Treatment of human influenza A (H5N1) infection with Ching-Wen-Bai-Du-Yin

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Abstract

The World Health Organization (WHO) has recently documented 383 confirmed human cases of H5N1 infection with a mortality rate greater than 62.9% by May 2008. Although the surveillance of the bird and human populations for the pathogenic H5N1 virus is being conducted, sporadic avian influenza /H5N1 occurs in various places of the world and cause serious illness and death in humans. Clinical symptoms of H5N1 influenza are mainly involved with pneumonia with infiltrates, respiratory distress, tachypnea, and inspiratory crackles. Multiorgan failure with renal and cardiac dysfunction is also common. Therefore, understanding its pathology, transmission route, clinical features, and treatments would help us preparing for the prevention and management of this infection. The Ching-Wen-Bai-Du-Yin (anti-pyretic and anti-toxic soup) is formulated for the treatment of symptoms of flu or pestilence in the past. Ching-wen-bai-du-yan (CWBDY) consists of gypsum, Rehmanniae Radix, rhinoceros (now, buffalo) horn, Coptidis rhizoma, Fructus Gardenia Jasminoides, Radix Platycodi Grandiflori, Radix Scutellariae Baicalensis, Anemarrhena Rhizome, Radix Paeonia Lactiflora, Fructus Forsythiae Suspensae, Radix Scrophulariae Ningpoensis, Radix Glycyrrhizae Uralensis, Cortex Moutan Radicis, and Herba Loaphatheri Gracilis. The formula was targeted for antipyretic, anti-inflammatory, analgesic, sedative, anti-bacterial, antiviral, hepatoprotection, detoxification, tonic and diuretic effects. The antipyretic and antiinflammatory may reduce the pulmonary...
injury and inflammation by H5N1 virus. In addition, other effects by CWBDY may be complimentary to the current therapy.

Keywords:avian influenza, Ching Wen Bai DuYin

Introduction

The avian influenza A/H5N1 virus is a public health threat. The World Health Organization (WHO) has now documented 383 confirmed human H5N1 infections with a mortality rate greater than 62.9%\textsuperscript{(1)}. Outbreaks of H5N1 in poultry have been associated with human transmission. Human contact with sick or dead bird is the most frequent cause of transmission of the avian influenza virus. Although the surveillance of the bird and human populations for the pathogenic H5N1 is being conducted, sporadic avian influenza /H5N1 occurs in various places of the world and cause serious illness and death in humans. Therefore, understanding its pathology, transmission route, clinical features, and treatments would help us preparing for the prevention and management of H5N1 infection.

An influenza-like illness, fever (more than 38°C), and a lower respiratory tract symptoms are common in most patients with H5N1 infection, but upper respiratory tract symptoms are only in some cases. In some patients, diarrhea, vomiting, abdominal pain, pleuritic pain, and bleeding from the nose and gums were found in the course of illness\textsuperscript{(2-5)}. Watery diarrhea is more common than in influenza due to human viruses\textsuperscript{(6)} The major radiologic abnormalities were extensive pneumonic infiltration with segmental and multifocal distribution, mostly located in lower zones of the lung. No pleural effusion and hilar lymphadenopathy was noted \textsuperscript{(7)}. Two patients from Vietnam had acute encephalitis and diarrhea without apparent respiratory symptoms. In another case, from Thailand, the patient presented with fever and diarrhoea, but no respiratory symptoms. All the patients had a recent history of direct exposure to infected poultry\textsuperscript{(8-10)}.

Lower respiratory tract manifestations develop early in the course of illness. Dyspnea developed a median of 5 days after the onset of illness (range, 1 to 16 days)\textsuperscript{(11)}. Almost all patients have clinically apparent pneumonia; radiographic changes include diffuse, multifocal, or patchy infiltrates; interstitial infiltrates; and segmental or lobular consolidation with air bronchograms.\textsuperscript{15} The most common abnormality among patients is in the lungs with multifocal consolidation, respiratory distress, tachypnea, and inspiratory crackles. It is mainly caused by a primary viral pneumonia, usually without bacterial supra-infection. Progression to respiratory failure has been associated with diffuse, bilateral, ground-glass infiltrates and manifestations of the acute respiratory distress syndrome (ARDS). The median time from the
onset of illness to ARDS was 6 days (range, 4 to 13) \(^{(11)}\). Multiorgan failure with signs of renal dysfunction and cardiac compromise, including cardiac dilatation and supraventricular tachyarrhythmias, has been common\(^{(2-5)}\). Other complications have included ventilator-associated pneumonia, pulmonary hemorrhage, pneumothorax, pancytopenia, Reye’s syndrome, and sepsis syndrome without documented bacteremia\(^{(10)}\).

The three-year mortality rate of H5N1 infection is high (62.9\%)\(^{(1)}\). In contrast to 1997 avian influenza, which most deaths occurred among patients older than 13 years of age, recent H5N1 infections have caused high mortality rates among infants and young children. The case fatality rate was 89 and 90 percent in Thailand and Indonesia, respectively among those younger than 15 years of age. Death has occurred an average of 8 to 11 days after the onset of illness (range, 6 to 30 days) and most patients have died of progressive respiratory failure\(^{(3,4,9)}\).

**Historical pandemic**

The earliest known pandemic occurred in 1641, it wiped out a large portion of the population in China. After extensive research on this pestilence, a Chinese physician, Wu Youhsing (1580-1660 published a book *Wenyilun* (*On Pestilence*) in 1642, which described the specific symptoms of different kinds of epidemic disease and proposed the theory of *lichí* (excessive influences or pestilence)\(^{(12)}\). His theory of *lichí* stated that pestilence was not caused by exogenous factors (such as wind, cold, summer-heat and wet), but rather by the result of infection by excessive influences. The features of *Lichí* are understood as follows: firstly, it could be cured by herb medicine; secondly, it may penetrate the body through the mouth and nose; thirdly, the occurrence of disease depends on the amount and virulence of the excessive influence and the body resistance; and fourthly, each pestilence is associated with its paritcular *lichí*. Wu Youhsing also claimed that the shapeless *lichí* affecting humans was different from that occurring in animals, such as in cattle, goats, chickens and ducks. The reason that a cattle was sick but not a goat, a chicken sick but not duck, human sick but not bird, is because of the different sources of infected *chi*. This ancient description of avian influenza may provide us valuable information for dealing with avian influenza when we are still struggling to its control and treatment.

From 1918 to 1919, about 20 to 40 percent of the worldwide population became ill and that over 50 million people died of the Spanish flu pandemic. Those who did not succumb to the disease within the first few days often died of complications from the flu (such as pneumonia) caused by bacteria. One of the most unusual aspects of the Spanish flu
was its ability to kill young adults. The reasons for this remain uncertain. Mortality rates of the Spanish flu were high among healthy adults as well as the usual high-risk groups. The attack rate and mortality was highest among adults 20 to 50 years old. The severity of that virus has not been seen again\(^{(13)}\).

The Asian influenza pandemic occurred in 1957. People under 65 years of age, had no immunity to this strain and a pandemic was predicted. This pandemic virus was quickly identified, due to advances in technology and vaccine was available in limited supply. Infection rates were highest among school children, young adults, and pregnant women in October 1957. Most influenza-and pneumonia-related deaths occurred between September 1957 and March 1958. The elderly had the highest rates of death. Although the Asian flu pandemic was not as devastating as the Spanish flu, about 69,800 people in the U.S. died. The Hong Kong influenza pandemic was detected in Hong Kong in early 1968. Deaths from this virus peaked in December 1968 and January 1969. Those over the age of 65 were most likely to die. The number of deaths between September 1968 and March 1969 for this pandemic was 33,800, making it the mildest pandemic in the 20th century. In 1997, a few hundred people became infected with the avian A/H5N1 flu virus in Hong Kong and 18 people were hospitalized. Six of the hospitalized persons died. This virus was different because it moved directly from chickens to people, rather than having infecting pigs as an intermediate host. In addition, many of the most severe illnesses occurred in young adults similar to illnesses caused by the 1918 Spanish flu virus. Hong Kong government slaughtered all chickens (estimated 1.5 million) in order to prevent the spread of this virus. The avian flu did not easily spread from one person to another, and after the poultry slaughter, no new human infections were found\(^{(13)}\).

From 1997 to May 2005, H5N1 viruses were largely confined to Southeast Asia, but after they had infected wild birds in Qinghai Lake, China, they rapidly spread westward. The deaths of swans and geese marked H5N1’s spread into Europe, India, and Africa. Infections with highly pathogenic H5N1 viruses were confirmed in poultry in Turkey, Korea and Japan\(^{(14)}\). Therefore, the World Health Organization (WHO) is coordinating the global response to human H5N1 infections and monitoring the corresponding threat of an influenza pandemic.

**Treatment**

Vaccines and antiviral drugs are the two most important medical interventions for reducing morbidity and mortality during a pandemic, but will not be available in adequate supplies. Vaccines are considered the first line of defense, but it is not available at the present.

Current therapy with antiviral drug,
Oseltamivir (Tamiflu) and corticosteroid has been considered to be an effective treatment of H5N1 infection but the morbidity and mortality remains high\(^{(9,10)}\). In addition to the safety concerns of Tamiflu that causing psychological disturbance, the development of drug resistance in human influenza A (H5N1) virus were reported\(^{(15)}\). Influenza A/H5N1 virus with an amino acid substitution in neuraminidase conferring high-level resistance to oseltamivir was isolated from two of eight Vietnamese patients during oseltamivir treatment. Both patients died of H5N1 virus infection, despite early initiation of treatment in one patient. Surviving patients had rapid declines in the viral load to undetectable levels during treatment. The resistance of treatment can emerge during the currently recommended regimen of oseltamivir therapy and may be associated with clinical deterioration\(^{(1,2,16,17)}\).

Therefore, the strategy for the treatment of H5N1 virus infection should include additional antiviral agents as well as other measures to reduce morbidity, mortality, and social disruption. The ancient experience of pestilence (wenyi) recorded in the book of Chinese medicine might offer insight to the treatment of this disease. The Ching-wen-bai-du-yin (antipyretic and anti-toxic soup) is formulated for the treatment of symptoms of flu or pestilence\(^{(18)}\). Ching-wen-bai-du-yin (CWBDY) consists of gypsum (shi gao), Rehmanniae Radix (sheng di huang), rhinoceros (now, buffalo) horn (xi jiao), Coptidis rhizoma (huang lian), Fructus Gardenia Jasminoides (zhi zi), Radix Platycodi Grandiflori (jie geng), Radix Scutellariae Baicalensis (huang qin), Anemarrhena Rhizoma (zhi mu), Radix Paeonia Lactiflora (chi shao), Fructus Forsythiae Suspensae (lian qiao), Radix Scrophulariae Ningpoensis (xuan shen), Radix Glycyrrhizae Uralensis (gan cao), Cortex Moutan Radicis (dan pi), and Herba Loaphatheri Gracilis (zhu ye). The prescription was searched from ‘My understanding with the pestilence’ by Yu Shiyu (1794) for the antipyretic and antitoxic effect. Pharmacological action of this prescription is targeted for antipyretic, anti-inflammatory, analgesic, sedative, anti-bacterial, antiviral, hepatoprotection, detoxification, tonic and diuretic\(^{(18)}\). Clinical application of CWBDY for treatment of epidemic hemorrhagic fever has been reported and beneficial effects including shortening the duration of fever, disease course and duration of hospital stay as compared with the control groups\(^{(19,20)}\). Application of CWBDY was also successful in the treatment of patients with the herpes-induced encephalitis and bacterial-induced meningeal encephalitis\(^{(21)}\).

**Possible Mechanism of CWBDY**

Antipyretic effect of CWBDY has been reported in animal study with intra gastric or intrarectal administration of 10 ml/kg to rabbits.
Both routes are effective and the continuing intrarectal injection has a more rapid anti-pyretic effect\(^{(22)}\). Radix Glycyrrhizae Uralensis, Cortex Moutan Radicis, Radix Scutellariae Baicalensis and Radix Paeonia Lactiflora have anti-inflammatory effects. Radix Glycyrrhizae Uralensis, Cortex Moutan Radicis, and Radix Paeonia Lactiflora have analgesic effect. Radix Paeonia Lactiflora and buffalo horn have sedative effect\(^{(18)}\).

The compounds purified from traditional Chinese medicine remedies were investigated for the antiviral effect. Baicalein, baicalin (from Radix Scutellariae Baicalensis), glycyrrhizic acid (Radix Glycyrrhizae Uralensis) had no toxic effect on host cells but had a moderate ability to reduce hepatitis B virus (HBV) production by transfected HepG2 cells\(^{(23)}\).

Antioxidant activity of alkaloids from Coptidis Rhizoma is compared using 3-morpholinosydnonimine (SIN-1)-induced LLC-PK\(_1\) cells for peroxynitrite (ONOO\(^{-}\)) generation. Coptidis Rhizoma extract and its alkaloids, except for berberine, reduced the cellular ONOO\(^{-}\} level. In addition, DNA fragmentation induced by SIN-1 was significantly decreased by the extract, and also by coptisine, epiberberine, jatrorrhizine, groenlandicine and magnoflorine. Coptidis Rhizoma extract, epiberberine, jatrorrhizine, groenlandicine and magnoflorine significantly increased cell viability even at a concentration as low as 10 µg/ml and coptisine is the most effective for protection against SIN-1-induced cellular injury\(^{(24)}\).

Geniposide from Fructus Gardenia Jasminoides has anti-inflammatory effect in an experimental rat model of type II collagen-induced arthritis. Geniposide at high dose or medium dose, delays the starting time of right paw edema significantly, and reduces the serum interleukin (IL)-1β and tumor necrosis factor (TNF)-α levels significantly\(^{(25)}\). Geniposide is found to possess a potential for detoxification by inducing GSH S-transferase (GST) activity and the expression of GST M1 and GST M2 subunits. The signaling pathway of geniposide leading to the activation of GST has been investigated in primary culture of rat hepatocytes. Geniposide induced increased protein levels of GST M1 and GST M2 (1.76- and 1.50-fold of control, respectively). This effect of geniposide is inhibited by the MEK-1 inhibitor PD98059, but not by other mitogen-activated protein kinase (MAPK) inhibitors\(^{(26)}\).

Aqueous extract from Platycodi radix (AEPR), a traditional drug used to treat acute lung inflammatory disease, was tested on lipopolysaccharide (LPS)-induced inflammation in human airway epithelial A549 cells. Nuclear factor-κB (NF-κB) and its inhibitory regulator, inhibitory κB (I-κB), play crucial roles in LPS-induced inflammatory response. LPS-induced NF-κBp65 and I-κBα are inhibited by AEPR. AEPR suppressed LPS-induced gene expression of TNF-α, inducible nitric oxide synthase (iNOS) and cyclooxygenase-2
Platycodin D is the major constituent of triterpene saponins in the root. Platycodin D-induced apoptosis in human keratinocytes HaCaT cells is confirmed by DNA fragmentation, caspase-3 activation, and caspase-8 activation. Platycodin D can activate inhibitor of NF-κB, IKK-β in the NF-κB activation of upstream level, but not IKK-α. Platycodin D-mediated apoptosis of HaCaT cells upregulates Fas receptor and Fas ligand expression, but did not exhibit p53 activation (28).

The Radix Scutellariae Baicalensis has been widely employed for many centuries in traditional Chinese herbal medicine as popular anti-bacterial and antiviral agents. They are effective against staphylococci, cholera, dysentery, pneumococci and influenza virus. Baicalein is a potent free radical scavenger. Baicalein possesses a multitude of pharmacological activities, such as anti-inflammatory and anti-tumor agent. Anti-inflammatory action of baicalein and wogonin, flavonoids from the root of Scutellaria baicalensis has been demonstrated by inhibition of LPS-induced nitric oxide (NO) production in a macrophage-derived cell line, RAW 264.7 (29).

Rhizomes of Anemarrhena asphodeloides Bunge (Liliaceae), has been prescribed as antipyretic, anti-inflammatory, diuretic and hypoglycemic agents in Chinese traditional medicine. Two xanthone glycosides I and II, have isolated as mangiferin and 7-O-β-D-glucopyranosyl-mangiferin (30). Six steroidal saponins, anemarrhenasaponin (An-I and An-Ia), timosaponin (TB-I, TB-II and TB-III), and timosaponin A-III inhibit the platelet aggregation, and delay the activated partial thromboplastin times. It might be used as a novel antithrombotic therapeutic agents in post-myocardial infarction (31).

The root of Paeonia lactiflora and the root cortex of Paeonia suffruticosa, are important Chinese crude drugs used in many traditional prescriptions. Paeonia lactiflora selectively inhibited cyclooxygenase activity. Paeoniflorin (PF) is one of the main effective components of the total glucosides of paony (TGP) extracted from the root of Paeonia lactiflora which has been used for gynaecological problems and for cramp, pain and giddiness. Anti-inflammatory, antioxidative, antihepatic injury and immunoregulatory activities of TGP have been proved. The effects and mechanisms of paeoniflorin on immunological liver injury was induced by tail vein injection of bacillus Calmette-Guerin (BCG) and LPS in mice. Serum alanine aminotransferase (ALT) activities were significantly decreased by PF (25, 50, 100 mg/kg). Histological examination demonstrated that paeoniflorin could attenuate the area and extent of necrosis and reduce the immigration of inflammatory cells. The increase in TNF-α, IL-6, LPS binding protein (LBP) and CD14 mRNA expression in mouse liver was significantly decreased by PF (100 mg/kg) and was changed by PF (25, 50 mg/kg) at different
time-point. The protective mechanism of paoniflorin might be partially related to modulation of TNF-α, IL-6, LBP and CD14 mRNA expressions in mouse liver.\(^{32}\)

Another major bioactive constituent of both crude *Paeonia* drugs is 1,2,3,4,6-penta-O-galloyl-beta-D-glucose (PGG). PGG has been shown to possess potent antioxidant, anti-mutagenic, anti-proliferative and anti-invasive effects. Activated macrophages produce excessive amounts of NO and prostaglandin E2 (PGE2), which play key roles in the processes of inflammation and carcinogenesis. PGG, epigallocatechin gallate (EGCG), and gallacetophenone treatment except gallic acid significantly inhibited LPS-induced NO and COX-2 activity in LPS-activated macrophages. Among the four compounds examined, PGG is the most potent in both iNOS (IC\(_{50}\) 18 µg/mL) and COX-2 inhibitory activity (IC\(_{50}\) 8 µg/mL and 12 µg/mL, respectively for PGE2 and PGD2).\(^{33}\)

Fructus Forsythiae Suspensae has been used for anti-bacterial, antipyretic, anti-inflammation, hepatoprotection, anti-vomiting, blood circulation, and diuretic effects. Forsythin, flavonol glycosides, rutin and isoquercitrin, lignan glycosides, arctiin and matairesinoside, as well as phenylethanoid verbascoside, ursolic acid and β-sitosterol have been isolated from the flowers of Forsythia viridissima. Aqueous extracts of Lianqiao (Fructus Forsythiae) blocked the activity of the initiator caspase-8 as well as the effector caspase-3 and caspase-7 in a dose-dependent manner with an IC\(_{50}\) 10 µg/ml. Identification of caspase inhibitory activity of this drug, allows the formulation of testable hypotheses and design of further investigations.\(^{34}\)

Radix Scrophulariae Ningpoensis has been known for vasodilation, anti-bacterial, anti-inflammatory, sedative, and antipyretic effect. One of its components, harpagoside inhibits LPS-induced iNOS and COX-2 mRNA and protein expression in HepG2 cells. These inhibitions correlate with the suppression of NF-κB activation by harpagoside. Furthermore, harpagoside dose-dependently inhibited LPS-stimulated NF-κB promoter activity in a gene reporter assay in RAW 264.7 cells. These results suggest that the inhibition of the expression of COX-2 and inducible nitric oxide by harpagoside involves suppression of NF-κB activation, thereby inhibiting downstream inflammation and subsequent pain events.\(^{35}\) A study shows that daily doses standardized to 50 mg or 100 mg of harpagoside are better than placebo for short-term improvements in patients with pain and rescue medication.\(^{36}\)

Radix Glycyrrhizae Uralensisanti has been know for anti-ulcer, anti-convulsive, insulin promoting, detoxificative, anti-inflammatory, antiviral, anti-bacterial and anti-cancer activities. Glycyrrhizin (GL) and glycyrrhizic acid (GA) from Radix Glycyrrhizae Uralensis, under the name of Stronger Neo-Minophagen C (SNMC) preparation has been used clinically for 60 years in Japan as an anti-allergic and anti-hepatitis
agent. GL and GA reduce alanine transaminase (ALT) and aspartate transaminase (AST) values in the serum. This hepatoprotective effect has recently been explained as the inhibitory effects of GL and GA on immune-mediated cytotoxicity against hepatocytes and on NF-κB, which activates genes encoding inflammatory cytokines in the liver. In addition, GL and GA also induce interferon-γ and some other cytokines are related with their antiviral activities(37).

Cortex Moutan Radicis has circulatory, anti-bacterial, anti-inflammatory, and immune modulatory effects. The protective agents against sepsis-induced lethality from the root cortex of *Paeonia suffruticosa* led to the isolation of paeonol, 2,5-dihydroxy-4-methoxy-acetophenone, acetovanillone, paeonoside, paeoniflorin, oxypaeoniflorin, apiopaeonoside, and methyl 3-hydroxy-4-methoxybenzoate. Among them, three showed the highest survival rate (100% with a dose of 30 mg/kg vs. 17% for the control experiment) and reduced ALT level to be a half of the control value on the sepsis model induced by LPS/D-galactosamine(38). Paeonol significantly inhibits histamine release from the rat peritoneal mast cells treated with compound 48/80, a mast cell degranulator. The release of TNF-α, mast cell activating cytokine, is significantly suppressed in RBL-2H3 mast cells pretreated with anti-dinitrophenyl

Table 1. Target therapy for the influenza A (H5N1) virus infection

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Active ingredient</th>
<th>Mechanisms of action</th>
</tr>
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<tbody>
<tr>
<td>oseltamivir</td>
<td>Tamiflu</td>
<td>Antiviral</td>
</tr>
<tr>
<td>corticosteroid</td>
<td>Prednisone</td>
<td>Immunosuppression, anti-inflammatory</td>
</tr>
<tr>
<td>Ching Wen Bai Du Yin Gypsum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radix Rehmanniae</td>
<td>β-sitosterol, campesterol, rehmannin, katol, arginine</td>
<td>increase blood pressure, diuretic, hyperglycemic</td>
</tr>
<tr>
<td>Rhinoceros (buffalo) horn</td>
<td></td>
<td>antipyretic, sedative</td>
</tr>
<tr>
<td>Coptidis rhizoma</td>
<td>berberine, coptisine,</td>
<td>antibiotic, circulation, antioxidant</td>
</tr>
<tr>
<td>Fructus Gardenia Jasminoides</td>
<td>geniposide</td>
<td>antiinflammatory</td>
</tr>
<tr>
<td>Radix Platycodi Grandiflori</td>
<td>platycodin D</td>
<td>antiinflammatory</td>
</tr>
<tr>
<td>Radix Scutellariae Baicalensis</td>
<td>baicalein, baikalin</td>
<td>antiviral, diuretic</td>
</tr>
<tr>
<td>Anemarrhena Rhizome</td>
<td>mangiferin, saponin and hypoglycemic</td>
<td>antipyretic, antiinflammatory, diuretic</td>
</tr>
<tr>
<td>Radix Paeonia Lactiflora</td>
<td>paeoniflorin</td>
<td>antioxidant, antipyretic,</td>
</tr>
<tr>
<td>Fructus Forsythiae Suspensae</td>
<td>1,2,3,4,6-penta-O-galloyl-β-D-glucose</td>
<td>antiinflammatory</td>
</tr>
<tr>
<td>antiinflammatory, diuretic</td>
<td>Forsythin, flavonoids</td>
<td>antibacterial, antioxidant,</td>
</tr>
<tr>
<td>Radix Scrophulariae Ningpoensis</td>
<td>harpagoside</td>
<td>antipyretic, antiinflammatory, sedative</td>
</tr>
<tr>
<td>Radix Glycyrrhizae Uralensis</td>
<td>glycyrrhizic acid Glycyrrhizin</td>
<td>antiviral, antiinflammatory</td>
</tr>
<tr>
<td>Cortex Moutan Radicis</td>
<td>paeonol, paeoniflorin</td>
<td>antiinflammatory, analgesic, diuretic</td>
</tr>
<tr>
<td>Herba Loaphatheri Gracilis</td>
<td>arundoin, cylindrin, Taraxerol, friendlin</td>
<td>diuretic, antipyretic</td>
</tr>
</tbody>
</table>
immunoglobulin E (IgE) in a dose-dependent manner. Paeonol significantly inhibits IgE production in B cells activated by anti-CD40 mAb, IL-4 and recombinant histamine releasing factor. In mice, paeonol effectively inhibits anaphylactic shock by 90% at a dose of 0.5 mg/mouse vs. phosphate buffered saline-treated control 2 h after the i.p. injection of compound 48/80. These results suggest that paeonol has antianaphylactic activity by regulating histamine and TNF-\(\alpha\)\(^{39}\).

Paeonol has anti-inflammatory and analgesic effects. In a rat model of carrageenan- evoked thermal hyperalgesia, paeonol dose-dependently inhibits TNF-\(\alpha\), IL-1\(\beta\), but enhanced IL-10 production in the rat paw exudates both at the early (1.5 h) and late phase (4 h) after carrageenan injection. The mechanisms of paeonol exerts its anti-inflammatory and analgesic effects in this inflammatory model may be associated with decreased production of proinflammatory cytokines, NO and PGE\(_2\) and increased production of IL-10, an anti-inflammatory cytokine. In addition, attenuation of the elevated iNOS and COX-2 protein expression as well as neutrophil infiltration in carrageenan-injected paws may also be involved in the beneficial effects of paeonol\(^{40}\).

Conclusion

Since almost all patients have clinically apparent pneumonia, the control of pneumonia is very important. CWBDY has antipyretic, anti-inflammatory effect, anti-bacterial effects which may reduce the inflammation of pulmonary injury by H5N1 virus. In addition, antiviral, analgesic, sedative, hepatoprotection, detoxification, tonic and diuretic effects by CWBDY may be complimentary to the current therapy. Therefore, this Chinese medicinal herb may help to reduce the morbidity and mortality of human influenza A infection and warrant a randomized controlled trials for the efficacy and safety of CWBDY preparation.

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清瘟败毒饮对人类禽流感之治疗

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中文摘要

世界衛生組織統計到 2008 年 5 月時，人類禽流感總共有 383 個病例，死亡率達 62.9%。
雖然在禽類及人類都持續的進行監視這種致病的 H5N1 病毒，但還有零星的疫病發生，導致
嚴重病情甚至死亡。禽流感的症狀主要是浸潤性的肺炎、呼吸困難、呼吸急促、吸氣暴裂聲。
包括心、腎的多重器官衰竭亦為常見。因此須明瞭禽流感的病機、傳染途徑、病症及對策，
才有助於防治禽流感。古時清瘟敗毒飲用於治療瘟疫頗有成效，其方劑為石膏、生地、犀角
牛角、黃連、桅子、桔梗、黃芩、知母、赤芍、連翘、玄參、甘草、丹皮、竹葉，主治清熱解
毒、止痛鎮靜、殺菌抗病毒，保肝強心利尿。清熱解毒可緩解病毒引起的肺部傷害及炎症，
而清瘟敗毒飲之其他作用，亦可輔佐現行禽流感療效之不足。
關鍵詞：禽流感、清瘟敗毒飲