Key words: COX-1; platelet aggregation; aspirin resistance; antiplatelet;

Aspirin, one of theanti-platelet agents which most widely used in clinical has a significant effect on cardiovascular diseasein high-risk patients. Its main mechanism is irreversibly acetylates the enzyme cyclooxygenase(COX)-1 at serine 529 preventing conversion of arachidonic acid(AA) to thromboxane A2 in a dose-independent manner [1-2]. However, not all patients show an equal antiplatelet effect, some studies suggest that there're some multidrug resistence protein 4(MRP4) can overexpress in human platelet which can reducing aspirin action. Besides that other human tisuses can productthromboxane A2(TXA2),what's more, the residual platelet fuction is the most important reason which can result in aspirin resistance. This review aims to provide a brief mechanism summary on aspirin resistance,which including the pathway of TXA2 production and anion efflux pump.

1.Effect of TXA2 on antiplatelet effect Since the sensitivity of the platelets to antithrombotic effects of aspirin is largely determined by the inhibitory effect of the drug on COX-1, this inhibition is not completeso that it is a wide range of individual differences in the course of chronic treatment. It has been found thatsome patients can not inhibit platelet TXA2 formation in vitro or in vivo, requiring further addition of aspirin adjuvant therapy. In addition, studies have found that platelets are not the only source of TXA2 circulation [4]. Monocytes ,endothelial and vascular smooth muscle cells could synthesise TXA2 in response to stimuli[5], in a predominantly COX-1 mediated process which is poorly sensitive to the inhibitory effect of aspirin. What's more, COX-2, which is associated with thromboxane and prostaglandin synthase in platelets, is not susceptible to aspirin so that it could also form TXA2 by its own activation. These findings have shown that it is difficute in accutarely assigning in vivo measures of TXA2 synthesis to the action of aspirin specifically on platelet COX-1.

2. Anion efflux pump (the effect of MRP4 on antiplatelet effects) Multidrug resistance protein-4 (MRP4) is a member of the MRP / ABCC subfamily of ATP-binding cassette transporter. The expression of MRP4 has been found in many tissues,which can pumping a wide variety of endogenous and xenobiotic organic compounds out of the cells. Many studies have shown that aspirin is a target for MRP4 in human platelet and aslo determinate both aspirin and its metabolites ,salicylic acid are substrates of mouse ABCC4. In addition some studies have confirmed thatthe patients will synthesize a large number of multidrug resistance protein-4 (MRP4)increased with dosage of aspirin. However, theexpression is very littlein healthy patients.Mattiello etal found that the MRP4 over-expression is directly linked to anaspirin-reduced cell entrapment that leads to increased thromboxane B2（TXB2）production, as found in CABG patients, with residualplatelet activation despite aspirin treatment. Moreover, invitro inhibition of MRP4-mediated transport enhancesaspirin action in platelets. Above that aspirin can be mediated efflux by MRP4 transporter, thereby reducing its efficacy.

3. Discussion In summary, in vitro and vivo studieshave connected the antithrombotic effect of aspirin on the irreversible inhibition of platelet COX-1 with the formation of TXA2. Except as mentioned above, some other problems should be considered (1) although serum TXB2 can be used to determine the activity of platelet COX, whether TXB2 is a stable metabolite of TXA2 should be further exploration; (2)If platelets are able to obtain PGH2 by means of a mechanism that does not rely on COX, the effect of aspirin will fail. (3) Excepet COX-1, there are also isoforms COX-2 in human platelet. Somesurveys suggest that the production of TXA2 can be induced by COX-2 or other pathways. Despite this, our results paves the way to further studies of the possible direction about the aspirin resistance in anti-platelet.

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EXPERIENCE OF ACUPUNCTURE IN THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME

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Abstract Background Obstructive sleep apnea hypopnea syndrome (OSAHS) is a common and serious disease threatening people's health. Along with the changes of incidence increased year by year, the treatment of OSAHS is also developed, the continuous positive airway pressure (CPAP) and the surgical treatment is the preferred scheme at present, but because of poor compliance and acceptance. In the traditional medicine, Acupuncture has a significant effect on the treatment of the disease. This paper reviews the methods and thoughts of treatment, and draws the following conclusions.

Conclusion: In this paper, the main conclusions were

(1) Acupuncture has the exact curative effect on treating OSAHS, the clinical effect is prominent, the patient's compliance is good, the adverse reaction is few and so on.

(2) Acupuncture has various of treatment methods, and the main treatment is electroacupuncture, acupuncture and acupuncture with other special acupuncture. Acupoints are the local point of the neck, and they are mainly from Lianquan（RN23）, waijinjinyuye（Ex-HN14）, Fengchi（GB20）, yamen（DU15）, according to the syndromes in patients with dialectical acupoints.

(3) Acupuncture can not only improve the daytime sleepiness and sleep structure of the patients, but also can improve sleep quality and blood oxygen saturation in patients at night. Acupuncture can reduce sleep apnea hypopnea index, and some studies also found that patients with other symptoms may be improved, such as insomnia, memory loss, etc.

Because the level is limited, the research has some limitations or shortcomings, while acupuncture has many methods, but it is short of standardization. The multi center, large sample study is less. The systematicness is poor. Follow-up reports are few. For patients to maintain the efficacy of the treatment, there is lack of research reports.

Prospect : Acupuncture in the treatment of OSAHS, has a unique advantage, and should standardize the therapeutic plan, We have to do more central research, and follow up the treatment of patients in order to achieve better therapeutic effect of acupuncture.

Keyword：obstructive sleep apnea hypopnea syndrome（OSA）; acupuncture; research progress

RESEARCH PROGRESS ON THERAPEUTIC DRUGS AGAINST NEONATAL JAUNDICE

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Abstract: Neonatal jaundice is a physiological phenomenon in early neonatal stage and one of the clinical symptoms of various pathological diseases after birth. Drug treatment is one of the main therapeutic approaches for it. This paper summarized recent progress in therapeutic drugs against neonatal jaundice from reducing bilirubin generation, blocking bilirubin enterohepatic circulation, enhancing the ability of the liver to clear bilirubin, reducing unconjugated bilirubin, accelerating bilirubin transportation and other different aspects.

Key words: neonatal jaundice; neonatal;bilirubin; drug treatment

Introduction Neonatal jaundice is a common clinical problem encountered during the neonatal period, especially in the first week of birth [1]. Neonatal jaundice is caused by increased bilirubin in the neonatal blood, manifested as skin, sclera and mucous membranes yellowish discoloration [2]. The increase of serum bilirubin not only has obvious damage to the central nervous system, but also has different degrees of damage to the heart, lung, blood, immune system and other important organs. Therefore, it is important that we carry out the early prevention and treatment of neonatal jaundice and prevent the occurrence of nuclear jaundice. Drug therapy is one of the most important means of treatment of neonatal jaundice.

1. Inhibition of Bilirubin Production

Metalloporphyrins and D-penicillamine are heme oxygenase (HO) inhibition preparation which can inhibit HO activity and reduce hemoglobin transformed into biliverdin, thereby inhibiting the formation of bilirubin. In addition, Intravenous immunoglobulin can block the hemolytic process and reduce the destruction of red blood cells, thereby reducing the formation of bilirubin [3].

2. Blocking Bilirubin Enterohepatic Circulation, Reducing Bilirubin Reabsorption

Microecologics can promote the growth of intestinal flora which can inhibit β-glucosidase activity, reduce the enterohepatic circulation of bilirubin in the intestinal tract and reduce the level of bilirubin[4]. Insoluble and difficult to absorb particles also can absorb intestinal bilirubin and play bilirubin capture effect, mainly including activated charcoal, smectite powder, agar, zinc salts, calcium phosphate, cholestyramine. Besides, gastrointestinal excitomotor, bile salts and lipase inhibitor can prevent the enterohepatic circulation of bilirubin and effectively reduce the level of serum bilirubin.

3. Enhance the Ability of the Liver to Clear Bilirubin

Phenobarbitone, clofibrate and traditional Chinese medicine can induce the activity of UGT1A1 of the liver, which can enhance the ability of the liver to convert the unconjugated bilirubin into the conjugated bilirubin and promote the elimination of bilirubin. At present, the most commonly used traditional Chinese medicine for the clinical treatment of neonatal jaundice is Yinzhihuang oral liquid and Yinzhihuang injection. In addition to Yin Zhi Huang, the Yinchenhao Tang also has a good effect on the treatment of neonatal jaundice.

4. Reduce Unconjugated Bilirubin and Accelerate Transport of Bilirubin

Albumin can be combined with unconjugated bilirubin to promote the transport of bilirubin. Ademetionine can promote the excretion of bile, accelerate the excretion of bilirubin, and decrease the level of bilirubin. Besides, glucose can make bilirubin be excreted in vitro through glomerular filtration by causing osmotic dieresis.The latest re-