

# Effect of *Qing'e Pill* plus *Salvia* on Non-Traumatic Osteonecrosis of the Femoral Head of Idiopathic Type in Earlier Stage: A Case Report of a Twelve-Month of Period

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## Abstract

**Background:** Compromised circulatory and bone/lipid metabolic dysfunction are two major contributors to non-traumatic osteonecrosis of the femoral head (ONFH). *Qing'e pill* plus *Salvia* has significant anti-inflammatory and anti-atherosclerotic action, and it could also regulate bone formation and remodeling by suppressing osteoclasts. **Case Report:** We describe a case of a 62-year-old man with ONFH of idiopathic type in earlier stage that could not be adequately controlled with oral non-steroidal analgesics and restoring bone loss agents for past 3 years. After six months treatment with *Qing'e pill* plus *Salvia*, the plasma low-density lipoprotein (LDL), high-density lipoprotein (HDL), apolipoprotein A1 (apo A1), apolipoprotein B (apo B), total cholesterol (TC), triglycerides (TG), and blood viscosity were measured on an empty stomach. The Harris scores were maintained during a six months follow-up after discontinuation of *Qing'e pill* plus *Salvia*. **Discussion:** Our case has shown that plasma levels of inflammatory and atherosclerotic relaxed factors and the Harris scores may be controlled with herbal medication in ONFH of idiopathic type in earlier stage that could not be adequately controlled with oral non-steroidal analgesics and restoring bone loss agents.

## Keywords

*Qing'e Pill*, Osteonecrosis, Femoral Head, Ischemic, Biomarker, Traditional Chinese Medicine

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## 1. Introduction

Abnormal lipid metabolism and bone marrow fat cells hypertrophy/proliferation play important roles in non-traumatic osteonecrosis of the femoral head (ONFH) [1]-[4]. Fat emboli and/or thrombi may further compromise circulation to the femoral head [5]-[7]. In addition, repair capacity and bone remodeling play important roles in the progression and severity of nontraumatic ONFH [8].

In ONFH treatment, non-steroidal analgesics, Hypolipidemics, Anticoagulants, Vasodilators, and restoring bone loss agents are of vital importance to prevent the above complications, as confirmed by the Ajmal M. [9]. The non-steroidal analgesics are generally achieved by administration of Coxibs. And the restoring bone loss agents are generally achieved by administration of oral Bisphosphonates and Alendronate agents or intramuscular calcitonin as well as by weight-bearing. However, there are patients who, for various reasons, are unable to meet dietary or weight-bearing requirements or who remain unresponsive to drug treatment.

We observed a positive effect of *Qing'e pill* plus *Salvia*, an herbal extract used in Traditional Chinese medicine, on lowering plasma levels of inflammatory and atherosclerotic relaxed factors and reducing symptom in ONFH patients of idiopathic type in earlier stage that were unresponsive to oral non-steroidal analgesics and restoring bone loss agents.

## 2. Case History

Patient characteristics and diagnosis: A 62-year-old man (weight, 81 kg; height, 176 cm; waist, 36 inches, left leg) with non-traumatic ONFH of idiopathic type in stage II according to Association Research Circulation Osseous (ARCO) stage conformed by MRI at Union hospital of Tongji Medical College of Huazhong University of Science and Technology (HUST).

Five kinds of herbal materials of *Qing'e pill* were purchased from the Pharmacy of Union hospital of Tongji Medical College of HUST. The ingredients of *Qing'e pill* include 160 g of fried *Psoralea* which steep in wine; 80 g of fried *Eucommia* which peeled and dipped in ginger; 60 g of peeled *Walnut*; 160 g of *Salvia*. The above specimens were crushed into fine powder, and pasted for the pills with 60 g of garlic (Table 1). All five herbs were identified and authenticated by Prof. Shen Lin (The Botany and Drug Department of Union Hospital of Tongji Medical College). The patients were given every two pills and twice a day for six months.

After six months of the medicine treatment, blood viscosity was regularized, but LDL/HDL ratio level was remained unchanged. The follow up was started for twelve's months continuously. At the end of follow up period, Apo B/apo A1 ratio and Harris Score was raised significantly, blood viscosity and total cholesterol were decreased significantly, and LDL/HDL ratio was still not difference significantly (Table 2).

The blood pressure (140 - 150/90 - 100 mmHg) was mild high with nosymptom which was monitored after follow up period and it become normal after 3 months with no treatment.

During *Qing'e pill* administration, there was normalization of abnormal laboratory parameters of hemorheology indexes including 1/s (mPa.S), 5/s, 50/s, 100/s and 200/s. Four months after the last dose of *Qing'e pill*, the indexes were decreased significantly (Table 3).

Finally it was concluded after four months follow up period, the patient Harris Score was increased (80) with 29.03%, and (90) 45.16 at 12 months. Symptoms such as hip pain, limited mobility, and daily activities have been improved significantly.

## 3. Discussion

Currently, non-surgical femoral head-salvage therapy in Western medicine treats patients with non-steroidal

**Table 1.** Components of modified *Qing'e pill* and total dose of each herb.

No. Herbal name	Processing	Contents (g)
1 <i>Psoralea</i>	steep in wine	160
2 <i>Eucommia</i>	fried, peeled and dipped in ginger	80
3 <i>Walnut</i>	peeled	60
4 <i>Salvia miltiorrhiza</i>	levigation	160
5 garlic	steaming	60

**Table 2.** Serial routine laboratory measurements and immunohematological results.

	Total cholesterol mg/dl	LDL/HDL ratio	Apo B/apo A1 ratio	CRP	Harris score
resentation					
0 mounth	235.70	1.80	0.90	9.86	62
1 mounth	238.12	1.85	0.87	8.97	72
2 mounth	210.63	1.93	0.82	8.53	78
3 mounth	-	-	-	-	78
4 mounth	203.45	1.74	0.77	8.03	80
5 mounth	-	-	-	-	84
6 mounth	193.72	1.83	0.71	6.03	86
7 mounth	-	-	-	-	86
8 mounth	-	-	-	-	86
9 mounth	-	-	-	-	86
10 mounth	-	-	-	-	88
11 mounth	-	-	-	-	90
12 mounth	190.55	1.73	0.69	6.89	90

During Qing'e pill administration, there was normalization of abnormal laboratory parameters including total cholesterol, Apo B/apo A1 ratio, CRP, and Harris Score. Four months after the last dose of Qing'e pill, Harris score rose to 80.

**Table 3.** Serial routine laboratory measurements of hemorheology indexes.

Shear rate of whole blood	1/s (mPa.S)	5/s (mPa.S)	50/s (mPa.S)	100/s (mPa.S)	200/s (mPa.S)
resentation					
0 mounth	44.38	38.83	27.48	24.33	20.35
1 mounth	38.57	32.13	24.13	20.57	17.64
2 mounth	32.72	29.78	19.08	22.46	18.83
3 mounth	-	-	-	-	-
4 mounth	28.27	26.17	16.25	19.07	15.78
5 mounth	-	-	-	-	-
6 mounth	29.87	25.83	16.46	18.72	15.98
7 mounth	-	-	-	-	-
8 mounth	-	-	-	-	-
9 mounth	-	-	-	-	-
10 mounth	-	-	-	-	-
11 mounth	-	-	-	-	-
12 mounth	30.08	26.12	17.72	19.11	16.07

analgesics, Hypolipidemics, Anticoagulants, Vasodilators and Bisphosphonates while emphasizing the restriction of weight-bearing on the affected hip joint. One kind of Hypolipidemics drugs, Simvastatin, will increase the differentiation from marrow stromal cells (MSCs) towards osteoblasts, promoting mineralization of bones while inhibiting the differentiation from MSCs towards adipocytes, which can suggest the prevention of osteonecrosis. However, long-term effective dose of these drugs may bring severe adverse reaction of livers and muscles [10]. Enoxaparin, which is of Anticoagulants, and Iloprost, which is of Vasodilators, can relieve the pain of early-staged primary ONFH patients with tendency of thrombosis and with low fibrinolytic activity, but cannot reverse the necrotic process [11] [12]. Alendronate, as an osteoclast inhibitor, can improve clinical symptoms; retard joint collapsing and replacement time. But it also brings esophageal and gastrointestinal adverse reactions after long-term usage. For the patients who are suffering from gingivitis, it may also result in osteonecrosis of mandibular [13]. Other non-surgical treatments include electromagnetic stimulation, extracorporeal shock wave therapy, hyperbaric oxygen therapy and other physical therapies. However, there is a lack of large-sample study for all these therapies.

In recent years, we have harvested significant progress in traditional Chinese medicine of non-surgical treatment for ONFH patients. It will bring good clinical effect with absence of destructions, invasions, pains, and side effects, and therefore is very safe and reliable for the patients. All these advantages made traditional Chinese medicine therapy an international trend for treatment of osteonecrosis of the femoral head, and highly accepted by the scholars and the patients. Hence, comprehensive pharmacodynamics research and evaluation on representative prescriptions and therapies based on traditional Chinese medicine theory and combined with understanding of modern medicine are needed to filter out valid prescriptions and the rules, which are urgent priority and future direction of further research for prevention and treatment of the ONFH of early stage.

In Chinese medicine, ONFH is one kind of bone erosion and rheumatism diseases. In “*Qing’e pill*” prescription, *Eucommia ulmoides oliv* is warm-natured, with the effect of making kidney and bones strong, so in the book “Ben Cao Ji Yan”, there is such a description, “*Eucommia ulmoides oliv* is only herb to strengthen lower energizer, remove pains of foots and legs, and fix knees and loins.” Also in another ancient book named “Ben Cao Jing Shu”, it was said “*Psoralea corylifolia* can warm the kidney, raise ‘Yang’ from ‘Yin’, raise ‘fire’ from ‘soil’, can cure kidney weakness and difficulties in sitting up.” In “Ju Fang Qing’e pill”, it described that “Juglans regia can invigorating the kidney and promote blood circulation, garlic bulb can make the retention pass and dredging collaterals... The combination of these four kinds of herb is called ‘*Qing’e pill*’, which can not only cure kidney weakness and difficulties in sitting up, but also strengthen bone and musculature, promote blood circulation, make hair dark, and bring a good look.” With the use of *Salvia miltiorrhiza* which can activate blood circulation to dissipate blood stasis, we can harvest a very good effect in urinary system and circulatory system [14]. Compromised circulatory and bone/lipid metabolic dysfunctions were two major contributors to ONFH. *Qing’e pill*, which can significantly improve bone quality which has been recognized by most Chinese medical scholars, combined with *Salvia* which can activate blood circulation to dissipate blood stasis, can more effective for treating ONFH theoretically than one single. Our previous experimental studies have shown that this prescription can raise bone mineral density and biomechanical strength of an avascular necrosis of femoral head in rabbit model by inhibiting resorption activity of osteoclasts and promoting the proliferation of osteoblasts [15] [16], which results in production of more bony matrix and the balance of bone metabolism in rat model [17] [18]. Besides, this prescription brings an obvious effect in promoting of joint function, improving density of suffering hip and reversing the process of necrosis [19]-[22]. The MRI examination of this case was not different significantly before and after treatment, the patient was not deteriorating further on imaging. Our this case has also shown that plasma levels of inflammatory and atherosclerotic related factors, blood viscosity, and the Harris scores may be controlled with herbal medication in ONFH patient of idiopathic type in earlier stage without any toxicity and side effects. Further studies are required to investigate the exact compound responsible for ONFH treatment.

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