



北京中醫藥大學

BEIJING UNIVERSITY OF CHINESE MEDICINE

博士研究生學位論文

題 目：加味玉女煎治療退行性膝
關節炎的研究

專 業：方劑學

研究方向：古方新用的研究

博 士 生：王邦旺

導 師：謝 鳴 教授

二〇〇五年五月

中文摘要

退行性膝关节炎是以膝关节疼痛、僵硬及活动受限为主要表现。患此病的人，从年青到老年，从举步艰难到寸步难行，痛苦不堪，生活质量很差。由于病因及发病机理尚未完全阐明，目前缺乏有效药物和方法治疗。

本文以中医和西医治疗退行性膝关节炎的经验为背景，通过对与该病有关的中医历代文献资料的复习，在归纳本病的中医病机和治法方药的基础上，结合中医“肾主骨，肝主筋，阳明（胃）主宗筋束骨而利关节”的理论和新加坡本病的发病学特点，提出新加坡退行性膝关节炎的主要中医证候类型和其“劳伤过度，肝肾虚损，阳明蕴热，风湿痹阻，筋骨失养”的病机特点及“滋养肝肾，清泻阳明为主，兼行祛风除湿、舒经通络”治法思路；在立法思路指导下，以著名古方玉女煎的配伍和功效特点为依据，并在此方的基础上稍予加味（加味玉女煎）作为本病的治疗方剂，通过临床观察加味玉女煎治疗退行性膝关节炎的疗效。

本研究包括理论探讨和临床研究二部分：玉女煎治疗退行性膝关节炎理论与经验基础；加味玉女煎颗粒治疗退行性膝关节炎的临床研究。

研究一、玉女煎治疗退行性膝关节炎的理论探讨

从退行性膝关节炎的中医病名着手，分析前人有关本病类似病症的病机认识，认为退行性膝关节炎属于痹-痿证之范畴，其含义包括了本病以筋骨劳伤和肝肾不足为发病之背景，与痹证早期以客邪为主有所不同；疾病过程中，风寒湿热以及痰瘀等邪气客于膝部引起突出症状并促进病变之发展，与痿证以脏腑虚损、组织失养为主有所不同。从本病发病学、脏腑经脉定位、前人有关痹痿证的辨治经验的不同方面，阐发了本病以肝肾虚损为背景，复受外邪，经络瘀滞的基本病机；结合新加坡地域环境、新加坡人体质、生活习惯、发病特点以及药物治疗反应等特点，认为较之于中国大陆，本病新加坡患者偏于阴虚内热，瘀热阻络型。概括新加坡本病发病的主要病机为：肝肾不足，阳明蕴热，火热循经，或夹风冷或湿热或瘀血，经络瘀阻，筋骨失养。并根据中医阳明胃主宗筋束骨而利关节，肾主水生髓充骨，涵木荣筋的理论、古方玉女煎胃肾并治，清养并施，标本兼顾，存阴撤热之制方原理以及该方临床用于肾阴不足、牙齿松动或老年虚火牙痛或痛风性关节炎等经验，提出本方具有滋肾清火、荣筋壮骨、通络止痛等多向潜在功效和具有治疗本病用途的推测。

研究二、加味玉女煎颗粒治疗退行性膝关节炎的临床研究

采用前瞻性分组对照方法，对理论上提出的加味玉女煎方治疗退行性膝关节炎的疗效进行临床验证。临床设计中结合中医药的辨治特点，充分考虑到膝关节局部症状与局部外的其他症状、膝关节疼痛主症与中医证候中的症征特点，在总体疗效、局部疗效以及各症状改善等不同层面对加味玉女煎的疗效进行较为全面的考察和作用特点分析，以体现综合中、西医疗效评价标准和探讨中医的药证关系的学术特点。

临床研究中的二组入选病例治疗前在主症、局部症状、中医全身症状以及综合症状积分等方面经统计学处理无显著差异，疗效具有可比性。临床观察到，中药加味玉

女煎和阳性对照药吡罗昔康治疗退行性膝关节炎的总体有效率相当,但中药加味玉女煎组在临床显愈疗效上优于吡罗昔康。加味玉女煎和吡罗昔康对本病膝局部疗效的总有效率相当,其中加味玉女煎和吡罗昔康给药10天时膝关节局部均可显示疗效,但吡罗昔康对于膝关节局部改善效应随给药时间延长则更为突出。提示吡罗昔康在局部症状改善方面可能较加味玉女煎优。

临床观察到,加味玉女煎能明显改善膝局部之外的如心烦、口渴、牙齿松动、腰膝酸软症、舌象、脉象等中医症征;吡罗昔康虽对口渴、牙齿松动、腰膝酸软和舌质显示一定疗效,但显效时间较迟,效果不及加味玉女煎。

给药时程与疗效关系的分析中发现,加味玉女煎和吡罗昔康给药10天即出现明显疗效,之后随着给药疗程的增加,疗效也不断提高。其中吡罗昔康组在给药的第10天疗效变化最为明显,加味玉女煎于给药第20天后疗效呈明显的递进趋势。临床提示加味玉女煎或吡罗昔康治疗退行性膝关节炎的给药时间均不宜少于4周。

本次研究还观察到,在门诊随机就诊的100例退行性膝关节炎患者中,中医肝肾不足、气滞血瘀证的分布率明显高于风寒湿阻型,提示新加坡退行性膝关节炎患者发病的中医证型主要为肝肾不足型和气滞血瘀型。而在中医证候分型与疗效关系的分析中发现,加味玉女煎组和吡罗昔康对中医各型的总有效率无明显差异,但加味玉女煎组对肝肾不足和气滞血瘀两型的近愈率高于风寒湿阻型,且明显优于吡罗昔康,吡罗昔康的愈显疗效在中医各型之间无明显差异。表明中药疗效与其治疗的中医证型有关,加味玉女煎组对中医肝肾不足和气滞血瘀两型的疗效好,吡罗昔康的疗效与中医证型无关。

研究中的患者依从性好,未发现因服用加味玉女煎颗粒引起副反应。研究表明加味玉女煎颗粒是临床治疗退行性膝关节炎安全有效的新中药制剂,在新加坡及南亚地区将有广阔的运用前景。

本课题以中医学理论和临床经验为背景,在探讨新加坡地区退行性膝关节炎发病的中医病机特点和重新认识古方玉女煎功效的基础上,提出“玉女煎有防治退行性膝关节炎的效用”的推测;经临床研究证实,加味玉女煎对退行性膝关节炎的确具有较好的治疗作用。该课题不仅为发现治疗退行性膝关节炎的中医有效方药具有较大实用价值,而且对发掘古方临床新用途和探索方剂运用规律具有重要的学术意义。

关键词: 退行性膝关节炎 加味玉女煎 吡罗昔康

ABSTRACT

Main symptoms of osteoarthritis of knee (KOA) were pain in knee and difficulty in movement. Such patients, varied from young to old had greatly difficulty in movement, moving in pain and affecting their quality of life. Due to the cause and development of the illness had not unveiled totally; there is lack of efficient remedial at present stage.

Through the experience from western medical and traditional Chinese medical on KOA, with the knowledge from revision of past traditional Chinese medical research reports, on the basis of classification of KOA into traditional Chinese medical illness development, remedial method, prescription of herbs, together with traditional Chinese medicine theory of "Kidney function Bone, Liver function Tendon, Stomach meridian of Yang Ming controls all bone and tendons, and smoothen joints" and development of KOA with Singapore's characteristic of illness development pointed out that main types of traditional Chinese medical symptoms in Singapore's KOA and its illness development theory of "Over-exhausted, Dysfunctions of Liver and Kidney, gather heat in Stomach meridian of Yang Ming, dysfunction caused by Wind and Wetness, under-nutrition of Bone and Tendons", simultaneously with the inspiration of remedial, using mainly "Nutrition of Kidney and Liver, Clearing of gather heat in Stomach meridian of Yang Ming", selectively with "Removal of Wind and Wetness" or "Smoothened meridians"; under such positive influences, Yu Nü Jian formula decoction and its efficiency as evidence, using Yu Nü Jian together with additional herbs as remedial under clinical observation for its effectiveness on KOA.

Our research programme was divided into two sections: Investigation on its traditional Chinese medical theory and its experience for Yu Nü Jian formula used as prescription for KOA, and clinical research for Yu Nü Jian formula with additional herbs used as prescription for KOA.

Investigation on its traditional Chinese medical theory and its experience for Yu Nü Jian formula used as prescription for osteoarthritis of knee (KOA)

From the term 'osteoarthritis of knee (KOA)', analyzing its symptoms and illness development similar to the past traditional Chinese medical theory shows that KOA belong to 'Bi' and 'Wei' symptom, which both include the 'over-exhausted of Bone and Tendon' and 'dysfunction of Liver and Kidney' as development of illness, but their different where the early stage of 'bi', caused by external factors; during the development of the KOA, external factor causing the main symptoms and changes, where it is different from the development of 'Wei' symptoms which cause by dysfunction of inner organs. From the past experience, it is found that this illness is caused by 'dysfunction of Liver and Kidney, further damage by external factors and blockage at meridian'; given the environment in Singapore, eating habits

and lifestyle, compare to China, the symptoms mainly 'shortage of yin element and gather heat and blockage in meridian' which shown the development of illness in Singapore : 'Inadequate functioning of Liver and Kidney, gather Heat in Stomach meridian of Yang Ming', further damage by external factors. According traditional Chinese medical theory, Yu Nü Jian formula shows capability of resolving the cause of the illness and worth dissemination in conservative therapies.

Clinical research on Yu Nü Jian formula with additional herbs on KOA

Based from past experience and comparison method, theoretically clinical research will be using Yu Nü Jian formula as remedial for KOA . Traditional Chinese medical diagnosing specialties, symptoms on knee, pain in KOA as main symptom and traditional Chinese medical symptoms, together with other symptoms beside symptoms found on knee, considering its comprehensive efficacy, effectiveness on knee and other symptoms etc, a comprehensive analysis, assessment and observation done at different stages of prescription and its functions analysis were taken in consideration of clinical design, in order to show standards in both western medical and traditional chinese medical ,and investigation on relationship between the use of traditional chinese medicine and symptoms

Clinical research based on the pre-treatment knee symptoms and other symptoms beside knee, together with traditional Chinese medical observation on whole body, using clinical assessment scale (CAS) on the comparison of effectiveness, it was found that Yu Nü Jian with additional herbs in test group and use of Piroxicam in control group, the total effective rate had no obvious different, but Yu Nü Jian formula cure rate score better than use of Piroxicam. In duration of ten days, both test had obvious improvement on knee but use of Piroxicam improve more as the duration of prescription lengthen. This shows that use of Piroxicam had more improvement on knee than Yu Nü Jian with additional herbs

Clinical research shows that Yu Nü Jian with additional herb improved traditional Chinese medical body symptoms beside knee better than use of Piroxicam.

Analysis of duration in prescription of herbs, with 10 days grace time, both prescriptions shown significant effectiveness. Thereafter, the effectiveness would increase with consumption of prescription of medicine. The use of Piroxicam shows great improvement on the tenth day. Use of Yu Nü Jian with additional herbs shown better improvement on KOA symptoms after 20 days And thereafter, the improvement would increase steadily.. Clinical research shows that prescription of either Piroxicam or Yu Nü Jian with additional herbs is not advisable to be less than 4 weeks.

This research progamme observe that 100 cases of Singapore KOA patients, shows that based on traditional Chinese medical theory, belong to the symptom of "dysfunction of Liver and Kidney, blockage of both qi and blood". Both Yu Nü Jian with additional herbs and

Piroxicam have no obvious different in effectiveness, but Yu Nü Jian with additional herbs shown better result in traditional Chinese medical symptom while Piroxicam had no improvement in traditional Chinese medical symptom.

There were no negative effects on patients after prescription of Yu Nü Jian with additional herbs. This research shows that Yu Nü Jian with additional herbs will be a safe and new Chinese medical decoction in Singapore and south Asia region. It will become a worthwhile clinical prescription and dissemination in future.

This research programmer explores traditional Chinese medical theory and experience from clinical research; investigate KOA in Singapore, its causes and restudy of Yu Nü Jian formula points out the idea of Yu Nü Jian formula as remedial for KOA. Through clinical research, Yu Nü Jian formula with additional herbs does have better improvement in KOA. This research programmer shows not only the treatment on KOA by means of traditional Chinese medication had better result, it also explore new usages and ideas on use of traditional Chinese medicine as part of medical advancement.

Key words: Knee osteoarthritis; Modified Yu Nü Jian; Piroxicam