chemical

metabolism is altered and results in liver damage attributed to oxidative stress, inflammatory damage, apoptosis, necrosis or mitochondrial membrane breakdown and organ dysfunction (Garcia-Cortes, 2020). These chemicals have xenobiotic action and most of them are highly lipophilic compounds, that are poorly excreted by the kidneys (Zakin D B. T., 1996) . Chemical induced liver injuries are related to several molecular pathways and their effects vary depending on individual factors. Therefore, predicting of adverse reaction is not easy. Cytochrome P450 enzymes are prominent in converting chemicals into metabolites. These metabolites may be chemically reactive and exert cellular stress through covalent bonding between host macromolecules and leading to oxidative stress damage, accumulation of toxic metabolites or trigger a cascade of immune responses ultimately leading to cell death (Villanueva-Paz, 2021) Due to the effect of covalent binding of chemical metabolites disfunction of hepatic mitochondria might be happen by involving in the mitochondrial electron transport chain, leading to an increased formation of reactive oxygen species (ROS), which is prematurely reacting with molecular oxygen (Russmann, 2009). ROS further neutralize an endogenous cellular anti-oxidant, Glutathione (GSH) and GSH stores might be insufficient to reduce free radicals to prevent cellular component damage. Meanwhile activation of other interrelated biochemical pathways of ROS production, results in high concentration that contribute to cell death. Likewise, from liver cell injury to cell death cascade of biological pathways are involved like mitochondrial paralyzing, ATP depletion, inflammatory process and changing immunity function. This biological process leads to hepatotoxicity or hepatic disorders and appeared several symptoms like fever, jaundice, anorexia, abdominal pain, fatigue, anemia, and liver enlarge in further (Kavita Gulati, 2018).

Complimentary View of Chemical Induced Hepatotoxicity

In Ayurveda concept of visha (poison) is broad and informative. Any substance that contains, after administrating to body makes vishada (anguish) attributes is called visha. The Vagbhata text book of Ayurveda, has mentioned that all kinds of poison can be divided into two parts: natural and artificial. In artificial poison, there are two sub divisions named as Gara visha and Dushi visha. Under the gara visha, different kind of chemical poisons found in combination of toxic or non-toxic ingredients, incompatible food, incompatible drugs or metal were included (Murthy, 2021) and dushi visha explained bio-accumulation of poisonous constituents. Further gara visha is considered a poison that has combination of low potency poisons whether it cause instant death or chronic poisoning as per the potency of particular poison. In the past, it was believed that, Gara visha was administered to the body via foods or ornaments. So, it is obvious that contact poison and internal poison have both been referred to. Correspondingly, the precautions that had to be taken are widely explained regarding Kings meal and consumers (Srikanta, 2003). Dushi Visha is considered an anirgata (remain or not fully excreted)

portion of any kind of poison. The bioaccumulation occurs as per the biological half-life (dehadashesha) of the particular chemical (Acharya, 1980).

Meanwhile identification and discussion of the yakrut (liver) in Indian knowledge date back to Vedic era. In ancient text, Rig Veda was mentioned liver and called it "Takima" or "Yakna" and treatment, the use of milk of the red cows was explained to the liver disease. Yakrut and Pliha (spleen) were considered to be the moola of raktavahasrotas (emerging of blood circulating channel) by Caraka. The other teacher Sushruta included raktavaha dhamani (blood circulating vessel) and indicated that Yakrut and Pliha are other seats of raktadhatu (blood tissue). The function of the yakrut is mentioned as converting anna rasa (digested foods) into the form of ranjaka (formation of nutrients) after digestion. Yakrut is further considered as site of bhutgnivayapara (metabolism), Malapitta nirmana (kind of metabolites) (Gulabkunverba, 1949).

Ayurveda has explained common base for the pathogenesis of any kind of disorders and it is based on five contributory factors introduced: Dosha (three governing power of body), Dhatu (organised structural element of body), Agni (metabolic mediator), Ama (semi digested foods complex) and Srotovagunya (Obstructed micro transportive channel of body). In liver disease all the causative factors contribute to vitiated Vata dosha (one of the prominent governing powers of the body) which results in visamagni (unbalance state of Agni) and imbalance of the function of pitta and Kapha (rest of the governing power of body) that leads to mandagni, (state of reduction of action of agni) which further vitiates Kapha and restrain the action of agni. Afterward, Ama results in obstruction of cellular transportation. This condition create imbalance in the normal function of the tissue called doshadhatu vaisamya. In the context of liver disease imbalance, it results in raktha dhatu and pitta dosha and it affects to raktavaha srotas moola which is yakrut or pleeha (Srikanta, 2003).

Yakrut Vikaras (Liver disorders) comprehensively elaborated in Ayurveda but in scattered form. All basic texts have explained liver disease in term of the structural and functional integrity which the liver is affected. These diseases are Kamala (conditions of Jaundice) and its types, Yakrutdora or Yakrutvidhi, (Enlargement of liver or hepatomegaly) Yakrutvidradhi (liver abscess) Raktapitta, (Kind of bleeding disorder) Jalodara (conditions of Ascites), Madatyaya (Alcohol Use Disorders) and Pittaja Jvara. (Fever due to vitiated pitta). Among these, the type of Udara roga (diseases in abdominal cavity) Yakrutdora, Yakrutvidhi, Jalodara, and Madatyaya bare a role of toxic in causative factors.

Udara roga is the disease in Ayurveda which is characterized by enlarge of abdomen due to collection of fluids, flatus or enlargement of the organs in abdominal cavity. Under this disease Yakrutdodara was mentioned. The some causative factors of the udara roga are, taken of excessive usna (hot potency), ksara (alkali) , vidahi (produce hot and acidity both in body), amla (acetic) foods, Gara visha, improper samsrajana karma (post operative activities of purification), viruddhahara oushadi, (Incompatible foods and drugs), vitiation of the channels of circulation, continued presence of ama (content of semi digestive food) in the body, intake of irritating foods and drinks, and atisantarpana (over nutrition) (Acharya, 2009). Mostly the causative factors of Udara roga related to poisonous, unhealthy, inappropriate or incompatible foods and kind of harmful chemical contents. Gara visha janya yakruth vikara lakshana are jwara, agnimanda (anorexia or weak digestive capacity), krusha (emaciate), pandu (pallor), Shawasa (dyspnea), Jwara (fever), peetha varnatha (jaundice) Shopa (Swelling), and Yakrutplihavridhi (Liver & Spleen enlarge). Finally, it clearly emphasizes all kind of udara roga including yakrut vikara terminated as Jalodara (asities) in critical stage. Hence the Udara roga is considered as a fatal disease (Ashtamahagada) clinical importance of yakrut roga is remarkable in Ayurveda system (Sharma, 2021).

Management

Ayurveda is holistic care which define health is the balance of body, mind and spirit through rejuvenation, regeneration, reversible imbalance, and self-realization. Vise versa imbalance cause to disease and Shodhana, (purification) Shamana (pacification) and Nidana Parivarajana (absentia from causative factors) are the main lines of treatment for any disease. In parallel with any kind of treatment application of Pathya (proper diet and regimen) and avoiding Apathya (improper diet and regimen) is as important as medicine in Ayurveda.

Pathya is proper Ahara (Diet) and Vihara (regimen) that give proper nutrition to body and mind, clear the micro channels of body. In liver disease it is essential to follow the criteria and advice of pathya and apathya are indicated in the classical text according to the aetiology, nature and the severity of the disease (Shastri, 2003). Special treatment procedures are explained for Yakrut vikara due to gara visha in the text. Vamana (emesis) and application of gold and silver with honey as primary treatments are explained and in chronic condition, special drug preparation known as agada are mentioned. Apart from that, in Udara roga milk is specially mention as pathya. Simultaneously detoxification drugs are placed in treatments. Both a single herb drug and formula are prescribed in the text. Some of these drugs are herbal and some are herbo-mineral preparations. Single herb preparation of Yasti Madhu (Glycyrrhiza Glabra), Bhumi Amla (Phyllanthus Niruri), Kirata tikta (Andrographis paniculata), Haridra (Curcuma Longa) Katuki (Picrorrhiza Kurroa) and Guduchi Tinospora Cordifolia are supreme drugs for liver disorders having hepatoprotective, detoxification and anti-inflammation action. The special preparation of Agada is best form of drug for detoxification treatment named: Bilwadi agada, Dushi Vishari agada and Maha agada which are in classical text (Murthy, 2021; Acharya, 1980). There are number of pathya kalpana that have been explained for yakrut vikara with special focus on body constitution of person and further dealing with the nature of the dosha imbalance. Hence, at the beginning of treatment the agni has to be corrected where the preparation of rice has mentioned Manda, Peya, Vilepi, Yavagu (different preparation of rice gruels) that help to increase Agni and reduce the production of Ama which is very vital in Yakrut vikara. Mamsa Rasa (meat soup) is a regular preparation as a protein supplement in Yakrut vikara (Sharma, 2021). Treatment of chemical induced hepatotoxicity in Ayurveda has broad spectrum from dietary management, behavioural modification to internal medicine in critical care.

DISCUSSION

Chemical induced hepatotoxicity is more compatible with gara visha janya yakrut vikara in Ayurveda. Both diseases mostly bare common root in, aetiology and clinical manifestation. It is obvious that normal function of liver is vital to human health and liver has ability to recover itself. Though the live has remarkable capabilities it has limitation in advance and can worsen without proper management. Consequently, abstention from causative factors and symptomatic management is not enough to reverse the liver damage. An incidentally complementary view is critical and crucial in this era. With this informative review, a ray of enlightenment can be brought to the common platform of scholars in different principles

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