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SURVEY ON KNOWLEDGE AND HERBAL INTAKE AMONG PATIENTS WITH ELEVATED LEVEL OF HEPATIC TRANSAMINASE ENZYMES IN MEDICAL WARD HUSM

by

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CERTIFICATE

This is to certify that the dissertation entitled Survey on Knowledge and Herbal Intake among Patients with Elevated Level of Hepatic Transaminase Enzymes in Medical Ward HUSM is the bonafide record of research work done by Khairunnisa Bt. Abas, Matric No. 87436 during the period of July 2008 to April 2009 under my supervision. This dissertation submitted in partial fulfillment for the degree of Bachelor of Health Sciences (Nursing). Research work and collection of data belong to Universiti Sains Malaysia

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RESEARCH TITLE: SURVEY ON KNOWLEDGE AND HERBAL INTAKE AMONG PATIENTS WITH ELEVATED LEVEL OF HEPATIC TRANSAMINASE ENZYMES IN MEDICAL WARD HUSM.

ABSTRACT

The purposes of this study are to determine the knowledge of herbal safety among patients with elevated level of Hepatic transaminase enzymes, to determine the type of herbal taken among patients and to examine the significant difference in alanine transaminase (ALT) and aspartate transaminase (AST) levels between patients in medical ward HUSM who take and do not take herbal. The use of traditional medication in Malaysia has increased from year to year and people now get more attracted to use a traditional medication like herbs in their health care although, the data about herbal intake and their safety in Malaysia are still lacking. This study recruited 50 patients as its respondents from medical ward and clinic in HUSM from July 2008 to March 2009. The research design used in this study was descriptive cross sectional design. This design was used to collect quantitative data. Descriptive statistic and non-parametric Mann Whitney U test were used in this study to analyze the data. The age of respondents are ranging from 30 years old to 90 years old. From the 50 respondents, (74%, n=50) of them were taking herbs while (26%, n=50) did not take herbal. From this study, the percentage of accurate knowledge regarding herbal safety is lower than the percentage of inaccurate knowledge among the respondent. Therefore, there is no knowledge regarding herbal safety among the respondents. There are significant difference in ALT and AST between patient take herbal or not (ALT, $p = 0.04$, AST, $p = 0.02$).

TAJUK KAJIAN: TINJAUAN BERKAITAN PENGETAHUAN DAN PENGAMBILAN HERBA DI KALANGAN PESAKIT YANG MEMPUNYAI TAHAP ENZIM HEPAR TRANSAMINASE YANG TINGGI DI WAD MEDIKAL HUSM.

ABSTRAK

Tujuan kajian ini dijalankan adalah untuk mengenalpasti tahap pengetahuan tentang keselamatan penggunaan herba di kalangan pesakit, mengenalpasti jenis herba yang diambil oleh pesakit dan mengkaji perbezaan signifikan tahap alanin transaminas (ALT) dan aspartat transaminas (AST) di antara pesakit yang mengambil herba atau tidak di wad medikal HUSM. Penggunaan ubatan tradisional di Malaysia telah meningkat dari tahun ke tahun dan penduduk kini banyak menggunakan ubatan tradisional contohnya herba dalam penjagaan kesihatan mereka. Namun begitu, data mengenai penggunaan herba dan tahap keselamatannya di Malaysia amat terhad. Kajian ini dijalankan ke atas 50 orang pesakit di wad dan klinik medikal di HUSM dari Julai 2008 sehingga Mac 2009. Kajian kuantitatif berbentuk deskriptif jenis keratan lintang digunakan untuk proses pengumpulan data. Statistik deskriptif dan ujian bukan parametrik 'Mann Whitney U' digunakan untuk menganalisis data yang diperolehi. Seramai 74% responden mengambil herba manakala 26% tidak mengambil herba. Kajian ini juga mendapati lebih ramai responden memberikan jawapan yang salah berbanding jawapan yang betul bagi pernyataan maklumat keselamatan herba. Hal ini menunjukkan responden tiada pengetahuan terhadap keselamatan herba. Terdapat signifikasi di antara tahap ALT dan AST dengan responden yang mengambil herba dan tidak (ALT, $p = 0.04$, AST, $p = 0.02$).

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Several recent surveys from Europe and the United State (US) have demonstrated a sharp rise in the use of botanical drugs within a few years and 21% of patients attending an out-patient liver clinic had taken herbal preparations, and 13% used herbal to treat liver diseases (Felix, Eleonora, & Detef, 2005). Another survey assessed the use of complementary medicine in the US and revealed a 380% rise in the use of herbals between 1990 and 1997 (Felix, Eleonora, & Detef, 2005). In Malaysia, the uses of herbal medication are increasing from year to year (Ernst, 2003). People take herbs to treat many kinds of diseases such as, diabetes mellitus, liver disease, gastrointestinal reflux disease, cancer, hyperlipidemia, hemorrhoid and also reproductive system diseases (Herbportal, 2004). Besides that, herbal also are using in beauty and body appearance maintaining in some people in Malaysia like for smooth skin, growing hair and diet for loosing their weight (Herbsportal, 2004). Moreover, herbal medication can maximize efficacy of western drugs and medical treatments, it also can be more effective than western drugs in treating chronic conditions and illness such as, diabetes and asthma (Han & Miller, 2003).

However, our knowledge of the potentials and risks of botanical drugs is still limited and efforts to elucidate them should be intensified. Therapies developed along the principles of conventional (Western) medicine are often limited in efficacy and

unaffordable for many individuals throughout the developing world (Felix, Eleonora, & Detef, 2005).

Hepatic damage from conventional drugs is widely acknowledged and most physicians are well aware of them. Herbals as a cause of adverse hepatic reactions, however, have only recently been recognized as their use has become more widespread (Felix, Eleonora, & Detef, 2005). Certain herbals have been identified as a cause of acute and chronic hepatitis, cholestasis, drug-induced autoimmunity, vascular lesions and even hepatic failure and cirrhosis. Risk factors for herbal toxicity have not been well identified, largely since hepatotoxic incidents have mostly been published as isolated case reports or small series (Felix, Eleonora, & Detef, 2005).

Hepatic transaminase tests such as alanine transaminase (ALT) and aspartate transaminase (AST) often are part of standard laboratory panels which included in Liver Function Test (LFT). ALT is the enzyme produced within the cells of the liver and the level of ALT abnormality is increased in conditions where cells of the liver have been inflamed or undergone cell death, as the cells are damaged, the ALT leaks into the bloodstream leading to a rise in the serum levels (Jonathan & Daniel, 2008).

According to Paul (2005), mild elevations in alanine transaminase and aspartate transaminase can reveal serious underlying conditions or have transient and benign etiologies. Potential causes of liver transaminase elevations include viral hepatitis, alcohol use, medication use, steatosis or steatohepatitis, and cirrhosis. The history should be thorough, with special attention given to the use of medications, vitamins, herbal, drugs, and alcohol; family history; and any history of blood-product transfusions (Paul, 2005).

1.2 Problem Statement

Herbal medicines are readily available in the market in health food section without prescriptions and are widely used all over the world. According to recent survey the majority of people who use herbal medicines do not inform their physicians about their consumption that can cause abnormal test result and confusion in proper diagnosis (Parmar, 2005).

Most individuals who take herbals do not admit their intake, even on repeated questioning, either because they do not consider herbals as 'drugs', or because they fear not to be taken seriously by their doctors for using herbals, furthermore, doctors who recommend herbals or patients who take them advocate the long-standing use of herbals in traditional medicine as proof of safety, in particular, since most herbals are available without prescriptions and at low costs, therefore, self-medication is frequent and, sometimes, patients even increase the dosage of herbal intake (Felix, Eleonora, & Detef, 2005).

Herbal hepatotoxicity has been recognized for many years, but the study and research about it is still less (Eran, Galia, Rifaat, Orit, Michal, Emilia, Lital, Zvi, Dorit, Boaz, & Danie, 2007). Toxic hepatitis is considered the most common adverse reaction resulting from use of herbs, for the majority of herbal, the proof of it's efficacy were by the anecdotal success and personal experience, frequently the driving force for acceptance of herbal in the population (Eran et al., 2007). On the other hand, reports on adverse reactions of herbal are numerous, but often lack the power to provide unequivocal evidence-based proof regarding the relative risk associated with intake of herbal (Eran et al., 2007).

For the examples, a 63 year-old Chinese woman presented with fulminate liver failure 4 weeks after taking herbal. The liver explants showed massive centrilobular necrosis with periportal ductular profileration and inflammation (Shivakumar & Geoffrey, 2000).

Interactions between herbal and chemical drugs are another source of problems associated with the intake of herbal compounds. As an example the St John's wort *Hypericum perforatum* (Felix, Eleonora, & Detef, 2005). Herbal can lead either to toxicity and make the treatment to become less effective (Kuo, Hawley, Weiss, Balkrishnan & Volk, 2004). This situation will make health professional especially doctors and nurses have a pressure, because they have to know the accurate data or information about their patients in given the effective treatment but, usually patients will not tell their health care provider the truth about the intake of herbal medications, this is proven by 43% the herbal user did not told their doctors or pharmacist about the herbal intake (Kuo et al., 2004).

Furthermore, the wrong intake of herbal species or wrong prescribed of herbal, wrong dosage of herbal intake and the belief of 'all natural are safe' are risk for the potential complication or side effects of the herbal. Nowadays people are still not aware about the safety of herbal and the information about the side effects and complications of herbal use also still lacking in world (World Health Organization, 2000).

Contrary to popular belief that 'natural are safe' herbal medicines can cause significant toxic effects, drug interaction and even morbidity or mortality (Parmar, 2005). Therefore, the data of awareness amongst people regarding the use of herbal and the possible complications associated with them are really important and needed (Parmar,

2005). Besides that, the data about the intake of herbal among the patients also important in providing the effective management of the patients and prevent any complications due to interaction between herbal medicines and conventional drugs (Woodward, 2005).

This study can be explained by the theory of Health Belief Model by Hochbaum, Rosenstock and Kegels, 1950 and the theory of factors that can cause elevation of Alanine Transaminase (ALT) and Aspartate Transaminase (AST) levels and induce the hepatic injury and necrosis.

1.3 Objectives

1.3.1 General Objectives

The objective of the study is to determine the knowledge of herbal safety among patients with elevated level of hepatic transaminase enzyme in medical ward HUSM.

1.3.2 Specific Objectives

The specific objectives are:

1. To determine the knowledge of herbal safety among patients with elevated level of hepatic transaminase enzyme in medical ward HUSM.
2. To determine the type of herbal taken among patients with elevated level of hepatic transaminase enzyme in medical ward HUSM.
3. To examine the significant difference in Alanine Transaminase (ALT) and Aspartate Transaminase (AST) levels between patients in medical ward HUSM who take and does not take herbal.

1.4 Research Questions

1. Is there any basic knowledge regarding herbal safety among patients in medical ward HUSM?

2. What type of herbal taken by patients in medical ward HUSM?

3. Is there any significant difference in Alanine Transaminase (ALT) and Aspartate Transaminase (AST) levels between patients in medical ward HUSM who take and do not take herbal?

1.5 Hypotheses

Null hypothesis (Ho): There is no significant difference in Alanine Transaminase (ALT) and Aspartate Transaminase (AST) levels between patients in medical ward HUSM who take and does not take herbal.

Alternate hypothesis (H_A): There is a significant difference in ALT and AST levels between patients in medical ward HUSM who take and does not take herbal.

Null hypothesis will be reject at $\alpha = 0.05$ and Alternate hypothesis will be accept.

1.6 Definitions

1.6.1 Herbal

Herbal materials include crude plant material such as leaves, flowers, fruit, seed, stems, wood, bark, roots, rhizomes or other plant parts, which may be entire, fragmented or powdered (World Health Organization, 2000). In this study, herbal are the selected roots, leafs and oats that have been process in modern way to become tablets, cream, capsule and drinks.

1.6.2 Herbal Intake

The process of taking herbal into the body through the mouth (as by eating) (Dictionary.com, 2008). In this study, researcher wants to know what kind of herbal intake by the patients in medical ward HUSM.

1.6.3 Hepatic Transaminase Enzymes

Hepatic transaminase enzymes consist of alanine transaminase (ALT) and aspartate transaminase (AST). ALT is the enzyme produced within the cells of the liver and the level of ALT abnormality is increased in conditions where cells of the liver have been inflamed or undergone cell death (Jonathan & Daniel, 2008). Alanine transaminase (ALT), also called serum glutamic pyruvate transaminase (SGPT) or alanine aminotransferase (ALAT) is an enzyme present in hepatocytes (liver cells). When a cell is damaged, it leaks this enzyme into the blood, where it is measured. ALT rises dramatically in acute liver damage. The normal value of ALT: 5-35 IU/L (Gale Encyclopedia of Medicine, 2002).

Aspartate transaminase (AST), also called serum glutamic oxaloacetic transaminase (SGOT) or aspartate aminotransferase (ASAT) is similar to ALT in that it is another enzyme associated with liver parenchymal cells. Level increased in acute liver damage, but is also present in red cells and cardiac and skeletal muscle and is therefore not specific to the liver. The normal value of AST: 0-35 IU/L (Gale Encyclopedia of Medicine, 2002).

Therefore, in this study, the researcher wants to know is there any increasing value of ALT and AST levels if the patients take the herbal.

1.7 Significant of Study

This study is very important because the uses of herbal medication in development countries are increase from year to year (Ernst, 2003). Malaysia for example is one of the countries that rich with the sources of herbal plants in the world (Ernst, 2003). However, information regarding herbal usage the data and a number of patient who utilize the herbs are difficult to find (Azriani, 2007). Therefore, the accurate data about the intake of herbs among patients in Malaysia is still lacking (Azriani, 2007). Besides that, the awareness about the complications and the side effects of herbal use is still lower among people (Jacqueline, Colleen, Lincoln, James, Chao & Sandra, 2007).

Therefore, the data about relationship between herbal use with ALT and AST levels and the awareness of complications of herbal is really important to health professional like doctors and nurses because of some herbal can give the adverse effect to patient's health especially to the liver (Felix, Eleonora, & Detef, 2005). Furthermore, the efficacy of the herbal to treat other disease like cardiovascular and endocrine diseases is still in research and did not has enough or accurate information and data yet (Paul, 2005). Therefore, this study could help doctors and nurses gain new knowledge about herbs in given the good and effective treatment or care to their patients. Furthermore, this study also will be very helpful to the other study or research like study of uses of herbs and disease process also the herbal as a treatment method. Herbal safety is in concern in order to create awareness of herbal safety and efficacy among people, doctors, nurses and other health professionals.

CHAPTER 2

LITERATURE REVIEWS

2.1 Alanine Transaminase (ALT) and Aspartate Transaminase (AST)

AST and ALT are jointly known as transaminases. They are associated with inflammation and/or injury to liver cells, a condition known as hepatocellular liver injury; damage to the liver typically results in a leak of AST and ALT into the bloodstream (Palmer, 2004).

Because AST is found in many other organs besides the liver, including the kidneys, the muscles, and the heart, having a high level of AST does not always (but often does) indicate that there is a liver problem (Palmer, 2004).

The normal ranges for AST and ALT are around 0 to 40 IU/L and 0 to 45 IU/L respectively (IU/L stands for international units per liter and is the most commonly accepted way to measure these particular enzymes.) (Jonathan & Daniel, 2008). Following the same reasoning, if the liver was damaged years before by excessive alcohol use the results of a blood test done today may be normal, but a damaged liver may still be present (Palmer, 2004).

To confuse issues even further, there are many other factors besides liver injury that could affect the levels of AST and ALT. For example, males have higher transaminase levels than females and, African-American men have higher AST levels compared with Caucasian men and also people appear to have higher transaminase levels in the morning and afternoon than in the evening (Palmer, 2004).

Elevations of the transaminases occur due to so many causes that they give the doctor only a vague clue of the diagnosis. Additional testing is required in order to determine more precisely what is wrong with the liver. Some possible causes of elevated transaminase levels include the following:

- Viral hepatitis
- A fatty liver
- Alcoholic liver disease
- Drug/medication-induced liver disease
- Autoimmune hepatitis
- Herbal toxicity
- Genetic liver diseases
- Liver tumors

(Palmer, 2004)

2.2 Herbal

The increasing popularity of herbal medicines is based on their perceived effectiveness in the treatment and prevention of disease, the belief that these treatments are 'natural' and therefore safe, a feeling of better control of the disease and its management, and a holistic philosophy behind complementary medicine that pays tribute to the patients' desire for wellness and quality of life in nature's womb, which apparently is not provided by conventional health care (Felix, Eleonora, & Detef, 2005).

Dissatisfaction with conventional medicine due to lack of treatment success in many instances, unfavorable side effects, lack of time with the doctor and insufficient empathy from health care providers also contribute to herbal medicine's appeal, in addition, most countries do not impose prescription regulations upon herbal preparations and, therefore, access to this kind of therapy is unrestricted and cheap (Felix, Eleonora, & Detef, 2005). According to study of herbal medicine use in parturients by Hapner et al, 2002, the prevalence of herbal intake is 7.1% among the respondents.

2.3 Herbal Hepatotoxicity

ALT and AST are two of the most reliable markers of hepatocellular injury or necrosis, their level can be elevated in a variety of hepatic disorders (Paul, 2005). Although levels of ALT and AST can be extremely elevated (exceeding 2,000 U per L in cases of hepatocyte injury and necrosis related to drugs, toxins, ischemia and hepatitis), elevation less than five times the upper limit of normal (250 U per L and below) are much more common in primary care medicine (Paul, 2005). The range of possible etiologies at this level of transaminase elevation is broader and the tests less specific and herbals are the one cause of adverse hepatic reactions or the elevated of transaminase level (Paul, 2005). Table 2.1 lists selected herbal supplements that may cause elevated transaminase levels.

Table 2.1: Common Agents That Can Cause Liver Transaminase Elevations

Common Agents That Can Cause Liver Transaminase Elevations
Herbal supplements
Chaparral leaf
Ephedra
Gentian
Germander
Jin bu huan
Kava
Scutellaria (skullcap)
Senna
Shark cartilage

(Pratt & Kaplan, 2000)

2.4 Herbal and Safety

In the United State, herbs are labeled dietary supplements which are not expected to meet the standards for drugs specified in the Federal Food, Drug, and Cosmetic Act and the only requirement is that these preparations follow the standards set forth in the Dietary Supplement and Health Education Act (DSHEA) issued in 1994 which allows marketing without prior approval of their efficacy and safety by the Food and Drug Administration (FDA), while, DSHEA allows manufacturers to claim that the sold product affects the body or its function, as long as there is no allegation that it prevents or treats certain diseases (Felix, Eleonora, & Detef, 2005). Therefore, this simplified

licensing practice does not guarantee efficacy and safety in the same strict way as with the approval of conventional medications and treatments (Felix, Eleonora, & Detef, 2005).

2.5 Herbal-Drug Interaction

The following are the examples of known interaction between popular herbal and over-the-counter drugs.

1. **Hawthorn**, touted as effective in reducing angina attacks by lowering blood pressure and cholesterol levels, should never be taken with Lanoxin (digoxin), the medication prescribed for most for heart ailments. The mix can lower your heart rate too much, causing blood to pool, bringing on possible heart failure (Holistic online, 2007).
2. **Ginseng**, according to research, can increase blood pressure, making it dangerous for those trying to keep their blood pressure under control. Ginseng, garlic or supplements containing ginger, when taken with the blood-thinning drug, Coumadin, can cause bleeding episodes. In rare cases, ginseng may overstimulate resulting in insomnia. Long term use of ginseng may cause menstrual abnormalities and breast tenderness in some women. Ginseng is not recommended for pregnant or lactating women (Holistic online, 2007).
3. **Garlic** capsules combined with diabetes medication can cause a dangerous decrease in blood sugars. Some people who are sensitive to garlic may experience heartburn and flatulence. Garlic has anti-clotting properties (Holistic online, 2007).

4. **Goldenseal** is used for coughs, stomach upsets, menstrual problems and even arthritis. However, the plant's active ingredient will raise blood pressure, complicating treatment for those taking antihypertensive medications, especially beta-blockers. For patients taking medication to control diabetes or kidney disease, this herb can cause dangerous electrolyte imbalance. High amount of consumption can lead to gastrointestinal distress and possible nervous system effects. Not recommended for pregnant or lactating women (Holistic online, 2007).
5. **Feverfew**, believed to be the natural remedy for migraine headaches, should never be taken with Imitrex or other migraine medications. It can result in the patient's heart rate and blood pressure to raise dangerous levels (Holistic online, 2007).
6. **Guarana**, an alternative remedy being used as a stimulant and diet aid, contains 3 percent to 5 percent more caffeine than a cup of coffee. So, if you are taking any medication that advises you against taking any drink with caffeine, you should avoid taking this stimulant. It may cause insomnia, trembling, anxiety, palpitations, urinary frequency, and hyperactivity. Avoid during pregnancy and lactation period. Long term use of Guarana may lead to decreased fertility, cardiovascular disease, and several forms of cancer (Holistic online, 2007).
7. **Kava**, an herb that has antianxiety, pain relieving, muscle relaxing and anticonvulsant effects, should not be taken together with substances that also act on the central nervous system, such as alcohol, barbiturates, anti depressants, and antipsychotic drugs (Holistic online, 2007).

8. **St. John's Wort** is a popular herb used for the treatment of mild depression.The active ingredient of St. John's Wort is hypericin. Hypericin is believed to exert a similar influence on the brain as the monoamine oxidase (MAO) inhibitors such as the one in major antidepressants. Mixing MAO inhibitors with foods high in tyramine, an amino acid, produces one of the most dramatic and dangerous food-drug interactions. Symptoms, which can occur within minutes of ingesting such foods while taking an MAO inhibitor, include rapid rise in blood pressure, a severe headache, and perhaps collapse and even death. Foods high in tyramine include aged cheese, chicken liver, Chianti (and certain other red wines), yeast extracts, bologna (and other processed meats), dried or pickled fish, legumes, soy sauce, ale, and beer (Holistic online, 2007).
9. **White Willow**, an herb traditionally used for fever, headache, pain, and rheumatic complaints may lead to gastrointestinal irritation, if used for a long time. It exhibits similar reactions as aspirin (aspirin is derived from white willow). Long term use may lead to stomach ulcers (Holistic online, 2007).

2.6 Conceptual Framework

The Health Belief Model (HBM) is a psychological model that attempts to explain and predict health behaviors (Glanz, Rimer, & Lewis, 2002). This is done by focusing on the attitudes and beliefs of individuals. The HBM was first developed in the 1950s by social psychologists Hochbaum, Rosenstock and Kegels working in the United State Public Health Services. The model was developed in response to the failure of a free tuberculosis (TB) health screening program (Glanz, Rimer, & Lewis, 2002). The HBM is based on the understanding that a person will take a health-related action if that person