Kanglaite Injection Combined with HAD Regimen in the Treatment of Adult Acute Non-Lymphocytic Leukemia

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Abstract

Objective: To observe therapeutic efficiency of Kanglaite Injection (KLT) combined with HAD regimen in the treatment of adult acute non-lymphocytic leukemia (ANLL)

Methods: 12 cases with ANLL admitted between Feb.1995 and Apr.1998 were analyzed. Regimen in the first cycle: KLT100ml iv, twice per day, d1-d7; HHT 2mg im, twice per day, d1-d7; Ara-C 100mg hypodermic, once every 12 hours, d1-d7; DNR 60mg plus saline 40ml iv, once per day, d1-d3. The 2nd cycle started after recovery from bone marrow inhibition, about 2-5 weeks after the 1st cycle. Results: 9 of 12 cases reached CR (75%) with an average of 1.22 cycles. Conclusion: KLT combined with HAD regimen to treat ANLL had higher CR rate, quicker therapeutic efficiency and less side and toxic reaction.

Key words: leukemia, non-lymphocyte, acute, Kanglait, HAD regimen, anticancer drug, multi-dosage application

HA and DA regimens are common effective therapies nowadays in treating ANLL\(^1\). The regimens include HHT, Ara-C and DNR. A lot of severe complications occur due to the fact that the treatment dosage and intensity reach the degree to cause inhibition of bone marrow regeneration. However KLT has remarkable inhibitive effect on various cancer cells with quite slight adverse reaction. From 1995 we have designed KLT + HAD regimen to treat 12 cases with ANLL and obtained initial positive outcomes to report as follows.

1. Materials & methods
12 cases with ANLL were confirmed by bone marrow smear between Feb.1995 and Apr.1998 among whom 7 were male and 5 female, age between 19-59 with median as 40, 9 as first visit and 3 as return visit (2 cases not remitted after 2 or 3 cycles of HOAP regimen and 1 case relapsed 8 months after DA regimen as CR). FAB classification: 3 cases as M\(_1\), 4 as M\(_2\), 3 as M\(_4\) and 2 as M\(_5\). WBC before treatment: 0.8 x10\(^9\)/L -260 x10\(^9\)/L, hemoglobin: 30g/L -100g/L, platelet: 7x10\(^9\)/L -85 x10\(^9\)/L

The 1st cycle of regimen included KLT 100ml iv drip, twice per day, d1-d7; HHT 2mg im, twice per day, d1-d7; Ara-C 200mg per day, 100mg hypodermic every 12 hours, d1-d7 and DNR 60mg plus saline 40ml iv injection, once per day, d1-d3. The 2nd cycle started after recovery from bone marrow inhibition with 2-5 weeks between the 2 cycles.

During the treatment patients stayed in ordinary ward sterilized by ultraviolet ray once per day for 30 minutes each time. During chemotherapy and bone-marrow inhibition period patients were instructed to rinse out with compound sodium borate solution and orally take floxacin and
mycostatin to prevent infection. When body temperature exceeded 38°C, infectious focus was
looked for and specimen was sent for bacterial culture. At the same time antibiotics (ampicillin
or cefradin plus aminoglycoside antibiotics) were administered intravenously. In case of
severe infection or bleeding, fresh or prepared blood was infused.

The assessment of efficiency was based on the criteria formulated in 1987 by national
symposia on leukemia chemotherapy.

2. Results

Remission rate: Among 12 cases, 9 were with CR of whom 2/3 as M₁, 3/4 as M₂, 2/3 as M₄
and 2/2 as M₅. 2 cases were with PR. Total effective rate: 91%. Out of 9 first visit patients 7
cases were with CR (77.8%). And 2 of 3 relapsed patients got CR.

No. of cycles and time to reach remission: Cycle for 9 CR cases to reach remission was 1-2
(21-50 days) with an average of 1.22 cycles among whom 7 cases reached CR after 1 cycle
(77.8%) and 2 cases got CR after 2 cycles (22.22%).

Toxic/side effects & complications: (1) In non-hematopoietic system: 3 cases had slight
nausea and vomit which were remitted after muscular injection of metoclopramide. 1 case had
liver function damage with ALT (GPT) up to 60u and was back to normal within 1 week after
oral administration of glucuronolactone and Yi Gan Ling (a traditional Chinese medicine).
Renal function, EKG, echocardiogram and myocardial enzyme analysis of these patients had
no apparent change before and after the treatment. (2) In hematopoietic system: 12 cases had
bone-marrow inhibition after chemotherapy and were recovered after 2-5 weeks. Before
treatment bone-marrow regeneration for all patients was active or super-active and after the
treatment 10 cases became reductive or heavily reductive. The patients with WBC≤0.5x10⁹/L
and BPC≤20x10⁹/L accounted for 60% and 66% of the total treated cases respectively. 5
cases had skin petechiae, ecchymosis or nasal hemorrhage. 6 cases were with combined
infection, 3 cases with pneumonia, 1 case with acute paranasal sinusitis and 2 cases with
periodontitis. All of them got controlled after empiric antibiotics treatment (cephalosporin +
aminoglycoside + metronidazole). 1 case applied Fortum to control infection.

3. Discussion

HA and DA regimens are common effective therapies in treating adult acute non-lymphocytic
leukemia (ANLL). Some patients not responded to HA or DA regimen induction can still get
remitted after interchanging the regimens. This shows that there is no cross resistance
between HHT and DNR\[^2\]. Fraction of proliferative leukemia cells in patient bone-marrow is
often quite low before treatment and this may lead to low sensibility to cell specific drugs and
requires high dosage and more treatment cycles to reach remission. Combined application of
various non-cell cycle specific drugs is conducive to the enhancement of chemotherapeutic
sensitivity so as to elevate treatment efficiency[^3]. Both HTT and DNR belong to non-cell cycle specific drug and HAD regimen theoretically is reasonable in the treatment of ANLL. Modern concept holds that intensive chemotherapy is the most important factor to mark the progress in improving clinical treatment efficiency for acute leukemia and the remission speed of induction remains a main factor to decide patient prognosis. The HAD regimen belongs to intensive therapy with severe toxicity and complications. That is why we considered to apply KLT.

KLT is an emulsion with major substance extracted from traditional Chinese medicine “*semen coicis*”. It is a new dual-function anticancer drug. KLT blocks cancer cells division, inhibits their proliferation and eventually causes apoptosis of cancer cells. KLT has no apparent toxic and side effect. It can reverse multi drug resistance (MDR) of cancer cells and at the same time significantly elevates immune-function of cancer patients. We combined in this observation KLT with HAD regimen to treat ANLL. CR rate of 12 cases reached 75% and CR rate was 77.7% after 1 cycle with satisfactory outcomes which were obviously better than HA or DA regimen. General toxicity in the study group remained the same as those with other induction regimens to treat ANLL. This showed that KLT combined with HAD regimen could enhance efficiency as a synergist and reduce chemotherapy toxicity. Due to limited case number and short observation period this combination regimen still needed further data accumulation and a long-term observation.

**References**