

DICE Regime as the Second for Refractory or Relapsed Non-Hodgkin's Lymphoma

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Abstract Objective To explore efficiency and toxicity of DICE regimen as second-line chemotherapy in refractory or relapsed non-Hodgkin's lymphoma. **Methods** 28 patients of refractory or relapsed non-Hodgkin's lymphoma were treated by DICE regimen. Blocking acupuncture points of Zusanli with dexamethasone or granulocyte colony-stimulating factor(G-CSF) against myelosuppression induced by chemotherapy. **Results** A complete response was seen in 7 patients (25.0%), and a partial response was observed in 8 patients (28.6%). A significantly higher response rate was seen in patients with relapsing non-Hodgkin lymphoma compared with those in patients with refractory non-hodgkin lymphoma. (10/16 vs 4/12, $p < 0.01$). Low response rate in high LDH group compared to that in normal group. Toxicity was nausea/vomiting, alopecia and reversible myelosuppression. All the patients can tolerance the side effects and there was none drug-related death associated with myelotoxicity. **Conclusion** DICE regime was a relatively safe and highly efficient salvage for relapsed but not refractory NHL, this suggested the there may be different biology character between both them and the different strategies should be provided for them. LDH may be a marker for sensitive chemotherapy.

Key Words refractory or relapsed non-Hodgkin's lymphoma; Second-line salvage regime

CHOP regimen containing adriamycin was viewed as "gold" standard for non-Hodgkin lymphoma(NHL)^[1-2] and its rate of cure was about 30% , however, the regime was poor for refractory or relapsed NHL. High-dose chemotherapy combing stem-cell transplantation was limited because its cost was very expensive and its effective was disputing^[3-5], therefore, effective second-line salvage agent was paid close attention to NHL. Our data suggested that DICE regimen viewed as the second-line combination was ideal for refractory or relapsed NHL.

MATERIAL AND METHODS

General data

In all 28 cases, including 21 males and 7 females, their median age was 42 years old(14~63 years old) and karnofsky score was over 70. All patients had measuring tumor size and they were routinely carried out puncture procedure of bone marrow and measurement of lactate dehydrogenase (LDH). The functions of liver, kidney and heart of

the patients were normal. All patients was pathologically diagnosed as NHL with middle and high-grade. In all cases, 8 patients associated with infiltrating bone marrow and 12 cases with ascending LDH. 16 patients was with replapsed disease and 12 cases with refractory.

Therapy methods

The programme consisted of dexamethasone 20mg/m² intravenously daily for 5 days, ifosfamide 1200 mg/m² mixed with equal dosing of mesna continuously intravenous infusion daily for 5 days, cisplatin 20 mg/m² intravenously each day for 5 days and etoposide 75 mg/m² continuously intravenous infusion daily for 5 days, all administered every 3 weeks. Blocking acupuncture points of Zusanli with dexamethasone or G-CSF support was provided for 6-10 day, 21-28 day repeat above procedure which is regard as a cycle. Effect evaluation was carried out after 2 cycles. All 28 patients was administered 69 cycles, mean 2.6 cycles(2-8 cycles).

Evaluation standard

Evaluation standard by WHO for solid carcinoma was used, including complete remission (CR), part remission(PR), stead(SD) and progress(PS) and response rate was binding of CR and PR. Toxic

reaction was divided into 0-IV grade according to WHO.

RESULTS

Resent effect

Of 28 patients, 15 (53.6%) achieved a significant response consisting of 7 complete remissions (CR) (25%) and 8 (28.6%) partial remissions (PR). There were 62.8% objective responses in relapsed group comprised of 31.3% CR and 31.3% PR and there were 33.3% objective responses in refractory group comprised of 8.3% CR and 25% PR, however, there was no significant difference between them ($P < 0.01$). In addition, there was also no significant difference between the group for diffusion of bone marrow and non-diffusion group (CR: 2/8 Vs 5/20 respectively). Nevertheless, significant difference existed between escalated LDH group and normal LDH group (CR: 2/12 Vs 5/16, $P < 0.01$, Fisher's exact test). Long-term follow-up study was under way.

Adverse reactions

Toxicity was mainly nausea, bone marrow impression and alopecia. none% developed grade III-IV toxicity after prevention of Kang Ouan and blocking acupuncture points of Zusanli with dexamethasone or G-CSF support. All patients could well tolerate toxicity response of the drugs well and there were no death associated with chemotherapy.

DISCUSSION

In recent years, half of patients with NHL was difficult to complete remission or relapsed after standard therapy. Prognosis was poor for the patients. 40%-60% patients could achieve the second-remission by high-dose chemotherapy containing stem-cell transplantation, however, the death associated to this therapy was up to 5%-10%^[6] and the treatment was limited because of high price. Therefore, selection of effective and economic therapy was becoming a focus.

Ifosfamide (IFO) was a broader anti-tumor drug and it had longer half life in serum and stronger anti-tumor activity than cyclophosphamide. Its total remissive rate for NHL was up to 57%^[7-9]. Cisplatin was one of the strongest anti-tumor drugs and combination with IFO could be more effective for malignant tumor. Etoposide was inhibitor of topoi-

somerase I and it was one of the effective drugs for lung cancer and lymphoma. It was showed that etoposide and dexamethasone could reverse drug resistance because of multidrug resistance gene. On these grounds, DICE regimen was designed for relapsed and refractory NHL^[10-11] and it showed higher remission rate (53.6%) and non-associated death. So the regimen should be worth further studying and extending, however, the view should be showed that the effect was different for relapsed or refractory NHL and it was better in relapsed group than that in refractory group. The result showed there could be different biology character in both groups and the latter could be drug resistance at the beginning; on the other hand, the result could also show different therapy method should be selected in both groups and it was coincident with Haim'^[12-13]. In addition, the study showed the regimen was the same effect between infiltrative bone marrow group and non-infiltrative group, but, it was statistically different between high LDH group and normal LDH group (CR was 2/12 Vs 6/16, $P < 0.01$). The result showed that LDH could be related to chemotherapy sensitivity, but bone marrow diffusion had nothing to do with this.

The study suggested that DICE regimen may be considered as the second salvage for relapsed NHL not refractory NHL, and LDH could be used as one of index of chemotherapy sensitivity.

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