Available online at SciVarse ScienceDirect

**Chinese Herbal Medicines (CHM)**

ISSN 1674-6384

Journal homepage: www.tiprpress.com E-mail: chm@tiprpress.com

## Original article

# Cost-effectiveness Assessment of Commonly-used Drugs for Hepatoprotection and Enzymes Reduction Based on Decision Tree and Multi-utility Theory

Jia-qi Xu[1†], Rui-fang Xie[1†], Zhi-cheng Li[2], Jing-yi Tang[1*], Xin Zhou[1*]

*1. Department of Pharmacy, Longhua Hospital Afflicted to Shanghai University of Traditional Chinese Medicine, Shanghai 200032, China*

*2. Department of Surgery, Shanghai Pudong Hospital, Shanghai 200032, China*

ARTICLE INFO

*Article history*

Received: May 10, 2014

Revised: June 30, 2014

Accepted: July 20, 2014

Available online: October 28, 2014

DOI:

10.1016/S1674-6384(14)60046-0

ABSTRACT

**Objective** Drugs for hepatoprotection and enzymes reduction are widely used in China but their economic analysis has been ignored in a rather long period of time. A suitable protocol for hepatoprotection and enzymes reduction was recommended in Longhua Hospital. **Methods** This study was conducted as a retrospective piece. Three therapeutic protocols (compound glycyrrhizic glycoside combined with aspartic ornithine injection, compound glycyrrhizic glycoside combined with phosphatidylcholine, and compound glycyrrhizic glycoside combined with tiopronin) were selected. Seventy inpatient cases from January 2011 to February 2012 were enrolled and divided into three groups according to different regimens. The cost effectiveness of the three groups was respectively evaluated by incremental cost-effectiveness ratios (ICERs). A decision tree model and multi attribution utility theory were also adopted to analyze the data. **Results** All the three regimens exhibited good effects on protecting liver functions and reducing the levels of enzymes. Among them, the protocol of compound glycyrrhizic glycoside combined with tioproni expressed the least ICER, the lowest cost but the highest score in the multi-utility. **Conclusion** The therapeutic method of compound glycyrrhizic glycoside combined with tiopronin is the most cost-effective option in this study.

*Key words*

decision tree; hepatoprotection and enzymes reduction; incremental cost-effectiveness ratios; multi attribution utility theory; retrospective analysis



## 1. Introduction

Hepatitis is a common disease, which often expresses abnormal liver functions and elevated levels of enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) (Su, 1998). Therefore, protection of liver function and reduction of related enzymes are crucial for the treatment of liver diseases. Drugs for hepatoprotection and enzymes reduction are widely used in China but the economic analysis has been ignored for a long period of time.

* **Corresponding authors: Xin Z** Tel: +86-21-6438 5700-7204 E-mail: 2479707904@qq.com

**Tang JY** E-mail: dr_tang@163.com

† These authors contributed equally to this work. Xu JQ E-mail: xujiaqi0914@126.com Xie RF E-mail: 510706346@qq.com

Fund: Longhua Medical Project (LYTD-14); Shanghai Pharmaceutical Association Research Fund (2011-YY-05-05)

Neglect of economic consideration could increase health-care costs. In Longhua Hospital, the top three frequently-used injections are including ornithine aspartate, polyene phosphatidylcholine, and tiopronin, which are often combined with compound glycyrrhizin injection. The aim of our study is to assess the cost-effectiveness of these strategies in order to provide data support and optimize decision-making in clinic.

## 2. Methods

This trial was a retrospective and observational study. This study was approved by Medical Ethics Committee of Longhua Hospital (20101201).

### *2.1 Patients*

Patients at the infectious ward of Longhua Hospital from January 2011 to February 2012 were considered for enrollment in this study. Inclusion criteria were as follows: > 18 years old; abnormal laboratory results of liver function; receiving the treatment of ornithine aspartate, polyene phosphatidyl-choline, or tiopronin injection combined with compound glycyrrhizin injection. Exclusion criteria were liver cirrhosis, liver cancer, mental illness, pregnancy, and breast-feeding women. Then all included cases were divided into three groups: compound glycyrrhizin injection combined with ornithine aspartate injection (A), compound glycyrrhizin injection combined with polyene phosphatidylcholine injection (B), and compound glycyrrhizin injection combined with tiopronin injection (C). The general information such as gender, age, cost, diagnosis, and laboratory results was retrieved as a database. It should be noted that the three groups of patients had been carefully matched so that they were comparable in age, medical history, health condition, and so forth.

### *2.2 Effectiveness evaluation*

#### *2.2.1 Effectiveness*

The measurement criteria are as follows. Cure: The laboratory results become normal and symptoms (e.g. xanthochromia, isteric, etc) disappear. Remission: The laboratory results turn better and symptoms are alleviated. Invalid: The laboratory results and symptoms are stable or become worse. Valid includes cure and remission. The effective rate is obtained with the numbers of cure and remission cases divided by total case numbers (Su, 1998).

#### *2.2.2 Classification*

The biochemical marks for ALT and AST were classified into three layers: normal (< 40 U/L), 1−2 folds higher than normal (40−80 U/L), and 2 folds higher than normal range (> 80 U/L). The physical examination was classified into positive and negative layers (Su, 1998).

### *2.3 Calculating costs*

All costs were charged according to the price standards enacted by Shanghai government in 2011 in Longhua Hospital. The cost calculation was based on the bills of inpatients. In this study, we only took direct costs into consideration because it was difficult to estimate exact indirect costs. The direct costs are brought by health-care services, such as the expenses of hospitalization, diagnosis, and drugs; The indirect costs are some implicit expenses to meet specific needs of individuals, including nutrition fee, transportation fee, etc (Doubilet et al, 1986).

### *2.4 Statistic analysis*

From a hospital perspective, cost-effectiveness studies were carried out by three analytic models (incremental cost-effectiveness ratios, decision tree, and multi attribution utility theory which were applied to evaluate the cost and health outcomes of three strategies. The parameters were established based on the above standards of efficacy and costs.

#### *2.4.1 Incremental cost-effectiveness ratios (ICERs)*

ICERs are calculated as the following equation: ICERs = costs difference between two programs / health effects difference between programs (Pichereau et al, 2010).

#### *2.4.2 Decision tree*

The treatment options were displayed in a decision-tree. As a decision node (□), a treatment option must be selected and at a chance node (○), a variety of outcomes may occur, each one with some degree of probability. Several concepts are very important about the decision tree method: expected costs (the sum of costs and probability multiplication of different strategies), cost-effectiveness ratios (the ratio of cost to effectiveness), and cure costs (required costs for curing a patient) (Pauker and Kassirer, 1980).

#### *2.4.3 Multi attribution utility theory (MAUT)*

Effectiveness, costs, and hospital days were recognized as parameters, and the weighting coefficient values were 0.5, 0.3, and 0.2, respectively. The value of MAUT is calculated according to the equation below (Bettinger et al, 2007).

$$U_f = 100\ (f_n - V_{min}) / (V_{max} - V_{min})$$

Where $f_n$ represents a specific value of a parameter. $V_{min}$ and $V_{max}$ are respectively the minimum and maximum values of this parameter. $U_f$ represents the result of evaluation.

#### *2.4.4 Sensitivity analysis*

Economic modeling is fundamentally an accumulation of assumptions adopted from diverse sources. Therefore, it is imperative to appraise the stability of the model. We perform One-way sensitivity analysis for our model assumptions. Assuming reductions or increasing of transition probabilities brought about by treatment are changed by ± 5%, the variance of expected costs will be calculated to evaluate the stability of model.

All the statistical data were displayed as $\bar{x} \pm s$. The variances of liver function among different groups before treatment were analyzed with one-factor ANOVA (One-way analysis of variance) using SPSS 17.0 software; The

differences of laboratory results for a subject before and after the treatment were performed by paired-*t* test; The curative ratio or remission ratio were carried out by chi-square test. $P < 0.05$ was considered as statistical significance.

## 3. Results

### *3.1 Baseline evaluation*

Baselines of relevant variables are shown in Tables 1−4. The statistical results showed the baselines were consistent.

#### *3.1.1 Age hierarchy*

Altogether 70 cases were enrolled in this study with 36 males and 34 females, most of which were between 20 and 60 years old (65.71%). The average age was 49.10 ± 17.93, with the maximum age of 83 and minimum age of 19. Most cases (82.86%) were married. The age distribution of three groups had no statistical significance ($P > 0.05$) (Table 1). RSD showed there was no statistical significance between any two of the groups.

#### *3.1.2 Past medical history*

A large part of patients had medical history such as hepatitis history, viral hepatitis (54.29%), fatty liver (2.86%), drug hepatitis (2.86%), and autoimmune hepatitis (1.43%), indicating that liver dysfunction might be contributed to hepatitis especially viral hepatitis. Approximately half of patients had other medical history such as high blood pressure (22.86%), diabetes (4.29%), and cardiovascular diseases (5.17%), while a small part of patients (8.57%) had allergic history. In addition, there was no significance in three groups for the past medical history ($P > 0.05$) (Table 2).

#### *3.1.3 Present illness*

More than half of cases were viral hepatitis (60%), followed by drug-induced hepatitis (14.29%) and fatty liver (8.57%). Furthermore, disease distribution among three groups appeared no statistical significance with $P > 0.05$ (Table 3).

#### *3.1.4 Laboratory results*

Before therapy, the laboratory results of the three groups, such as ALT, AST, alkaline phosphatase (ALP), choline esterase (CHE), and total bile acids (TBA), had no obvious variances ($P > 0.05$) (Table 4).

### *3.2 Effect evaluation*

Tables 4−6 demonstrated that all regimens were effective but had not obvious differences. The efficacy rates ranged between 91% and 93%.

#### *3.2.1 Physical examination*

Physical examination results are shown in Table 5. After treatment the proportion of xanthochromia decreased from 24.29% to 11.43% as well as isteric sclera from 31.43% to 17.14%, indicating that drug treatments might be effective to relieve the symptoms of abnormal liver function.

#### *3.2.2 Effective rate*

According to criteria, after the treatment all three strategies obtained satisfactory effects with effective rate above 90% (Table 6). Furthermore, there were no significant differences between groups with chi-square test ($\chi^2 = 0.101$, $P > 0.05$).

**Table 1 Age hierarchy**

| Groups | Below 20 years old | 20−60 years old | 60−80 years old | Average age | *P* |
|---|---|---|---|---|---|
| A | 1 | 25 | 8 | 45.06 ± 18.36 | |
| B | 0 | 11 | 10 | 52.90 ± 17.88 | 0.188 |
| C | 0 | 10 | 5 | 52.93 ± 15.99 | |
| total | 1 | 46 | 23 | 49.10 ± 17.93 | |
| proportion / % | 1.43 | 65.71 | 32.82 | | |

**Table 2 Past medical history and allergy history**

| Medical and allergy history | Group A | | Group B | | Group C | | Total | | *P* |
|---|---|---|---|---|---|---|---|---|---|
| | *n* | Proportion / % | *n* | Proportion / % | *n* | Proportion / % | *n* | Proportion / % | |
| hypertension | 7 | 20.59 | 5 | 23.81 | 4 | 26.67 | 16 | 22.86 | 0.890 |
| diabetes mellitus | 1 | 2.94 | 1 | 4.76 | 1 | 6.67 | 3 | 4.29 | 0.832 |
| viral hepatitis | 20 | 58.82 | 9 | 42.86 | 9 | 60.00 | 38 | 54.29 | 0.453 |
| fatty liver | 1 | 2.94 | 1 | 4.76 | 0 | 0.00 | 2 | 2.86 | 0.699 |
| drug hepatitis | 0 | 0.00 | 2 | 9.52 | 0 | 0.00 | 2 | 2.86 | 0.091 |
| autoimmune hepatitis | 1 | 2.94 | 0 | 0 | 0 | 0.00 | 1 | 1.43 | 0.584 |
| gall-stone | 0 | 0.00 | 1 | 4.76 | 0 | 0.00 | 1 | 1.43 | 0.306 |
| cholecystitis | 0 | 0.00 | 1 | 4.76 | 2 | 13.33 | 3 | 4.29 | 0.104 |
| transfusion | 0 | 0.00 | 1 | 4.76 | 2 | 13.33 | 3 | 4.29 | 0.104 |
| thyroidea/hyperthyreosis | 0 | 0.00 | 1 | 4.76 | 0 | 0.00 | 1 | 1.43 | 0.306 |
| kidney stone | 0 | 0.00 | 1 | 4.76 | 0 | 0.00 | 1 | 1.43 | 0.306 |
| heart disease | 1 | 2.94 | 2 | 9.52 | 1 | 6.67 | 4 | 5.71 | 0.584 |
| others | 4 | 11.76 | 6 | 28.57 | 1 | 6.67 | 11 | 15.71 | 0.139 |
| age hierarchy | 7 | 20.59 | 2 | 9.52 | 3 | 20.00 | 12 | 17.14 | 0.541 |
| allergic history | 3 | 8.82 | 1 | 4.76 | 2 | 13.33 | 6 | 8.57 | 0.662 |

**Table 3 Present illness of three groups**

| Illness | Group A | | Group B | | Group C | | Total | | *P* |
|---|---|---|---|---|---|---|---|---|---|
| | *n* | Proportion / % | *n* | Proportion / % | *n* | Proportion / % | *n* | Proportion / % | |
| viral hepatitis | 19 | 55.88 | 12 | 57.14 | 11 | 73.33 | 42 | 60.00 | 0.491 |
| drug hepatitis | 5 | 14.71 | 3 | 14.29 | 2 | 13.33 | 10 | 14.29 | 0.992 |
| fatty liver | 2 | 5.88 | 3 | 14.29 | 1 | 6.67 | 6 | 8.57 | 0.533 |
| chronic hepatitis | 1 | 2.94 | 0 | 0.00 | 0 | 0.00 | 1 | 1.43 | 0.584 |
| alcohol liver | 2 | 5.88 | 0 | 0.00 | 1 | 6.67 | 3 | 4.29 | 0.507 |
| cholecystitis | 0 | 0.00 | 3 | 14.29 | 0 | 0.00 | 3 | 4.29 | 0.026 |
| autoimmune hepatitis | 3 | 8.82 | 0 | 0.00 | 0 | 0.00 | 3 | 4.29 | 0.190 |
| others | 2 | 5.88 | 0 | 0.00 | 0 | 0.00 | 2 | 2.86 | 0.336 |

**Table 4 Laboratory results of three groups before and after treatment**

| Groups | | ALT /(U·L$^{-1}$) | AST /(U·L$^{-1}$) | GGT /(U·L$^{-1}$) | LDH /(U·L$^{-1}$) | ALP /(U·L$^{-1}$) |
|---|---|---|---|---|---|---|
| A (*n* = 34) | before treatment | 363.94 ± 441.65 | 198.32 ± 224.51 | 167.38 ± 123.14 | 177.62 ± 46.46 | 112.21 ± 47.31 |
| | after treatment | 58.65 ± 34.17 | 50.12 ± 46.25 | 147.09 ± 159.03 | 157.38 ± 36.61 | 88.82 ± 27.28 |
| | *P* | < 0.01 | 0.001 | 0.398 | 0.007 | 0.002 |
| B (*n* = 21) | before treatment | 364.19 ± 397.32 | 198.19 ± 217.11 | 215.00 ± 178.36 | 171.76 ± 27.80 | 146.00 ± 95.44 |
| | after treatment | 71.76 ± 54.63 | 53.19 ± 34.95 | 161.90 ± 150.67 | 151.71 ± 27.31 | 119.00 ± 83.94 |
| | *P* | 0.003 | 0.006 | 0.005 | 0.016 | 0.8 |
| C (*n* = 15) | before treatment | 260.38 ± 203.70 | 150.00 ± 127.04 | 293.62 ± 363.07 | 182.81 ± 52.86 | 229.00 ± 562.31 |
| | after treatment | 66.80 ± 62.34 | 65.60 ± 57.97 | 222.40 ± 168.32 | 170.73 ± 40.08 | 87.67 ± 18.27 |
| | *P* | 0.001 | 0.001 | 0.129 | 0.171 | 0.002 |
| *P* | | 0.728 | 0.800 | 0.064 | 0.560 | 0.125 |

| Groups | | CHE /(U·L$^{-1}$) | TBIL /(μmol·L$^{-1}$) | dBIL /(μmol·L$^{-1}$) | TBA /(μmol·L$^{-1}$) |
|---|---|---|---|---|---|
| A (*n* = 34) | before treatment | 6780.03 ± 2477.15 | 56.80 ± 66.05 | 28.96 ± 42.33 | 38.40 ± 50.83 |
| | after treatment | 6638.97 ± 2429.53 | 22.81 ± 13.23 | 8.43 ± 6.73 | 16.81 ± 18.12 |
| | *P* | 0.552 | 0.001 | 0.003 | 0.018 |
| B (*n* = 21) | before treatment | 7592.81 ± 2054.03 | 25.97 ± 20.80 | 11.95 ± 14.74 | 55.86 ± 117.82 |
| | after treament | 7445.62 ± 2287.34 | 18.29 ± 10.25 | 6.06 ± 4.70 | 20.93 ± 37.78 |
| | *P* | 0.506 | 0.081 | 0.068 | 0.196 |
| C (*n* = 15) | before treatment | 6853.33 ± 2298.88 | 44.49 ± 78.95 | 20.42 ± 41.74 | 21.70 ± 32.94 |
| | after treatment | 5882.40 ± 1633.66 | 17.16 ± 8.35 | 5.45 ± 3.63 | 12.44 ± 9.63 |
| | *P* | 0.023 | 0.077 | 0.154 | 0.130 |
| *P* | | 0.448 | 0.018 | 0.035 | 0.299 |

**Table 5 Physical examination results before and after treatment**

| Symptoms | Degrees | Before treatment | | After treatment | |
|---|---|---|---|---|---|
| | | *n* | Proportion / % | *n* | Proportion / % |
| xanthochromia | normal | 53 | 75.71 | 62 | 88.57 |
| | slight | 9 | 12.86 | 6 | 8.57 |
| | obvious | 8 | 11.43 | 2 | 2.86 |
| icteric sclera | normal | 48 | 68.57 | 58 | 82.86 |
| | mild | 12 | 17.14 | 10 | 14.29 |
| | moderate | 9 | 12.86 | 2 | 2.86 |
| | serious | 1 | 1.43 | 0 | 0.00 |
| liver palms | positive | 7 | 10.00 | 7 | 10.00 |
| | negtive | 63 | 90.00 | 63 | 90.00 |
| spider angioma | positive | 1 | 1.43 | 1 | 1.43 |
| | negtive | 69 | 98.57 | 69 | 98.57 |

**Table 6 Effective rate of three strategies**

| Groups | Valid | Invalid | Total | Effective rate / % |
|---|---|---|---|---|
| A | 31 | 3 | 34 | 91.18 |
| B | 19 | 2 | 21 | 90.48 |
| C | 14 | 1 | 15 | 93.33 |
| total | 64 | 6 | 70 | 91.43 |

#### *3.2.3 Laboratory results*

Figure 1 illustrated the proportion for patient number of normal liver function parameters increased rapidly after therapy, especially for ALT (from 17.14% to 61.43% ) and AST (from 8.57% to 52.86%); Equally the absolute values of liver function parameters were also improved especially ALT and AST ($P < 0.05$) (Table 4). In addition, the differences

before and after therapy were obvious for some marks ($P < 0.05$) (Table 4). This indicated that the three strategies could relieve the exacerbation of liver function.

### *3.3 Costs*

As shown in Table 7, drug costs occupied the largest proportion (about 50%) of the total costs, followed by laboratory costs. The average costs and hospitalized days of group A were more than those in the other groups. Meanwhile, the mean costs and the hospitalized days of groups B and C were similar.

### *3.4 Cost-effectiveness evaluation*

#### *3.4.1 ICERs*

Results of ICERs by one-factor ANOVA are shown in Table 8, most of the laboratory parameters exhibited no significant differences with $P > 0.05$. However, for liver function marks, especially main parameters such as ALT, AST, and ICERs of group C were lower than those in the other two groups.

#### *3.4.2 Decision tree analysis*

Decision tree is a model constructed to list all the potential outcomes of choices, in order to provide statistical foundation for decision-making. As shown in Figure 2, the expected costs of group C including cure cost and relief cost were lower than those in the other groups, which indicated that group C was the most cost-effective regimen.

#### *3.4.3 Sensitivity analysis*

Sensitivity analysis is a tool for evaluating the reliability of econometric model, which removes the uncertainty of the results by assuming the changes of the several major variables within a certain range. In this paper, under the variable range

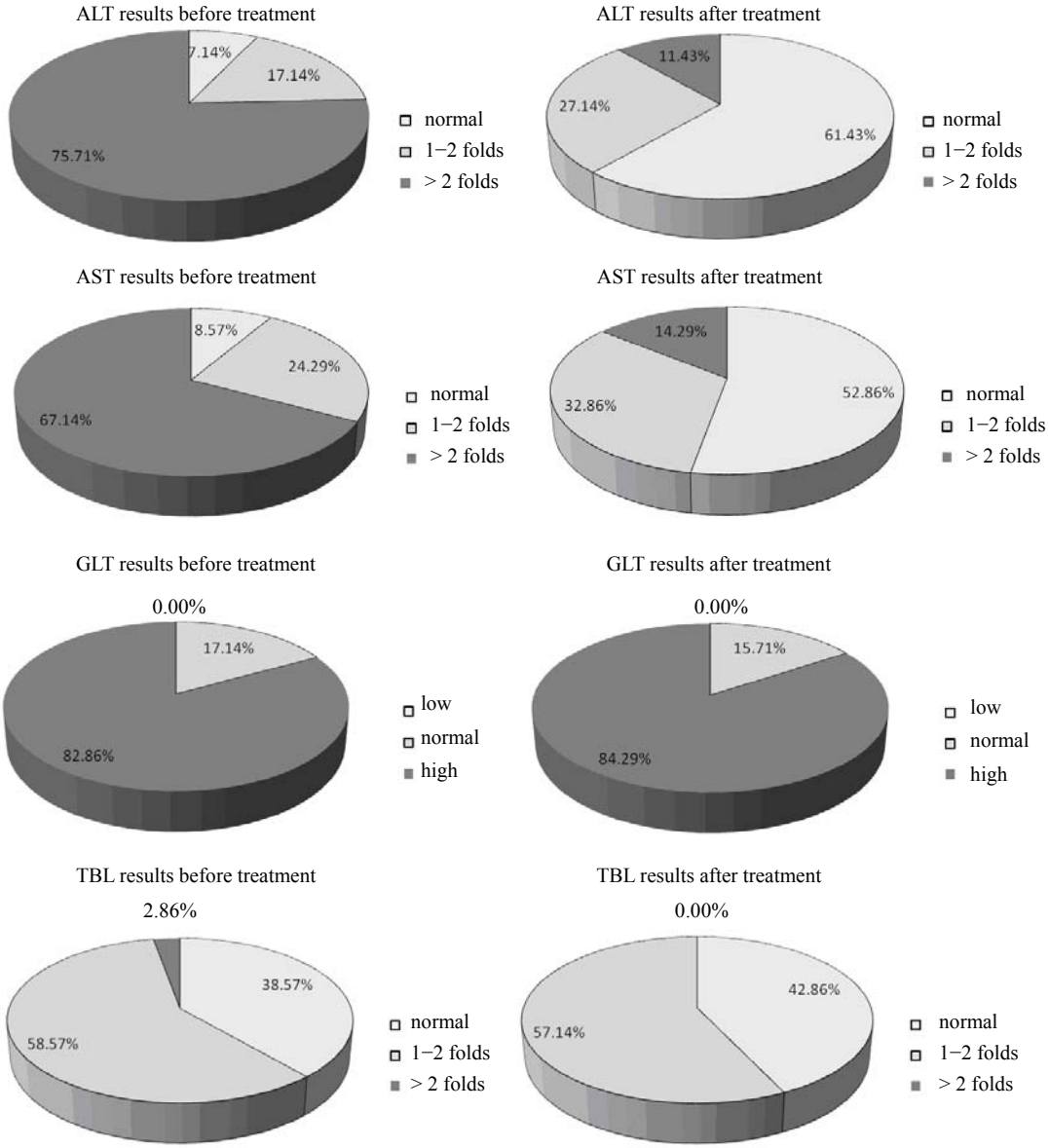


**Figure 1 Proportion of liver function parameters for patient numbers before and after treatment**

**Table 7 Costs of patients in hospital**

| Costs | Group A ($n$ = 34) | | Group B ($n$ = 21) | | Group C ($n$ = 15) | |
|---|---|---|---|---|---|---|
| | Cost / RMB | Proportion / % | Cost / RMB | Proportion / % | Cost / RMB | Proportion /% |
| bed fee | 1009.56 ± 508.96 | 7.26 | 825.95 ± 369.23 | 7.54 | 815.17 ± 294.66 | 7.85 |
| nursing cost | 246.97 ± 100.94 | 1.78 | 220.19 ± 97.76 | 2.01 | 218.67 ± 79.78 | 2.1 |
| chemical medicine | 8107.94 ± 6256.78 | 58.34 | 5180.98 ± 3371.77 | 47.3 | 4837.40 ± 1912.23 | 46.56 |
| herbal medicine | 302.68 ± 199.61 | 2.18 | 389.87 ± 260.36 | 3.56 | 278.73 ± 114.97 | 2.68 |
| chinese patent medicine | 396.18 ± 472.68 | 2.85 | 606.07 ± 828.42 | 5.53 | 404.91 ± 456.70 | 3.9 |
| curing fee | 135.66 ± 78.26 | 0.98 | 119.19 ± 65.11 | 1.09 | 133.87 ± 64.14 | 1.29 |
| operating costs | 2.94 ± 17.15 | 0.02 | 0.00 ± 0.00 | 0 | 0.00 ± 0.00 | 0 |
| laboratory costs | 2977.41 ± 856.14 | 21.42 | 2841.29 ± 1101.74 | 25.94 | 2773.33 ± 1182.70 | 26.69 |
| transfusion fee | 0.00 ± 0.00 | 0 | 0.05 ± 0.22 | 0 | 0.00 ± 0.00 | 0 |
| oxygen fee | 0.35 ± 2.06 | 0 | 0.05 ± 0.22 | 0 | 0.13 ± 0.52 | 0 |
| imagine fee | 30.66 ± 48.51 | 0.22 | 26.71 ± 38.61 | 0.24 | 16.00 ± 44.85 | 0.15 |
| examination fee | 333.53 ± 255.92 | 2.4 | 374.05 ± 378.32 | 3.41 | 386.00 ± 295.41 | 3.72 |
| diagnosis cost | 207.06 ± 83.71 | 1.49 | 185.24 ± 81.72 | 1.69 | 184.00 ± 66.34 | 1.77 |
| others | 146.02 ± 164.75 | 1.05 | 187.06 ± 184.97 | 1.71 | 140.38 ± 139.57 | 1.35 |
| total | 13 896.96 ± 7542.47 | 100 | 10 954.42 ± 5544.52 | 100 | 10 389.99 ± 3302.69 | 100 |
| hospitilized days | 20.56 ± 8.31 | | 18.29 ± 8.15 | | 18.93 ± 8.70 | |

**Table 8 ICERs of different groups**

| Marks | Group A ($n$ = 34) | Group B ($n$ = 21) | Group C ($n$ = 15) | $P$ |
|---|---|---|---|---|
| ALT | 230.25 ± 735.46 | 261.09 ± 746.88 | 29.82 ± 27.33 | 0.537 |
| AST | 364.88 ± 842.15 | 357.26 ± 746.76 | 144.15 ± 346.32 | 0.290 |
| GGT | 1285.48 ± 1584.37 | 1677.27 ± 3374.10 | 997.79 ± 1486.51 | 0.106 |
| LDH | 1113.73 ± 1663.79 | 1243.39 ± 1582.01 | 867.42 ± 1225.90 | 0.900 |
| ALP | 835.23 ± 1384.89 | 1171.54 ± 1775.83 | 510.89 ± 775.58 | 0.700 |
| CHE | 1722.96 ± 2589.89 | 1372.74 ± 1858.46 | 811.65 ± 1918.98 | 0.188 |
| TBIL | 1024.42 ± 1565.15 | 2461.72 ± 3234.28 | 1737.51 ± 1550.14 | 0.043 |
| DBIL | 2567.10 ± 4411.06 | 6863.39 ± 1 6509.88 | 2167.23 ± 1303.66 | 0.190 |
| TBA | 2040.26 ± 4497.95 | 2963.46 ± 4092.67 | 4153.89 ± 7738.10 | 0.685 |

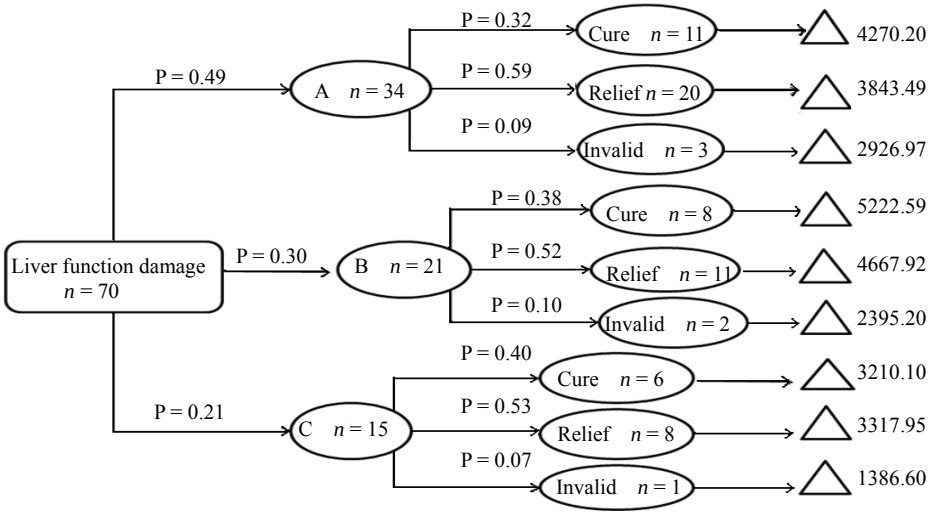


**Figure 2 Decision tree analysis of treatment of liver diseases**

*n*: sample number p: probability

of the total efficiency between 95% and 105%, the results kept consistent (Table 9) expected the costs of group C were the lowest while total effective rates were the highest, which indicated that this model was feasible in the study. Group C remained to be the most cost-effective.

#### *3.4.4 MAUT*

According to the analysis results of MAUT (Table 10), group C obtained the highest score with 84.9, suggesting that group C might be the most economical strategy among the three groups.

**Table 9 Sensitivity analysis of decision tree**

| Groups | Expected costs / RMB | Cure costs / RMB | Total effective rate / % | | Expected cost / RMB | |
|---|---|---|---|---|---|---|
| | | | Plus 5% | Minus 5% | Plus 5% | Minus 5% |
| A | 3900.67 | 4270.20 | 95.74 | 86.62 | 3949.36 | 3851.99 |
| B | 4662.77 | 5222.59 | 95.00 | 85.95 | 776.15 | 4549.39 |
| C | 3146.05 | 3210.10 | 98.00 | 88.67 | 2939.39 | 2791.51 |

**Table 10 Analysis results of MAUT**

| Groups | Valid rate | | Treatment cost | | Hospital days | | Total score |
|---|---|---|---|---|---|---|---|
| | value | score | value | score | value | score | |
| A | 91 | 45.5 | 75 | 22.5 | 62 | 12.4 | 80.4 |
| B | 90 | 45 | 83 | 24.9 | 68 | 13.6 | 83.5 |
| C | 93 | 46.5 | 84 | 25.2 | 66 | 13.2 | 84.9 |

## 4. Discussion

As far as we know, therapeutic methods for liver function damage have not yet reached a worldwide consensus. In some countries, the first-line regimens are not liver-protected therapies but etiological treatments. However, in China, the laboratory results reflecting liver function are important. For example, the results of liver functions are usually essential to probability of the entrance and employment. Ironically, the therapies for liver dysfunction in our country are commonly in an empirical way (Sun et al, 2010). Furthermore, the categories and the prices of drugs are considerably diverse. Many medicines such as chemical structures, herbs, and Chinese patent drugs are applied in clinic but their effects and effectiveness have been seldom systematically evaluated.

In this case, we compared three protocols on a retrospective basis. The effectiveness and cost-effectiveness were conducted in order to provide the data support for the choice of the best regimen.

### *4.1 Strategies*

In Longhua Hospital, two kinds of medicines are often used together: one contributes to the normalization of liver enzymes, the other protects liver function. Compound glycyrrhizin glycosides can be used as former and other drugs can protect liver function as latter. Given in this situation, all strategies in this study are combination regiments in Longhua Hospital.

The primary mechanisms of hepatoprotective drugs were generally attributed into anti-inflammatory, anti-oxidation, etc (Liu et al, 2001; Koh et al, 2005). The main drugs were applied showing as followed.

#### *4.1.1 Compound glycyrrhizin glycosides*

It is belonged to glycyrrhizic acid preparation, which can be metabolized into glycyrrhetinic acid by glucuronosyl transferase *in vivo*, exhibiting pharmacological activities, such as decreasing enzymes, anti-inflammatory, and regulating immune system. This preparation is widely applied with or without other drugs in clinic. Similarly, in Longhua Hospital, this drug is recognized as routine drug for liver protection.

#### *4.1.2 Aspartic ornithine injection*

Aspartic ornithine injection is able to decrease the level of ammonia in blood through participating in urea metabolism to remove toxic materials in liver, so it can be widely used in the treatment of various hepatic encephalopathy and liver dysfunction. In this paper, this drug is classified into group A.

#### *4.1.3 Polyene phosphatidylcholine injection*

Polyene phosphatidylcholine injection contains abundant high-energy polyene phosphatidyl choline and unsaturated fatty acid, which can be easily absorbed *in vivo* to stabilize liver cell membranes. This medicine can protect the liver function and prevent the recurrence of gallstones and liver damage, so it is suitable for all types of acute or chronic liver diseases. In this article, this medicine belongs to group B.

#### *4.1.4 Tiopronin*

Tiopronin is a kind of glycine derivatives, containing free sulfhydryl which can reduce the activities of ATP in liver mitochondria and increase the content of intracellular ATP. So this injection is also widely applied to reduce liver damages. In this article, the drug is categorized into group C.

### *4.2 Evaluation of effects*

This study only evaluated the effects of inpatients. In all laboratory results of liver function, ALT and AST are very important for the assessment of liver function. ALT is a sensitive parameter expressing the acute liver cell damage while AST is an indicator reflecting the degree of liver damage. Results showed that the levels of ALT and AST obviously were decreased after the treatment, indicating the treatment protocols could improve liver function. In addition, the results of both physical examination and effective rates also suggested these regiments effective (Tables 5 and 6).

### *4.3 Cost-effectiveness and decision tree analysis*

#### *4.3.1 Cost-effectiveness analysis (CEA)*

CEA refers to analyses that consider both cost and effectiveness, where effectiveness is an objective measure (Pichereau et al, 2010). It compares the costs and health effects

of an intervention to assess the extent to which it can be regarded as providing value for money. This informs decision-makers who have to determine where to allocate the limited healthcare resources (Kosuda et al, 2000). Cost-effectiveness ratios (CERs) are calculated as the division of cost to effect for each program. However, in reality the likelihood is that choices will have to be made between different treatment regimens for the same condition. In order to resolve such a problem, ICERs are used (Pichereau et al, 2010). In this study, we used ICERs to compare cost-effectiveness of different strategies before and after the treatment. Our results showed although there were no significant difference among the three groups ($P > 0.05$), the value for ICERs of group C was lower than those in the other two groups (Table 8).

#### *4.3.2 Decision tree analysis*

It is constructed of the choices and potential outcomes of the choices in general (Pauker and Kassirer, 1980; Kosuda et al, 2000). In our research, choices meant therapeutic strategies while the potential outcomes of therapy presented decision branch. Sensitivity analysis is to test the impacts of different hypothesis or estimation on the decision-tree results. In this study, the price variances of groups A, B, and C were unpredictable. Under the similar effective rate, the lower costs, the more effective the strategy is. For this reason, the sensitivity analysis was based on the fluctuation of effective rates. Ultimately the chart of decision tree (Figure 2) showed that the strategy C had the lowest expected cost and kept consistent when the effective rates fluctuated ± 5%.

#### *4.3.3 MAUT*

MAUT analysis is a method in order to systematically identify, measure, and compare the different variables involved in decision-making. When the MAUT analysis is used to compare medical protocols, it allows the users to select various attributes (e.g., efficacy, costs, and adverse reaction) of the agents being studied, compare the relative values of the agents, and then guide the users in making right decisions (Tawny et al, 2007). In our paper, three factors were taken into account such as effectiveness, hospitalization, and total cost in hospital. After analysis, group C had the highest score with 84.9 (Table 10).

## 5. Conclusion

In this article, we compare three strategies of hepato-protection and enzyme reduction with three pharmaco-economic methods including ICERs, decision tree analysis, and MAUT. The same conclusion has been resulted. Lycyrrhizic glycoside combined with tiopronin (protocol C) could be the most cost-effective protocol among the three studied strategies. This investigation focuses on the hepatoprotection and enzyme reduction drugs from a view of pharmacoeconomics and make an explicit conclusion. The outcomes could provide the statistical supports for medical decision-maker to make the sound judgment under a rational cost-conscious circumstance. Nevertheless, the study is conducted in a constrained situation such as small size samples amount and sole hospital data, which could bring some limitation to this study, a further study should be done to confirm the conclusion.

### Authors' contributions

Dr. Xin Zhou has contributions to conception and design, revising this paper critically for important intellectual content and final approval of the version to be published. Miss Rui-fang Xie has contributions to the acquisition, analysis, and interpretation of data. She also prepared drafts of this paper. Miss Jia-qi Xu has contributions to acquisition of data, analysis and interpretation of data. Dr Zhi-cheng Li has contributions to editing the article. All authors agreed on submitted paper.

### References

Bettinger TL, Shuler G, Jones DR, Wilson JP, 2007. Schizophrenia: Multi-attribute utility theory approach to selection of atypical antipsychotics. *Ann Pharmacother* 41: 201-207.

Doubilet P, Weinstein MC, McNeil BJ, 1986. Use and misuse of the term "cost effective" in medicine. *New Engl J Med* 314: 253-256.

Koh HS, Matsui A, Mimura S, Inao M, Saitoh E, Ohno A, Nagoshi S, Yoshimoto T, Mochida S, Fujiwara K, 2005. Increased cytoprotective function in the liver of transgenic mice expressing osteopontin in hepatocytes. *Hepatol Res* 32(1): 46-51.

Kosuda S, Ichihara K, Watanabe M, Kobayashi H, Kusano S, 2000. Decision-tree sensitivity analysis for cost-effectiveness of chest 2-fluoro-2-D-[18F] fluorodeoxyglucose positron emission tomography in patients with pulmonary nodules (non-small cell lung carcinoma) in Japan. *Chest* 117: 346-353.

Liu L, Mei QB, Li BL, Zhou SY, Cao ZX, 2001. Antioxidation of *Tanguficum* Maxim polysaccharide on acute liver injury mice. *J Fourth Mil Med Univ* 22: 530-533.

Pauker S, Kassirer J, 1980. The threshold approaches to clinical decision making. *New Engl J Med* 302: 1109-1117.

Pichereau S, Le Louarn A, Lecomte T, Blasco H, Le Guellec C, Bourgoin H, 2010. Cost-effectiveness of UGT1A1*28 genotyping in preventing severe neutropenia following FOLFIRI therapy in colorectal cancer. *J Pharm Pharm Sci* 13: 615-625.

Singer ME, Applegate KE, 2001. Cost-effectiveness analysis in radiology. *Radiology* 2001: 611-620.

Su CT, 1998. The clinical observation about self-JiangMei decoction treating on 68 cases of abnormal liver function. *J Guangxi Coll Tradit Chin Med* 15(2): 16-17.

Tawny LB, Garyn S, Donnamaria RJ, James PW, 2007. Schizophrenia: Multi-Attribute Utility Theory Approach to Selection of Atypical Antipsychotics. *Ann Pharmacother* 41: 201-207.