



RESEARCH ARTICLE

Effects of Intravenous Pharmacopuncture with Harmonizing and Releasing Formulas on Hepatic Recovery after Partial Hepatectomy in Rats



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Abstract

The objective of this study was to find out the effect of intravenous pharmacopuncture on hepatic recovery after partial hepatectomy in rats. Male Sprague–Dawley rats were randomly divided into five groups: normal group, control group, saline group, and two experimental groups. Except for those in the normal group, the rats underwent partial hepatectomy. Those in the control group did not receive any treatment. Those in the saline group received an intravenous injection with saline. Those in the two experimental groups received intravenous pharmacopuncture with SihoJigak-tang or DanchiSoyo-san extracts (10 mg/kg). Serum total bilirubin and liver regeneration rate were measured on Day 7 after partial hepatectomy. Intravenous pharmacopuncture with SihoJigak-tang significantly increased the liver regeneration rate, and intravenous pharmacopuncture with DanchiSoyo-san significantly decreased serum total bilirubin after partial hepatectomy.

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1. Introduction

Partial hepatectomy is required in the presence of primary or secondary liver tumors [1]. Liver cancer is the leading cause of death in Korea, especially for people in their 40s or 50s [2]. In fact, liver transplantation is the only option in many cases of acute liver failure and end-stage liver

disease. However, liver transplantation is not a general therapy due to the limited supply of donated livers [3]. Therefore, partial hepatectomy is performed more often than liver transplantation. It is generally considered that partial hepatectomy is warranted due to the large hepatic mass; however, it poses a high risk of fulminant hepatic failure [1].

Posthepatectomy liver failure is the leading cause of postpartial hepatectomy death (>60%) [4]. Many risk factors are already known, which are related to the patient's comorbidity, underlying liver disease, treatments received, and the type of resection. The principal risk of liver resection is posthepatectomy liver failure, which is mainly related to the quality and the volume of the remnant liver. Posthepatectomy liver failure incidence varies from 0% to 2% after resection on healthy parenchyma, but can reach 7% after major partial hepatectomy. Posthepatectomy liver failure on cirrhotic liver ranges from 0% to 10% after limited resection and reaches >30% after major partial hepatectomy. To prevent posthepatectomy liver failure, physicians are trying various methods, such as portal vein embolization, two-stage hepatectomy, and splenectomy [5].

To recover well from partial hepatectomy and to avoid postoperative hepatic failure, morphological regeneration and functional restoration may be concerned. A previous study [6] reported that GamiSoyo-san (GSS) intravenous pharmacopuncture (intravenous injection of herbal extract) promoted the restoration of liver function, but not the regeneration of liver tissue after partial hepatectomy in rats.

On the basis of Korean medical theory, GSS is one of the formulas to treat Lesser Yang syndrome [7], including the diseases in half-exterior and half-interior [7], the diseases in the liver and gall bladder, and their meridians. These medicinal formulas are called harmonizing and releasing formulas [7].

From the previous study [6], we came up with an idea that these formulas may be applied to the patients who are going through a partial hepatectomy. Through a literature study on the classics of Korean medicinal prescriptions, two harmonizing and releasing formulas; SihoJigak-tang (SJT) and Danchisoyo-san (DSS) were selected for the present study.

Due to the low metabolic rate and the unconscious state of the patient, oral administration of herbal medicine is not appropriate after partial hepatectomy. Considering this problem, intravenous pharmacopuncture was applied in the present study, as it was in the previous study [6].

As a preliminary experiment to investigate the effects of harmonizing and releasing formulas on the recovery from partial hepatectomy, we performed intravenous pharmacopuncture with SJT and DSS, and analyzed the liver regeneration rate and serum total bilirubin (TBIL) after a partial hepatectomy in rats.

2. Materials and methods

2.1. Animals

Male Sprague–Dawley rats (aged 7 weeks, 247.54 ± 17.06 g; DaeHanBiolink, Chungcheongbuk-do, Korea), were acclimated to the housing facility (2–3 rats/cage, $22 \pm 2^\circ\text{C}$,

$20 \pm 3\%$ humidity, 12-hour light/dark cycle) for 1 week. The animals were allowed free access to standard rat chow and water during this period. The rats were fasted overnight before the experiment, but were given free access to water. The animals were randomly allocated to five groups: normal group, control group, saline group, SJT group and DSS group. Except for those in the normal group, the rats underwent partial hepatectomy. Those in the control group did not receive any treatment. Those in the saline group received an intravenous injection with saline. Those in the SJT and DSS groups received intravenous pharmacopuncture with SJT or DSS extracts. Five rats were assigned to each group.

This study was approved by Daejeon University Institutional Animal Care and Use Committee (Approval no. DJUAR2015-002).

2.2. Medicinal herbs

The herbs were purchased from the Daejeon Korean Medicine Pharmacy (Daejeon, Korea), and washed using an ultrasonic cleaner (Branson 5210R; Branson Ultrasonics, Danbury, CT, USA) for 1 hour and dried using a dry oven (FD-600M; JEIO TECH, Daejeon, Korea) at 60°C . The compositions of SJT and DSS and the amounts of the herbs in these two formulas are listed in Tables 1 and 2, respectively.

2.3. Herbal extracts

The herbs of each formula were ground and mixed well. Fifteen grams of each formula compound was diluted with 70% ethanol (150 mL), which was extracted using Soxhlet Apparatus System at 80°C for 1 hour, and filtered using Whatman Filter Paper (Cat No. 1001 150; Whatman International, Maidstone, UK). The ethanol was removed using a rotary evaporator (N-1000; EYELA, Tokyo, Japan) at a reduced pressure and the residues (SJT: 0.43 g, DSS: 1.2 g) were gained.

The extract of each formula (0.270 g) was dissolved in 100 mL phosphate-buffered saline and put in a sterilized container. The container was sealed and kept at room temperature.

2.4. Partial hepatectomy

Partial hepatectomy was carried out following Higgins and Anderson's method [8]. Under anesthesia with avertin (0.3 g/

Table 1 Composition of SihoJigak-tang.

Scientific name	Amount (g)
<i>Bupleurum falcatum</i> Linne	12
<i>Scutellaria baicalensis</i> Georgi	8
<i>Platycodon grandiflorum</i> A. De Candolle	8
<i>Citrus aurantium</i> Linne	8
<i>Pinellia ternata</i> Breitenbach	4
<i>Zingiber officinale</i> Roscoe	4
<i>Zizyphus jujuba</i> Miller var.	4
<i>Glycyrrhiza uralensis</i> Fischer	2
Total amount	50

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