

Clinical Efficacy of Decitabine/Azacitidine in Combination with HAG in the Treatment of Elderly Patients with Acute Myeloid Leukemia

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Abstract: This study was conducted to investigate the clinical effect of combining decitabine/azacitidine with HAG in the treatment of single elderly patients with acute myeloid leukemia. Patients in Shaanxi Provincial People's Hospital were selected for this study from January 2020 to January 2022, and all of the patients were elderly patients with acute myeloid leukemia. Around 23 patients were selected for this study, subsequently the patients were divided into two groups; Group A contained 11 patients and was given decitabine in combination with HAG; and Group B contained 12 patients, and was given azacitidine in combination with HAG. This study showed that the treatment effective rates of patients in both groups were 90.91% and 58.33%, respectively, with a small difference ($p > 0.05$) in the data comparison. The incidence of adverse reactions in the two groups was 63.64% and 16.67%, respectively, with the incidence in group B is significantly ($p < 0.05$) lower compared with group A. Meanwhile, compared with group B, patients in group A had a significantly ($p < 0.05$) shorter mean time to WBC normalization, higher HB and PLT levels, lower WBC levels were lower, all the survival duration times were longer, and subpopulation indicators of peripheral blood T lymphocytes were more in line with normal values. In summary, this study demonstrated that the combination of azacitidine and HAG therapies for the treatment of elderly patients with acute myeloid leukemia is more effective, furthermore can reduce significantly the incidence of adverse treatment effects in patients.

Keywords: Decitabine; Azacitidine; HAG; Elderly patients with acute myeloid leukaemia

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1. Introduction

Acute myeloid leukemia (AML) is a heterogeneous hematological malignancy, where the patient with this disease presents with abnormal differentiation of the bone marrow and peripheral hematoma or clonal proliferation of undifferentiated myeloid cells [1,2]. The outcome of the treatment for this disease is poor, and commonly, patients developed various adverse events following the treatment. One of the most common types of AML is senile acute myeloid leukemia with an increase in the incidence rate yearly, and sadly this disease predominating in older patients over 60 years of age. Therefore, it is particularly important to treat the patients with an appropriate treatment, to minimize the incidence of adverse effects in patients [3-6]. In this study, we used two different treatment regiment, which are decitabine combined with HAG, and azacitidine combined with HAG in elderly patients with AML, and compared the clinical outcomes in patients with the different treatment type.

2. Data analysis and methodology

2.1. General information

The study was conducted in the Shaanxi Provincial People's Hospital from January, 2020 and January, 2022. Around 23 elderly patients with acute myeloid leukemia were selected for this study, subsequently they are divided into two groups; Group A: 11 patients, the male and female patients were 6 and 5, respectively, and the age range of the patients was 62 years to 88 years with a mean age of (72.12 ± 1.33) years; Group B: 12 patients, the male and female patients were 7 and 5, respectively, the oldest being 90 years old and the youngest 61 years old, with a mean age of (72.78 ± 1.67) years. There is no significant difference ($P > 0.05$) in terms of the patient's demographic data between these two groups, which met the criteria for comparative studies.

2.2. Research methodology

Patients in group A were given decitabine combined with HAG treatment regimen, in which decitabine was administered at a dose of 25 mg, drug intervention by intravenous drip, on days 1-5, and granulocyte colony-stimulating factor was applied at a dose of 300ug/d, intervention by subcutaneous injection. High trichostatin was administered intravenously at a drug dose of 1mg/m², and intervened on days 1-7. An aclarubicin was used intravenously, intervening on days 4, 6, 8, and 10. Agranulocyte was administered at a dose of 10mg/m², q12h, on days 1-7 intervention. During the course of the therapeutic intervention given to the patient, if the patient's WBC was at $20 \times 10^9/L$, the use of G-CSF was stopped immediately, and the patient will be given symptomatic treatment.

Patients in group B were treated with azacitidine combined with HAG regimen, in which the dose of azacitidine used were 75mg/m² by subcutaneous injection for intervention on days 1-7, and G-CSF is applied at a dose of 300ug/d by subcutaneous injection, and hypertrigonelline is applied at a dose of 1mg/m² by intravenous drip, intervention on days 1-7, and the application of Aconitine at a dose of 10mg/m² by subcutaneous injection, q12h, intervention on days 1-7. The patient-specific interventions is given based on the patient's actual condition.

2.3. Observed indicators

The treatment effect of the two groups of patients was observed by applying the International Working Group on AML criteria, consist of three main indicators; namely, (1) Complete remission, mainly refers to the improvement of the patients' symptoms after treatment and no progression of the disease; (2) Remission mainly refers to the partial control of the patients' symptoms; and (3) Non-remission mainly refers to the deterioration of the patients' disease and no improvement of their symptoms. Few indicators as described below were used to compare the effectiveness of different treatment regimens in this study.

- (1) The total effective rate is calculated by excluding non-remission.
- (2) The incidence of adverse reactions in the two groups was compared.
- (3) The recovery time of white blood cell (WBC), hemoglobin (HB), platelet (PLT) levels and various peripheral blood T lymphocyte subpopulation indicators were compared between the two groups.
- (4) Patients were followed up, and their disease-free survival time and overall survival time were observed, recorded, and compared.

2.4. Statistical analysis

For statistical analysis, SPSS 20.0 software was used for the calculation of the measurement data, and the results were expressed as $(\bar{x} \pm s)$, and the validation data were based on t-values, while for the statistics of the count data, the comparison results were counted using (n/%) for validation, which was expressed as 2 values, in which the results showed a data ratio of 0.05 hours, indicating the calculated data is significant.

3. Results

3.1. Efficient comparison

The treatment effective rates for the two groups, group A and B were 90.91% and 58.33%, respectively, with a small difference ($p > 0.05$) observed in the comparison as shown in **Table 1**.

Table 1. Comparative analysis of the effective rates of the two groups [n (%)]

| Group | Completely relief | Relief | No relief | Efficient |
|----------------|-------------------|-----------|-----------|------------|
| Group A (n=11) | 8 (72.73) | 2 (18.18) | 1 (9.09) | 10 (90.91) |
| Group B (n=12) | 4 (33.33) | 3 (25.00) | 5 (41.67) | 7 (58.33) |
| \bar{x} | | | | 3.159 |
| p value | | | | 0.076 |

3.2. Incidence of adverse reactions

The incidence of adverse reactions in the two groups, group A and B was 63.64% and 16.67%, respectively, with a significantly lower ($p < 0.05$) incidence in group B, compared to group A as shown in **Table 2**.

Table 2. Comparison of the incidence of adverse reactions in the two groups [n (%)]

| Group | Bone marrow suppression | Anemia | Neutropenia | Incidence |
|----------------|-------------------------|-----------|-------------|-----------|
| Group A (n=11) | 2 (18.18) | 3 (27.27) | 2 (18.18) | 7 (63.64) |
| Group B (n=12) | 1 (8.33) | 1 (8.33) | 0 (0.00) | 2 (16.67) |
| \bar{x} | | | | 5.316 |
| p value | | | | 0.021 |

3.3. Comparison of WBC recurrence times

Patients in group A, has a significant ($p < 0.05$) shorter mean time to WBC recurrence compared to group B as shown in **Table 3**.

Table 3. Comparison of the duration of normalization of WBC in the two groups ($\bar{x} \pm s$)

| Group | Mean time to recurrence of WBC (d) |
|----------------|------------------------------------|
| Group A (n=11) | 6.12±0.56 |
| Group B (n=12) | 8.77±1.53 |
| t | 5.413 |
| p value | 0.000 |

3.4. Comparison of patients' HB, WBC, and PLT levels

After the treatment, compared to group B, patients in group A have higher ($p < 0.05$) levels of HB and PLT, and lower WBC levels as shown in **Table 4**.

Table 4. Comparison of HB, WBC, and PLT levels in the two groups after treatment ($\bar{x} \pm s$)

| Group | HB (g/L) | WBC ($\times 10^9/L$) | PLT ($\times 10^9/L$) |
|----------------|-------------------|-------------------------|-------------------------|
| Group A (n=11) | 108.34 \pm 5.44 | 5.66 \pm 1.00 | 87.34 \pm 3.24 |
| Group B (n=12) | 97.56 \pm 5.33 | 7.66 \pm 1.13 | 81.35 \pm 3.41 |
| t | 4.798 | 4.478 | 4.309 |
| p value | 0.000 | 0.000 | 0.000 |

3.5. Comparison of peripheral blood T lymphocyte subsets in the two groups

Various peripheral blood T-lymphocyte subpopulation indicators for both groups are shown in **Table 5**.

Table 5. Comparison of peripheral blood T lymphocyte subsets between the two groups ($\bar{x} \pm s$)

| Group | CD8 ⁺ (%) | CD4 ⁺ (%) | CD4 ⁺ /CD8 ⁺ |
|----------------|----------------------|----------------------|------------------------------------|
| Group A (n=11) | 24.34 \pm 4.33 | 39.46 \pm 5.23 | 1.54 \pm 0.44 |
| Group B (n=12) | 32.12 \pm 4.56 | 32.41 \pm 5.56 | 1.12 \pm 0.34 |
| t | 4.187 | 3.125 | 2.574 |
| p value | 0.000 | 0.005 | 0.018 |

3.6. Survival time of the patients in both groups

Group A patients showed a significant ($p < 0.05$) different in both the disease-free survival time and overall survival time of patients, than patients in group B as shown in **Table 6**.

Table 6. Comparison of survival times of patients in the two groups ($\bar{x} \pm s$)

| Group | Disease-free survival time (months) | Total survival time (months) |
|----------------|-------------------------------------|------------------------------|
| Group A (n=11) | 14.23 \pm 1.23 | 16.56 \pm 1.43 |
| Group B (n=12) | 9.44 \pm 0.23 | 14.34 \pm 1.22 |
| t | 13.267 | 4.016 |
| p | 0.000 | 0.000 |

4. Discussion

In terms of actual clinical developments, there are two main type of DNA demethylation drug, which are decitabine and azacitidine. These are used to promote the recovery of AML cells by expressing oncogenes that have a multiple silencing function on DNA methyltransferases (DNMTs), allowing the normal differentiation and apoptosis [7-11]. In the case of azacitidine, this drug acts mainly on RNA, mRNA, and protein metabolism, converting them into decitabine triphosphate, subsequently inhibit the DNMTs, in contrast decitabine act on DNMTs by acting on DNA [12,13]. This study demonstrated that decitabine has a better demethylation effect, meanwhile azacitidine has a positive effect on reducing cellular activity, and provides effective inhibition of protein synthesis [14-17]. In addition, the data also showed that both the demethylating drugs, azacitidine and decitabine, have better clinical outcomes compared to conventional treatments method, and both are effective in improving patients' adverse symptoms [18,19]. However, the use of these drugs can cause damage to patients and lead to adverse reactions, whereas azacitidine is less effective but has reduce level of adverse symptoms in patients, thereby may facilitate their recovery [20].

In conclusion, the combination of azacitidine and HAG therapy in the treatment of elderly patients with AML is more effective, where it can reduce the incidence of adverse effects in patients, subsequently

improve the treatment effect in patients.

Disclosure statement

The authors declare no conflict of interest.

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