中藥治腦方劑對腦缺氧治療效果之研究

Therapeutic Effects of Chinese Medicine on Ischemic Stroke-A Study of Cerebral Active Regimens

中文摘要

腦血管老化會導致腦中風，而腦中風是國人第二大死因，更是老年人最常見的疾病之一。利用核磁共振攝影，可快速診斷是否有腦中風引起之腦組織缺血，其至腦細胞老化引起腦梗塞，但在治療腦中風方面，西醫仍無有效藥物可供使用。中藥治腦方劑流傳已久，用以治療腦中風，但仍無科學化的證據顯示的確有療效。本研究目的即在探討這些中藥治腦方劑，是否具保護缺血腦組織之作用。

本研究採大白鼠大腦皮質缺血動物模式來測試中藥方劑之療效。使用大白鼠重約 450+ 50 公克，利用 chlorohydrate (400mg/kg)腹腔注射麻醉，再利用顯微手術，把雙側頸動脈及右側中大腦動脈結紮，60 分鐘後再放開，使大皮質血管恢復流通。48 小時後，大白鼠再次麻醉，取腦作 2% 的 triphenyltetrazollium chloride (TTC) 染色梗塞皮質區則呈白色。

實驗的第一階段，以十五種不同的治腦方劑逐一測試其對缺血性損傷之療效。這些方劑依臨床病患服用方式調理，然後灌食大白鼠 3 天，再行暫時性血管結紮手術。48 小時後再測動物大腦皮質梗塞體積。

實驗的第二階段，以第一階段中有效果的五種治腦方劑測試其對缺血性損傷之治療效果。這五種方劑在大白鼠先行暫時性血管結紮手術後，灌食兩天後犧牲，再測動物大腦皮質梗塞體積。

兩次實驗的主要發現爲：第一階段中在各組實驗動物分別餵食不同的治腦方劑 3 天後 (依給於人體的計量換算成動物的計量後，依其體重給予每天兩次的餵食) ，實行中大腦動脈結紮 60 分鐘後放鬆血管以產生腦梗塞，如此動物經過 48 小時的恢復後犧牲，取腦進行 TTC 染色並計算腦梗塞的體積以比較與對照組 (無治療組)的差異。我們完成十五種治腦方劑的測試，包括十全大補湯、右歸飲、聖愈湯、補陽還五湯、五苓散、牛黃丸、育生丸、小續命湯、四逆湯、參附湯、大柴胡湯、血府還瘀湯、健翎湯、復元活血湯、與黃耆五物湯等十五種。

在計算過各組之腦梗塞體積與統計後，各組之體積 mean+ SEM mm3 (如表一) ，統計後之圖表 (如圖一)。我們發現其中牛黃丸、育生丸、小續命湯與黃耆五物湯對於我們所測試之急性缺血造成之腦組織損傷有保護的作用 (mean+ SEM mm3 分別爲牛黃丸 152.3+ 21.0；育生丸 115+ 10.4；小續命湯 137.6+ 30.8；黃耆五物湯 94.4+ 29.3 與對照組 203+ 9.03)。另外我們發現在參附湯這一組動物中僅發生 50% 的腦梗塞機率。

第二階段的主要發現係以第一階段中有效果的五種治腦方劑餵食已行暫時性血管結紮手術的大白鼠，兩天後犧牲，取腦切片進行 TTC 染色並計算腦梗塞體積比較與對照組的差異。發現有兩組腦梗塞體積有顯著縮小，分別是參附湯、育生

丸(mean+SEM mm3 參附湯 134+12.5；育生丸 118+16.4)。(如表二、三，圖二)
由兩次的實驗結果，初步發現有急性腦缺血的保護作用的這幾種治腦方劑爲牛黃丸、育生丸、小續命湯、黃耆五物湯、參附湯。再進一步探討其對於急性腦缺氧的治療效果。以這五種中藥方劑繼續進行動物實驗，研究其對於腦缺血治療效果，結果發現參附湯及育生丸兩種中藥方劑對於急性腦缺氧者有顯著治療效果。

英文摘要

Stroke is the leading cause of handicaps in Taiwan. It can be diagnosed at the very ealiest time when the cerebral artery is occluded. However, there is no any drug proven to be clinically effective in the protection of the ischemic brain. Many Chinese herbs have been used for treating stroke for more than thousands of years. But no one has been proven scientifically to be effective. The purpose of this study was to test scientifically in stroke animals with 15 Chinese herbs which have been considered effective Chinese medicines for treating stroke patients, so that we could find out some potential useful Chinese herbs for clinical use in stroke patients.
Sprague-Dawly rats weighing 450+50g were used. In the first stage, these animals were divided into 16 groups. Each group of animals were fed for 3 days with one kind of Chinese herb medicine chosen from lists of the more frequently and effectively used by Chinese herb medical doctors for treating stroke patients. The control group was fed with saline. Thereafter, the animals were anesthetized and subjected with a transient occlusion of the carotids and the right middle cerebral arteries for 1 hour. The brains of these animals were perfused with saline and stained for 30 minutes with 2% TTC 48 hours after brain reperfusion.
Our results showed that the brain infarction volume of the control animals was 203+9.03 mm3 (mean+SEM). The mean infarction volumes of the groups treated with the 15 herb medicines were listed in Table 1. and figured in Figure 1. Among the 15 treatment groups, five had significant lower infarction volume than the control.
Liu Hung Wang (牛黃丸), Yu San Wang (育生丸), Siu Su Ming Tang (小續命湯), Hung Chi Wu Wu Tang (黃耆五物湯), and San Fu Tang (參附湯) were effective in prevention of ischemic brain injury.
In the second stage, those animals were divided into 6 groups. Five groups of animals underwent ligation procedures and the other one as control. Five ligation groups were fed for 2 days with one kind of 5 effective Chinese herb medicines demonstrated in the first stage of the experiment and the control group fed with normal saline.
The results of the second stage showed that two groups had significant lower infarction volume than the control group. The mean infarction volumes of the groups treated with the five herb medicines were listed in Table 2. and figured in Figure2.

In conclusion, San Fu Tang (參附湯)、Yu San Wang (育生丸) deserved further investigation for clinically treating ischemic brain injury.

Key words: stroke, cerebral ischemia, infarction volume, Chinese herb