

# Quality of Peptic Ulcer Healing and Selection of Antiulcer Drugs

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**Abstract.** *Peptic Ulcer is a Common and Frequently-Occurring Disease in Clinical Practice, Which Has Always Troubled People and Affected the Health of Patients. Factors Affecting Ulcer Healing Quality Include Growth Factors and Receptors, Antiulcer Drugs, Mucosal Protective Drugs, Prostaglandins (Pgs), Helicobacter Pylori (Hp), Mucosal Blood Flow, Etc. Eradication of Helicobacter Pylori, Combination of Anti-Acid Drugs and Mucosal Protective Agents, Rational Use of Non-Steroidal Anti-Inflammatory Drugs and Traditional Chinese Medicine Are Helpful to Improve the Quality of Ulcer Healing. This Article Reviews the Concept of Ulcer Healing Quality, How to Improve the Quality of Ulcer Healing and the Selection of Anti-Ulcer Drugs.*

**Keywords:** *the Quality of Ulcer Healing, Antiulcer Drugs, Choose*

## 1. Introduction

The Core Problem of Peptic Ulcer Treatment is How to Improve the Quality of Ulcer Healing. the Healing Quality is High and Recurrence is Low. on the Contrary, the Healing Quality is Low. Not Only Are There Many Recurrences, But Also There Are Many Complications. the Healing Rate of Peptic Ulcer is High, But the Recurrence Rate is Still High, Which is a Difficult Problem That Must Be Solved Clinically At Present. Recurrence Rate of Peptic Ulcer is Related to Quality of Peptic Ulcer Healing (Qouh) [1]. a Large Number of New Anti-Ulcer Drugs Have Also Been Developed. the Eradication of Helicobacter Pylori (Hp) Has Resulted in a Ulcer Healing Rate of More Than 95%, But There is Still the Problem of Ulcer Recurrence [2]. Studies Have Found That Although the Epithelium of the Newly Healed Ulcer is Intact, the Tissue Structure is Obviously Abnormal. These Abnormalities Reduce Cell Oxygen and Ability, Energy Supply and Mucosal Defense Function, and Become the Pathological Basis for Ulcer Recurrence [3]. Recurrence of Ulcer Disease is Affected by Many Factors, Such as Duodenal Erosion, Smoking, Drinking, Mental Stimulation, Taking Nsaids, Etc. Recent Studies Have Shown That the Recurrence Rate of Completely Cured Ulcers is Very Low. Liu Jianqiang et al. Found That the Recurrence Rate of Hp Positive Ulcers is 62%, of Which 100% Recurred in Grade Sa Healing, 88% in Grade Sb Healing, and

94% in Grade Sc Healing. There is No Recurrence after 2 Years of Follow-Up [4]. in Recent Years, It Has Been Found That Acid Inhibition and Hp Treatment Can Promote Ulcer Healing, But If the Healing Quality is Not High, It is Easy to Relapse. Therefore, Attention Should Be Paid to the Quality of Ulcer Healing during Treatment. the Relevant Issues Are Briefly Described as Follows.

## **2. the Concept of Quality of Healing (Qouh) for Peptic Ulcer**

Tarnawski et al [5] Put Forward the Concept of Ulcer Healing Quality Qouh in 1991, Which Specifically Refers to the Repair and Regeneration of Epithelial Tissue Must Have Complete Mucosal Defense Capability. the Healing of Peptic Ulcer is an Extremely Complicated Process. the Research on the Healing Process of Ulcer Shows That Firstly, the Healing Zone is Generated in the Adjacent Tissues of the Ulcer; Enlargement and Expansion of Gastric Glands; Epithelial Cells Dedifferentiate and Proliferate, and Migrate Along the Surface of Proliferating Granulation Tissue from the Periphery of the Ulcer to Cover the Entire Ulcer. Then Gastric Glands Are Reconstructed in the Granulation Tissue and Microvessel Networks and Connective Tissue Are Formed and Reshaped. Clinical Observation Found That [6] Ulcers in Red Scar Stage Are More Likely to Recur Than Those in White Scar Stage. Healing of the Choice Requires Not Only General Healing, But Also Restoration of Its Normal Histological Structure and Function. among Them, Transforming Growth Factor (t g f-A) and Epidermal Growth Factor (e g f) Activate Receptors under Damaged Stimulation, Control Cell Proliferation, Rebuild Epithelial Tissue, and Fibroblast Growth Factor (B f g f) and Vascular Endothelial Growth Factor (V e g f) Promote Regeneration of Connective Tissue and Microvessels. Other Factors Such as Insulin-Like Growth Factor (Ilgf), Keratin Cell Growth Factor (Kcgf) and Hepatocyte Growth Factor (Hcgf) Trefoil Peptide Have Regenerative Effects on Injured Mucosa. Different Ulcer Healing Qualities Have Different Ulcer Recurrence Rates, with High Healing Quality and Low Recurrence Rate. on the Contrary, the Healing Quality is Low, the Recurrence Rate is High and the Complications Are Numerous. Obviously, Improving the Quality of Ulcer Healing is the Key to Prevent Recurrence.

## **3. Factors Affecting Ulcer Healing Quality**

### ***3.1 Growth Factors and Receptors***

The Main Factors Affecting Qouh Are Mucosal Damage Factors Not Removed, Especially Helicobacter Pylori Not Eradicated, Taking Glucocorticoids and Nsiad Drugs; the Whole Process of Mucosal Repair on Ulcer Surface is Regulated by Growth Factors and Receptors. under Mucosal Inflammatory Stimulation, Transforming Growth Factor -A(Tgf-A) and Epidermal Growth Factor (Egf) Receptors Are Activated to Reconstruct Epithelial Tissue. Stomach Sinusitis Persists. in Addition to the Obvious Low Healing Quality and High Ulcer Recurrence Rate Caused by Neutrophil Infiltration in Scars, Granulation Tissue Maturity is Measured

by the Number of Fibroblasts, the Number and Distribution of Neovascularization, the Regeneration of Collagen Fibers and Mucosal Muscularis. the Ideal Qouh Should Not Only Achieve Good Reconstruction of Tissue Structure, But Also Restore the Mucosal Protection and Mucus Synthesis Function of Normal Gastric Mucosa. Other Factors Such as Insulin-Like Growth Factor (Igf)-1, Keratin Cell Growth Factor (Kcgf), Hepatocyte Growth Factor (Hgf), Trefoil Peptide, Etc. Are Also Involved in Mucosal Regeneration and Repair [7].

### **3.2 Antiulcer Drug**

After Eradication of Hp with Proton Pump Inhibitor (Ppis) as the Main Triple, Ppis Were Given to Gastric Ulcer Patients Respectively. Teprenone (Schweitzer) or Ppis+ Teprenone Were Maintained for 6 Weeks. the Ulcer Healing Quality Was Evaluated by Gastroscopy and Eus. the Total Healing Rate of Ulcer Was 85.0%, the S2 Acquisition Rate of Ulcer Was 51.0%, and the High Quality Healing Rate of Ulcer Was 21.9%. Zhang Zhengzheng et al [8] Observed the Healing of Peptic Ulcer in Different Parts after Standard Treatment, and Found That Qouh (Sc/Sa+Sb) in the Group of Non-Prone Parts Was Significantly Better Than That in the Group of Prone Parts, and the Difference Was Statistically Significant ( $P < 0.05$ ). However, the Qouh(Sc+Sb/Sa) in the Non-Recurrent Site Group and the Recurrent Site Group Had No Statistical Difference ( $P > 0.05$ ), and Peptic Ulcer in Different Sites May Have Some Influence on Qouh. We Know That Mucosal Functional Maturity Can Be Determined by Evaluating the Microcirculation Status of Gastric Mucosa, Glycoprotein Content, Mucous Production Function of Regenerated Mucosa and Other Indicators. under Chromoendoscopy, the High Healing Quality Was Flat and the Low Healing Quality Was Nodular. the Experimental Study on Rat Gastric Ulcer Also Confirmed That Ppis+ Teprenone Has the Best Ulcer Healing Rate, Healing Quality Index and Various Ulcer Healing Quality Indexes [9]. the Increase of Blood Flow At the Edge of Fully Healed Ulcer is More Significant Than That At the Edge of Unhealed Ulcer. It is Suggested That the Quality of Microcirculation in Regenerative Mucosa of Ulcer Healing is Closely Related to Qouh.

### **3.3 Prostaglandins (Pgs)**

Numerous studies have confirmed that PGS is closely related to the occurrence and healing of ulcers, especially ulcers caused by glucocorticoids and NSAIDS. Li Wei et al. used EUS to measure the thickness of the mucosa and the presence of hypoechoic lumps in the submucosal tissue of the healed ulcer, and divided the ulcer into high, medium and low quality healing groups. The recurrence rates of the ulcer in one year were 4.5%, 40.5% and 75.0% respectively [10]. The decrease of PGS content in mucosa not only delays ulcer healing, but also thins regenerated epithelium, reduces gland height and aggravates gland cystic expansion, thus reducing ulcer healing quality. Administration of PGE1 can reverse the inhibition of non-steroidal anti-inflammatory drugs on DNA synthesis of epithelial cells on the edge of ulcer, and stimulate the repair of damaged blood vessels and the

reconstruction of microcirculation. Improve QOUH and reduce ulcer recurrence.

### **3.4 *Helicobacter Pylori (Hp)***

At present, it is known that most gastric ulcer and almost all duodenal ulcer patients have HP infection. Eradication of HP can significantly reduce the recurrence of gastric ulcer. If HP can be permanently removed, peptic ulcer is expected to be cured. It is an indisputable fact that eradication of Hp can shorten the healing time of most ulcers. Studies have found that Hp cytotoxin can inhibit the proliferation of ulcer marginal cells and affect the healing quality of ulcers. Animal experiments show that HP cytotoxin can inhibit cell proliferation at the edge of ulcer and affect the formation of ulcer scar [11]. Eradication of Hp cured peptic ulcer. The ulcer will not be complicated with complications such as hemorrhage or perforation when it is cured.

### **3.5 *Mucosal Blood Flow***

After acetic acid stimulation, experimental animals first experienced microvascular blockage, which gradually manifested as mucosal epithelium shedding and necrosis, and finally formed ulcers. During ulcer healing, obvious blood flow changes at the ulcer edge can be observed, and the blood flow increase of fully healed ulcers is more obvious than that of non-healed ulcers. Clinical observation found that EGF receptor in mucosa around ulcer increased obviously after the formation of ulcer, and there was aggregation in the ulcer area. Some of the EGF receptor was directly combined with ulcer marginal cells, and it could also indirectly increase the protective effect on regenerated mucosa and glands through the effects of PGs and somatostatin. The expressions of VEGF and FGF in gastric mucosa were from weak to strong, which were closely related to the repair of gastric mucosa. The formation of blood vessels in granulation tissue at the bottom of ulcer directly affected the quality of ulcer healing.

## **4. Drug Selection for Improving Ulcer Healing Quality**

All H p positive peptic ulcer, whether in active stage or not and with or without complication history in the past, must undergo H p eradication therapy. The principle of drug selection is: H p eradication rate > 90%; Due to various social or psychological factors, they cannot show high compliance, resulting in poor healing quality or recurrent ulcer. Studies have found that after cimetidine treatment, angiogenesis is poor and the density of neovascularization is 2 ~ 3 times less than that of surrounding normal tissues, which affects the healing quality. At present, western countries think that the best treatment for eradication of H p is OAC500 (omeprazole 20 mg, amoxicillin 1 g, clarithromycin 500 mg, bid, course of treatment 1 week), with an eradication rate of 96.4%. Wang Guozhong et al [12] studied the effect of raelidine and famotidine on gastric QOUH through randomized, multicenter and controlled trials. OMC250 (omeprazole 20mg, metronidazole

400mg, clarithromycin 250mg,bid, course of treatment for one week), eradication rate 94.6%. It was found that PPIs and mucosal protective agent significantly increased the ulcer healing rate compared with placebo, while only mucosal protective agent had significant effect on QOUH. After triple therapy, losers were treated with PPI+bismuth+2 antibiotics. These plans are more in line with China's national conditions. Antimicrobial drugs produced by different manufacturers are quite different in dosage form and dosage, and often the doctor's prescription is inconsistent with the patient's taking method. Doctors should try their best to let patients get more information about the disease and treatment, actively and correctly cooperate with treatment, so as to obtain the best therapeutic effect.

Whether peptic ulcer needs maintenance treatment with antacid after one course of Hp eradication treatment is still controversial. Some people think that eradication of Hp will cure the ulcer disease. Without Hp, the ulcer will not recur. According to the consensus of domestic scholars, Hp positive ulcers must be eradicated and treated according to the recommended treatment plan [13]. The principle of drug selection with the best cost-effective drug effect is: eradication rate>90%, good compliance and short course of treatment. Traditional Chinese medicine for invigorating spleen, clearing heat and removing blood stasis can promote gastrointestinal mucosal epithelial cell proliferation and tissue mucosal repair and improve QOUH by increasing EGF and EGFR levels. Therefore, it is advisable to maintain Hp eradication therapy for a period of time. In order to improve the quality of ulcer healing and reach the best state of ulcer healing. Therefore, it is suggested that duodenal ulcer should continue to take acid inhibitor for 4 weeks after Hp eradication, gastric ulcer should continue to take acid inhibitor for 6 ~ 8 weeks, and the medication time for senile giant gastric ulcer should be longer. Mucosal protectant can promote the synthesis of prostaglandins, EGF and FGF, promote the growth of epithelium and granulation, and repair tissues. Acid inhibitor can reduce the damage of gastric acid to newly-formed epithelial cells at the edge of ulcer and granulation tissues at the bottom of ulcer, thus synergistically promoting tissue repair and regeneration and maintaining the integrity of gastric mucosa structure and function.

According to the definition of peptic ulcer, the final formation of ulcer is caused by the digestion of gastric acid/pepsin itself. This concept has not changed in today's "Hp era". Furazolidone is a monoamine oxidase (MAO) inhibitor and has a good effect on killing HP. It has been used for 20 years to treat peptic ulcer. Studies have shown that [14] its anti-ulcer mechanism can not only kill Hp and promote mucus secretion, but also increase the content of dopamine in the brain and duodenum. Dopamine has a "dopamine cell protective effect" on gastrointestinal mucosa independent of PGs. At present, the best eradication plan still has a failure rate of 5% ~ 10%, so the maintenance treatment after HP eradication is conducive to improving ulcer healing quality. Wang Yingkun et al [15] advocated that the gastric ulcer should be maintained for 4 weeks after Hp eradication, the gastric ulcer for 6-8 weeks, and the maintenance treatment time for the elderly giant ulcer should be longer. This is a series of defense and repair mechanisms of gastroduodenal mucosa. Including mucus/bicarbonate barrier, mucosal barrier, mucosal blood flow, cell

renewal, acute healing of injury, prostaglandins and epidermal growth factor, etc. In the experimental study of gastric ulcer in rats, it is also confirmed that PPIs combined with Schweitzer has the best ulcer healing rate, healing quality index and QOUH indexes. It has good effects in preventing lipid peroxidation of biomembrane, increasing mucosal blood flow, reducing susceptibility to oxygen, and maintaining the integrity of gastric and small intestinal mucosa.

## 5. Conclusion

In a word, the quality of ulcer healing depends on the eradication of Hp and the maintenance treatment of acid inhibition for an appropriate period of time, the elimination of the risk factors of ulcer recurrence, and the reasonable selection of symptom self-control therapy. Factors affecting the quality of ulcer healing include Hp infection, gastric acid regurgitation, local gastrointestinal hormone deficiency and nutrient (blood supply) insufficiency, and improper selection of antiulcer drugs. QOUH focuses on the analysis and evaluation of the tissue state of local blast marks after ulcer healing. QOUH is closely related to ulcer recurrence. A more detailed and accurate evaluation of scar tissue after ulcer healing will provide a new way for drug selection, combination of drugs and finding methods to control ulcer recurrence.

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