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## **BI-Ning capsule on experimental study on HPRT gene in patients with gouty arthritis**

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**Abstracts: Objective:** This research observe the effect on patients of HPRT (hypoxanthine-guanine phosphoribosyltransferase) gene with 78 cases of acute gouty arthritis by bi-Ning capsule. **Methods:** 78 cases of acute gouty arthritis by random principles are divided into bi-Ning capsule group and the control group, observation of serum HPRT mRNA levels in both groups before and after treatment. **Results:** serum HPRT mRNA-expression is better than a control group of the pilot group. **Conclusion:** BI-Ning capsule is superior to the western medicine in the therapeutic effect on acute gouty arthritis, and it improves the expressing levels of HPRT mRNA in patients with acute gouty arthritis.

**Key words:** acute gouty arthritis; bi-Ning capsule; HPRT mRNA.

Gout and hyperuricemia is the disease of multifactorial inheritance. The serum uric acid rise is the important biochemical basis of gout. The exothermic of the scanty key enzyme in purine metabolism process is main causes of hyperuricemia, which through our topics group research further confirmed. HPRT gene is purine metabolism remedy synthesis way of key enzyme, HPRT gene defects can led to its activity reduced and can make bird purine nucleotide and times yellow purine nucleotide reduced, that eventually led to its end late product uric acid increased. The report is as follows:

### **1. Clinical data**

#### **1.1 Source of case**

In this research 78 gouty arthritis patients hail from the first affiliated hospital of Heilongjiang University of traditional Chinese medicine Rheumatology from 2007 to 2011, which male in 71 cases, women's 7. Normal human peripheral blood samples, taken from our 5 healthy volunteers.

Model group is the blood sample of 78 gout patients before treatment. On a random basis is divided into Group (bi-Ning capsule group) and control group (Western medicine colchicine groups), two groups of patients generally by statistical analysis, the difference was not significant meaning ( $P>0.05$ ), and comparability.

#### 1.2 Diagnosis standard:

Western diagnosis standard: reference 7th edition of internal medicine under<sup>[1]</sup> ("high uric acid blood syndrome and gout" in the of Western diagnosis standard and the Meng Zhaoheng authored of in the acute gout sexual arthritis of diagnosis standard<sup>[2]</sup>

1.2.2 The Chinese medicine diagnosis standard: according to early research conclusions and the bi Ning soup of group party principles, basis Guiding principle of clinical research on new drugs of traditional Chinese Medicine under<sup>[3]</sup> in the gout of TCM card type diagnosis standard, the enrolled cases meet a criterion of damp-heat syndrome .

### 2. Research technique

2.1 Treatment drug: BI Ning capsule main ingredient: desmodium 15g, fructus corni 20 g, semen plantaginis 12g, radix clematidis 15g, gentiana 15g, and Z Rhizome Dioscoreae Hypoglaucae mosses 15g, and smilax glabra 15g, forsythia 10g, and ligusticum wallichii 12g, caulis Ionicerae 20g, radix 10g., specifications for 0.5G/bag, each bag containing pharmacognostic 0.3mg, every time 4 capsules, tid, po.

2.2 Controlled drug: colchicine tablets (pharmaceutical limited liability company of Xishuangbanna), 2 tablets after meals. Two groups of patients were continuously taking them 7 days for a course, statistical effect after the two treatments, medication-ban serving a high purine diet, pungent irritants, drinking and so on.

2.3 Experimental groups: normal set of 5 cases of normal human peripheral blood samples; Model groups for the gout patients before the treatment of 78 cases of blood samples; after taking two courses are divided into group and control group, pilot group for bi-Ning capsule in the treatment of traditional Chinese medicine group, a total of 42 cases in the control group for Western medicine colchicine groups, a total of 36 cases.

2.4 Experimental reagents: Main reagents for PCR primers for  $\beta$ -actin length 432bp, HPRT length 476bp. Trizol RNA Isolation Kit, TaqDNA, and reverse transcriptase polymerase detection, UV gel Imaging System. 2.4 observing targets: serum HPRT mRNA levels

2.5 Experimental steps: expression by RT-PCR method for detection of serum HPRT mRNA in patients with gout, calculate total RNA extraction, RNA reverse transcriptase double-stranded cDNA, using DNA polymerase chain reaction (PCR) amplification of cDNA, amplification products in 1.5% in agarose gel electrophoresis, electrophoresis in observed and photographed under UV light after, VILBER-LOURMAT imaging system used for analysis, respectively measuring HPRT mRNA, Beta-actin electrophoretic band optical density and total area of expression level as representatives of HPRT/ $\beta$ -actin ratio HPRT mRNA

2.6 Statistic process The statistical description use means  $\pm$  standard deviation ( $\bar{x} \pm S$ ) ,and apply to STATA 12.0 programme.

### 3. Result

3.1 Serum HPRT mRNA in patients with gouty arthritis electrophoretic band brightness variation (see Figure 1, Figure 2). In Figure 1, 2 shows, agarose electrophoresis gel 653 observation under UV lights are visible on BP fragment, but various groups of electrophoresis with obvious differences in brightness. Group of  $\beta$ -actin electrophoresis with brightness, amplification of fragments are 432bp.

Above results indicates that, , two group gout sexual arthritis patients treatment Qian model group HPRT mRNA expression obviously declined ( $P<0.01$ ) and compared to normal group. Two group HPRT mRNA expression obviously rise after treatment ( $P<0.01$ ); normal group and against group and ramped patients compared to HPRT mRNA expression has obviously differences ( $P<0.01$ ); Chinese medicine bi Ning capsule group and against group compared to, serum

HPRTmRNA expression is obviously rise ( $P<0.01$ ). Gene point mutation, and insertion deletion polymorphism may result to decrease the enzyme activity and increased uric acid synthesis, or only present as Lasch-Nylan syndrome characterized by high uric acid or gout. Bi-Ning capsule can greatly improve the expression of the HPRTmRNA reduce serum uric acid without patients, which is root in treating this disease.

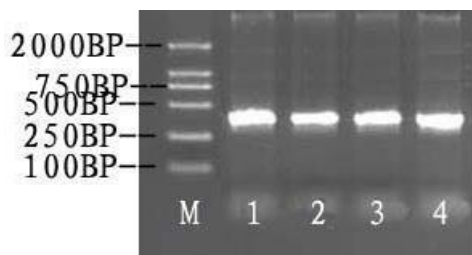


Figure 1: Beta-actin M:Ladder marker;1 mRNA by RT-PCR gel electrophoresis products: normal; 2: model group (prior to treatment); 3: pilot group (BI-Ning capsule); 4: control group (colchicine).

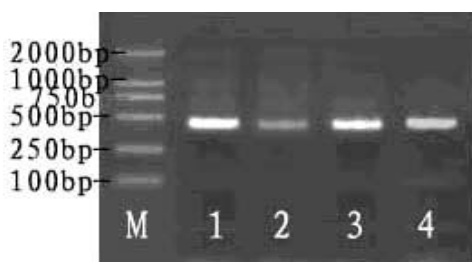


Figure 2: HPRTmRNA m RT-PCR electrophoresis products: is Ladder marker;1: normal; 2: model group (prior to treatment); 3: pilot group (BI-Ning capsule); 4: control group (colchicine).

### 3.2 Table 1 HPRTmRNA electrophoresis products of change comparison ( $\bar{x} \pm S$ )

Group	Case	HPRT/ $\beta$ -actin
normal group	5	0.8213 $\pm$ 0.0385
Model group	78	0.1826 $\pm$ 0.0355
Experimental group	42	0.8057 $\pm$ 0.0422 <sup>*</sup>
control group	36	0.5835 $\pm$ 0.0343 <sup>*</sup>

## 4. Discussion

Gout and hyperuricemia is the disease of multifactorial inheritance. The exothermia of the scanty key enzyme in purine metabolism process is main causes of hyperuricemia which phosphate ribose phosphate synthase and phosphate ribose phosphate amino transferase, and times yellow purine phosphate ribose transferase defects belonging to x with sexual genetic, yellow purine oxidation enzyme activity increased may for more gene genetic, our research mainly study related gene of uric acid generated increased. HPRT is key enzyme in the purine metabolism remedy synthesis way, which has become gene mutations mechanism and repair mechanism ideal of research target points in the recently research<sup>[4]</sup>. HPRT gene defects led to its activity reduced, which can make bird purine and times yellow purine changes for bird purine nucleotide and times yellow purine nucleotide reduced, and two species purine is incapable of fusing synthesis nucleic acid and eventually led to its final product (uric acid) increased. The study from the molecular level to further clarify the pathogenesis of hyperuricemia and gout. for early prevention and treatment of the disease and the development of new drug targets to provide the scientific basis and rationale.

Tongying think the substance of gout is the malfunction of spleen and kidney and the intrinsic heat of Zang-Fu. Gout with hot and humid cloud of phlegm drugs as standard<sup>[5]</sup>. Gout patients are damp heat constitution, addicted to drink, like greasy and surfeit flavour. That induced Zang-Fu organs dysfunction, ascending the clear and descending the turbid has no right to, and accumulation

of damp-heat syndrome delays in blood, stagnates in the condyles, and due to exogenous pathogenic wind attacks meridians, Qi and blood poor run, phlegm-damp in between the bones and tendons, muscles<sup>[6]</sup>. Lysimachia, Plantago as the principal drugs, enable promoting diuresis for stranguria, dehumidify, relieve internal heat or fever, detumescence. Its sweet and light permeability, and salt to soft, slightly cold heat, Tom Lee sanjiao, longer than the wet, wet treatment of bi syndrome what is preferred. Radix clematidis is ministerial drug, drugs diaphoresis, pungent warm, passing 12 meridians, both expelling wind and removing dampness, collaterals and take away the pain, while distribution of Gentiana, smilax glabra, Z Rhizome Dioscoreae Hypoglaucae Moss, rhizoma et radix notopterygii associate drugs, removing a total of rheumatism, clearing hot and humid, bi Tong, clear Interior heat. According to modern pharmacological research on decoction of Clematis have some immune suppression<sup>[7]</sup> edible Tulip colchicine-like role, also has significant inhibition of angiogenesis activity and role of synovial tissue, can be used to eliminate inflammation of the joints<sup>[8-9]</sup> Psyllium can inhibit the synthesis of uric acid, dihydro chlorothiazide lysimachia similar enhancing effect of ureteral peristalsis and increases urine flow, and two effects is parallelism, Z Rhizome Dioscoreae Hypoglaucae Moss. Gentiana, smilax glabra have diuretic effect, lead to blood uric acid decrease, and remedy gouty arthritis<sup>[10-11]</sup>

With the change of diet structure, we'll see the rate of gout arthritis among young and middle-aged people rising. Western medicine treatment have liver and kidney damage. Chinese medicine in the treatment of this disease have a great deal of progress, summed up many proven treatments and simple formula, the study of single herbs are also more. In the literature, it is rarely and superficial understanding to studies on the mechanism. Specific targets are not clear, no basis for experimental study. In addition, disease norms inconsistent, unreasonable, are problems of research design, these are further areas that need improvement and effort.

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