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Review article

Do herbal medicines negatively affect liver tests? A systematic review of Korean clinical studies on safety☆

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Abstract

Introduction: The use of herbal medicine (HM) is common, but there are concerns about the potential adverse effects of HMs on liver function. This study aimed to assess the effect of Korean HM in studies where liver function was measured. Additionally, the incidence of liver injury following the use of Korean HM was investigated.

Methods: This study involved systematic searches of eleven Korean Medical databases and two journals related to HM research through December 2013. All articles that reported clinical trials in which any type of human patient was treated with any type of HM were included. Three independent authors reviewed the literature based on specific inclusion and exclusion criteria.

Results: 43 studies met the inclusion criteria. 23 studies were performed prospectively. In terms of the incidence rate of liver injury, none of the prospective studies reported liver injury rate incidences. One study reported 3 cases of liver injury and another study reported 5 cases of liver injury in patients treated with HM in retrospective studies. Additionally, 4 case reports were on liver injury patients who were treated with HM. All retrospective studies were case-series studies. Among the prospective studies, 6 studies were randomized controlled trials, and 2 studies were case-control studies.

Conclusions: There was insufficient evidence suggesting that the use of HMs affected patients' liver injury incidence. The risk of liver injury caused by HMs is thought to be small, but it could not be determined whether this was the case for individual HMs due to both the heterogeneity of the patients and the range of HMs prescribed.

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Keywords: Korean herbal medicine; Safety; Liver injury; Hepatotoxicity; Hepatitis; Drug-induced

Introduction

Korean herbal medicine has had a long tradition of use outside of conventional medicine in Korea. It originally referred to those medicinal substances recorded in Chinese material medica [1]. However, it is different from herbal drugs which are usually those medicinal substances not recorded in Chinese material medica or only used in folk medicine, but are also called medicinal herbs [1]. The acceptance of herbal medicines (HMs) usage is growing with improvements in their quality control and associated regulations; advances in clinical research have also shown the value of HMs in the treatment and prevention of disease [2–5].

Drug-induced liver injury is defined as liver dysfunction caused by drugs, both HMs and conventional medicine, and it is diagnosed using strict criteria after excluding pre-existing liver diseases, such as hepatitis, infectious diseases, and biliary tract disease [6].

There are two medical systems in Korea: one is the conventional medical system and the other is the traditional Korean medical system, and these operate independently. As HM is used widely and is common in Korea, many conventional medical

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Table 1
Liver test follow-up for patients taking HMs in prospective studies.

[Ref] no.	Author (year)	Study design	Study population *N*(male) Average age(mean ± SD)	Patients' disease	Prescribed HM	Co-medication with other medicine	Measured liver tests	Duration of medication	Incidence rate liver injury
[11]	Kim (1993)	Case series Safety	52(26) 64.8 ± 9.8	Cerebrovascular disease	Unrestricted Herbs	Yes	AST, ALT, ALP	4 weeks	0/52
[12]	Kim (1998)	Case series Safety	13(8) 65.2 ± 15.7	Cerebrovascular disease	Woohwanhcheongsim-whan	NR	AST, ALT, ALP	4 weeks	0/13
[13]	Lim (2001)	Case series Safety	34(19) NR	Acute low back pain (Low back sprain 25, HIVD 9)	Whuallak-tang	No	AST, ALT, ALP	32 patients with 7-13days use of HM 1 patient with 14-20days use of HM 1 patient with more than 21days use of HM	0/34
[14]	Chung (2002)	Case series Safety efficacy	19(7) 63.0 ± 11.0	Cerebrovascular disease with hypertension	Samhwangsasim-tang	NR	AST, ALT	2 weeks	0/19
[15]	Hwang (2002)	Case series Safety	27(11) 50.7 ± 11.8	Bronchial athma	Socheongryong-tang	NR	AST, ALT, GGT	8weeks	0/27
[16]	Yoon (2002)	Case series Safety	54(22) 67.0 ± 17.8	Cerebrovascular disease	Unrestricted Herbs	Yes	AST, ALT	11 weeks	0/54
[17]	Bae (2003)	Case series Efficacy, safety	41(0) NR	Obesity	Bangpungtongsung-san extracts	NR	AST, ALT	8 weeks	0/41
[18]	Kim (2003)	Case-control Efficacy, safety	49(21) 59.6 ± 8.7	Hyperlipidemia	Chunghyuldan	No	AST, ALT	8 weeks	0/49
[19]	Song (2003)	Case series Efficacy, safety	38(0) 31.6 ± 11.5	Obesity	Slimdiet®	NR	AST, ALT, GGT	6 weeks	0/38
[20]	Seong (2004)	Case series Safety	15(4) 57.8 ± 10.4	Acute cerebrovascular disease with headache	Pasaekhwalhyeol-tang	NR	AST, ALT	2 weeks	0/15
[21]	Lee (2005)	Case series Safety	14(9) 11.0 ± 2.6	Obesity	Taeeumbiman-tang	No	AST, ALT, ALP, DB, TB	4 weeks	NR
[22]	Park (2005)	Case-control Efficacy, safety	42(25) 51.5 ± 9.2	Cerebrovascular disease high risk patients	Tongxinluo®	NR	AST, ALT	8 weeks	0/42
[23]	Seo (2005)	RCT Efficacy, safety	42(8) 57.5 ± 6.6	Degenerative arthritis	Jetongdan	Yes	AST, ALT	8 weeks	0/42
[24]	Paeck (2006)	Case series Efficacy, safety	160(120) age interval frequency analysis	Mental retardation, cerebral palsy, developmental disability, developmental speech disorder	Unrestricted HM	Yes	AST, ALT, ALP, GGT, TB, DB, LDH	More than 16 weeks	0/160