



## CHAPTER 1

### BACKGROUND AND RATIONALE:

Leukemia is one of a few malignant diseases that can be effectively treated by chemotherapy. Acute myelogenous leukemia (AML) is the most common type of acute leukemia in adults. In China, AML is also the most common type of leukemia of adults. With the introduction of chemotherapy 40 years ago, 50-70% of adult AML patients can achieve a complete remission with a median remission duration of 1 year<sup>[1]</sup>. Some patients can even be cured by chemotherapy.

Infection and bleeding are the most important direct causes of deaths in patients with hematologic malignancies<sup>[2]</sup>. With the improvement of blood transfusion, especially the wide availability of blood components, e.g. platelets and plasma, most bleedings can now be effectively controlled. Although new antibiotics are being introduced at an increasing speed, infection still remains a leading cause of excess morbidity and mortality among granulocytopenic patients with malignancies<sup>[3]</sup>. The risk of infection is particularly high in patients with acute leukemia, in whom fatal infection occurs in up to 25% or more of those receiving remission induction chemotherapy<sup>[4]</sup>. The control of infection requires a lot of money.

The primary site of infection is the alimentary tract where chemotherapy induced mucosal damage allows invasion by the potentially pathogenic microorganisms that colonize the gastrointestinal tract<sup>[6, 7]</sup>. Damage to the integument

by invasive procedures, such as bone marrow aspiration or placement and maintenance of vascular access devices, may also serve as a portal for infection.

Infections are principally caused by aerobic gram-negative bacilli (especially *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*) and gram-positive cocci (in particular, coagulase-negative staphylococci,  $\alpha$ -hemolytic streptococci, and *Staphylococcus aureus*). Fungi are common causes of secondary infections among neutropenic patients who have received broad-spectrum antibiotics<sup>[5]</sup>.

Prophylactic alimentary tract decontamination by oral antibiotics has been tried in neutropenic cancer patients and acute leukemia patients during granulocytopenia<sup>[4]</sup>. These include oral administration of nonabsorbable drugs such as gentamycin, nystatin, vancomycin, framycetin, polymyxin B, colistin, and absorbable drugs such as trimethoprim/sulfamethoxazole (TMP-SMZ) and the quinolone drugs. The nonabsorbable antibiotics are not recommended because of the controversial reports of the previous studies<sup>[5]</sup>. Some studies show that TMP-SMZ and quinolones are effective in preventing documented infections of neutropenic patients. The major disadvantages of oral prophylactic antibiotics include colonization of gastro-intestinal tract as well as other sites with antibiotic resistant pathogens, the potential bone marrow toxicity of TMP-SMZ<sup>[8]</sup> and fungal superinfection<sup>[9]</sup>, in addition to the cost of the drugs. So oral antibiotic prophylaxis is not widely accepted in China.

Garlic (*Allium sativum*) is a member of the family Liliaceae, or Lily. It has been used in both ancient and modern times to treat medical conditions including infections. The active component for many of its therapeutic effects is allicin, of

which the chemical composition is diallyl thiosulfinate<sup>[10]</sup>. A chemically stable final transformation product of allicin, diallyl trisulfide has been synthesized and available as oral capsules, intramuscular and intravenous preparations in China<sup>[11]</sup>. In vitro studies have shown that allicin is effective in inhibiting the growth of gram-positive (e.g. *Staphylococcus aureus*), gram-negative (e.g. *Pseudomonas aeruginosa*, *Escherichia coli*, enterococcus etc.) bacteria<sup>[12]</sup>, fungus<sup>[13]</sup> and virus<sup>[14]</sup>. Aqueous extract of garlic has been reported to effectively cure laboratory animals of experimental shigelosis<sup>[15]</sup>. In addition, allicin has been shown to be effective in lowering blood lipids and blood pressure and to inhibit platelet aggregation.

Since garlic is non-toxic, easily available, inexpensive, active against both G<sup>-</sup> and G<sup>+</sup> bacteria, fungus and virus, it may be used as chemoprophylaxis for neutropenic patients. If it can be proven effective in preventing infection of granulocytopenic patients or leukemic patients during chemotherapy, both the patients and the society would benefit. The objective of the present study was to prove the efficacy of garlic in preventing infection in chemotherapy induced neutropenic patients.

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