

Analysis of the Effect and Adverse Reaction of Cisplatin Metronomic Chemotherapy Combined with Radiotherapy in the Treatment of Stage II–IV Nasopharyngeal Carcinoma

Maimaiti Yiming Yasheng*, Mireguli Rouzi, Shokaya Yasen, Ainivarjiang Abdu Rousu Li

Department of Otolaryngological, the People's First Hospital of Kashi, Xinjiang 844000, China

*Corresponding author: Maimaiti Yiming Yasheng, 13579099018m@sina.cn

Copyright: © 2024 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To analyze the effect and adverse reaction of cisplatin metronomic chemotherapy combined with radiotherapy in the treatment of stage II–IV nasopharyngeal carcinoma. *Methods:* Fifty nasopharyngeal cancer patients (in stage II–IV) admitted to our hospital from January 2022 to December 2023 were selected and randomly divided into a control group and an observation group of 25 cases each. The control group was treated with cisplatin conventional chemotherapy combined with radiotherapy and the observation group was treated with cisplatin metronomic chemotherapy combined with radiotherapy. Both groups were compared in terms of recent efficacy, adverse effects, natural killer (NK) cell activity, T-cell subpopulation changes, and treatment adherence. *Results:* The clinical remission rate of the two groups were not significant ($P > 0.05$), but the incidence of adverse reactions in the observation group was lower than that in the control group, and the levels of NK cell activity, CD3, CD4, and CD4/CD8 cells in the observation group were higher than that in the control group after treatment ($P < 0.05$). The treatment compliance in the observation group was higher than that in the control group ($P < 0.05$). *Conclusion:* In the treatment of stage II–IV nasopharyngeal carcinoma, adopting cisplatin metronomic chemotherapy combined with radiotherapy therapy achieved better therapeutic efficacy, reduced adverse reactions, increased NK cell activity, regulated T-cell subsets, and has an overall high application value.

Keywords: Nasopharyngeal carcinoma; Stage II–IV; Cisplatin metronomic chemotherapy; Radiotherapy; Adverse reactions

Online publication: 3 July, 2024

1. Introduction

Nasopharyngeal cancer, whose cancer cells originate from nasopharyngeal mucosal epithelial tissue, is a relatively high-incidence class of head and neck malignant tumors. Most of the patients consult the doctor due to the discovery of neck masses, with insidious symptoms in the early stage. As the disease progresses, symptoms such as nosebleeds, head and face pains, and blurred vision may appear, which may even lead to speech and breathing

difficulties. There are also differences in the performance of symptoms corresponding to the metastasis of different sites of the cancer cells in later stages^[1]. The early diagnosis rate of nasopharyngeal cancer is low, and in clinical treatment, surgery, radiotherapy, chemotherapy or radio-chemotherapy synchronization can be chosen depending on the specific situation. In chemotherapy treatment, cisplatin is a commonly used drug that can kill cancer cells, and the principle of radiotherapy is to destroy DNA molecules of tumor tissues, thus killing cancer cells. It has become the main therapy treatment for nasopharyngeal cancer, as conventional chemotherapy can cause more adverse reactions and damage the body's functions. Metronomic chemotherapy is a new strategy for tumor treatment, which is characterized by low doses of conventional chemotherapeutic drugs, as well as frequent and continuous treatment without long chemotherapy intervals, and anti-tumor vascular treatment with vascular endothelial cells as the therapeutic target. When combined with radiotherapy, it can produce a synergistic effect^[2]. We studied the effect of cisplatin metronomic chemotherapy combined with radiotherapy in the treatment of stage II–IV nasopharyngeal carcinoma as well as analyzed the incidences of adverse reactions.

2. Data and methods

2.1. General information

Fifty cases of nasopharyngeal cancer patients admitted to our hospital from January 2022 to December 2023 were selected and randomly divided into a control group and an observation group of 25 cases each. The control group consisted of 17 males and 8 females aged 23–65, with an average age of 48.20 ± 5.59 years. There were 6 cases of patients in stage II of the disease, 15 cases in stage III, and 4 cases in stage IV. There were 21 cases of poorly differentiated squamous carcinoma, 3 cases of undifferentiated carcinoma, and 1 case of vesicular nucleated cell carcinoma. The observation group consisted of 19 males and 6 females aged 25–66, with an average of 48.11 ± 5.40 years. There were 6 cases of patients in stage II, 16 cases in stage III, and 3 cases in stage IV. There were 20 cases of poorly differentiated squamous carcinoma, 4 cases of undifferentiated carcinoma, and 1 case of vesicular nucleated cell carcinoma. The data of the two groups were comparable but were not significant ($P > 0.05$).

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Patients with nasopharyngeal carcinoma diagnosed by pathological examination and in stage II–IV; (2) patients with primary treatment or after 1–2 cycles of induction chemotherapy; (3) blood routine, liver, and kidney functions and other tests are normal; (4) no contraindication to radiotherapy; (5) no serious internal medicine disease; (6) complete clinical information. Exclusion criteria: (1) Patients with recurrence after radiotherapy; (2) primary diseases combined with liver and kidney function damage, cardiovascular and cerebrovascular damage; (3) combined with psychiatric diseases; (4) a history of local radiation therapy; (5) those who dropped out halfway.

2.3. Methods

The control group received cisplatin conventional chemotherapy combined with radiotherapy. Cisplatin was administered once a week at a 40 mg/m^2 dosage. A 6MV-X-ray intensity-modulated radiotherapy method was used to fix the head, neck, and shoulder. CT-enhanced continuous scanning was performed to determine the specific location of the target area and the actual size of the target area. According to the location, size, and CT image, a target plan was roughly outlined to develop an irradiation dosage. This treatment was carried out for 5 times a week for 6–7 consecutive weeks.

The observation group received cisplatin metronomic chemotherapy combined with radiotherapy. The radiotherapy method was the same as the control group and cisplatin treatment was administered twice a

week at 8 mg/m² each time. For patients with more serious conditions, both groups were given the following intervention program: one to two cycles of induction chemotherapy before radiotherapy, and three to four cycles of adjuvant chemotherapy after radiotherapy.

2.4. Observation indexes

The recent therapeutic effect between the two groups was compared [3]. The treatment effect was evaluated after one month. If the target lesion disappears completely and no new lesion appears, it is judged as “complete remission”; if the diameter of the target lesion is reduced by $\geq 30\%$ and the maintenance time is ≥ 4 weeks, it is judged as “partial remission”; if the diameter of the target lesion is reduced by $< 30\%$ and the maintenance time is ≥ 4 weeks, it is judged as “partial remission.” If the diameter of the target lesion is reduced by less than 30%, if the target lesion is enlarged, or if new lesions appear, it is included in the category of “stable/progressing.” Remission rate = complete remission rate + partial remission rate.

The incidence of adverse reactions between the two groups was compared, including nausea and vomiting, skin toxicity, and oral mucosal toxicity. The changes in NK cell activity and T-cell subsets, CD3, CD4, CD8, and CD4/CD8 cells were also compared.

The treatment adherence between the two groups was compared [4]. In the total course of treatment, the expected number of cisplatin doses in the control group and the observation group were 6 times and 13 times, respectively. The treatment adherence was judged according to the stipulated completion of the expected dosage, which was “Excellent” in the range of 75–100%, and “Good” in the range of 25–75%. The rate of treatment adherence was indicated as follows: “Excellent” for 75–100%; “Good” for 25–75%; and “Poor” for 0–25%. Good adherence = percentage of excellent + percentage of good.

2.5. Statistical methods

The data in the study were analyzed by the SPSS version 25.0 software. Measurement data sets were expressed as mean \pm standard deviation and the count data were expressed as %. Measurement data were analyzed using a *t*-test, and count data were analyzed using a chi-squared (χ^2) test. Results were considered statistically significant at $P < 0.05$.

3. Results

3.1. Recent therapeutic effect

As shown in **Table 1**, the difference in the remission rate between the two groups of patients in the treatment of nasopharyngeal primary foci and neck lymph nodes was not significant ($P > 0.05$).

Table 1. Recent therapeutic effect between the two groups [*n* (%)]

Focus	Cases, <i>n</i>	Group name	Full remission	Partial mitigation	Stabilization/progress	Mitigation rate
Nasopharyngeal primary focus	25	Control group	23	1	1	24 (96.00)
	25	Observation group	25	0	0	25 (100.00)
χ^2/P			-	-	-	1.020/0.312
Neck lymph nodes	-	Control group	23	1	1	24 (96.00)
	-	Observation group	24	1	0	24 (96.00)
χ^2/P			-	-	-	0.000/1.000

3.2. Adverse reactions

As shown in **Table 2**, the incidence of adverse reactions in the observation group was lower than that in the control group ($P < 0.05$).

Table 2. Incidence of adverse reactions between the two groups [n (%)]

Group	Cases, n	Nausea and vomiting	Dermal toxicity	Oral mucosal toxicity	Pharyngeal/esophageal toxicity	Salivary gland toxicity
Control group	25	23 (92.00)	23 (92.00)	22 (88.00)	22 (88.00)	23 (92.00)
Observation group	25	14 (56.00)	17 (68.00)	15 (60.00)	14 (56.00)	14 (56.00)
χ^2	-	8.420	4.500	5.094	6.349	8.420
P	-	0.004	0.034	0.024	0.012	0.004

2.3 NK cell activity and T cell subsets in the two groups

As shown in **Table 3**, the comparison of the indicators of the two groups of patients before treatment was not significant ($P > 0.05$). After treatment, the NK cell activity of the observation group was greater than that of the control group, and the levels of CD3, CD4, CD4/CD8 in the T-cell subsets were also higher than that of the control group ($P < 0.05$).

Table 3. NK cell activity and T-cell subsets between the two groups (mean \pm standard deviation, %)

Group	Cases, n	NK cell activity		CD3		CD4		CD8		CD4/CD8	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Control group	25	31.52 \pm 5.29	26.71 \pm 5.13	48.52 \pm 6.36	39.15 \pm 6.15	30.14 \pm 6.25	24.59 \pm 5.58	20.23 \pm 5.13	20.28 \pm 5.16	1.45 \pm 0.29	1.16 \pm 0.48
Observation group	25	31.47 \pm 5.15	38.79 \pm 6.12	48.38 \pm 6.24	57.45 \pm 6.20	30.22 \pm 5.59	39.17 \pm 5.16	20.15 \pm 5.22	20.32 \pm 5.29	1.48 \pm 0.32	1.89 \pm 0.51
t	-	0.034	7.564	0.079	10.478	0.048	9.592	0.055	0.027	0.347	5.212
P	-	0.973	0.000	0.938	0.000	0.962	0.000	0.957	0.979	0.730	0.000

3.4. Treatment adherence

As shown in **Table 4**, the treatment adherence of patients in the observation group was higher than that of the control group ($P < 0.05$).

Table 4. Treatment adherence between the two groups [n (%)]

Group	Cases, n	Excellent	Good	Poor	Rate of treatment adherence
Control group	25	7	7	11	14 (56.00)
Observation group	25	13	9	3	22 (88.00)
χ^2	-	-	-	-	6.349
P	-	-	-	-	0.012

4. Discussion

Nasopharyngeal cancer is a very high incidence of head and neck malignant tumors, with a high incidence in

South China and Southwest China, with certain family predisposition, regional aggregation, racial susceptibility, and high incidence in males^[5]. It directly infiltrates the neighboring tissues and organs and the rate of cervical lymph node metastasis is high. Early-stage nasopharyngeal cancer is usually selected to be radiated for radical treatment, and in middle and late-stage nasopharyngeal cancer, it is necessary to combine multiple treatments, such as radiotherapy and chemotherapy. Combining radiotherapy and chemotherapy can improve the local control rate and have a better overall benefit^[6]. Chemotherapy can synchronize with the tumor cell cycle to inhibit the G2/M phase, and cellular hypoxia and radiosensitivity can be improved. In addition, chemotherapy plays a role in systemic subclinical metastases, controlling the distant metastasis rate and the local recurrence rate. Cisplatin is a commonly used chemotherapeutic drug that has a good effect on many malignant tumors. As a first-line anticancer drug with a high application rate, it has no cross-resistance with other first-line anticancer drugs and exhibits a good synergistic effect^[7]. Cisplatin inhibits the replication of DNA of cancer cells, blocks the proliferation pathway, and destroys the structure of tumor cell membranes regardless of the cycle, thus killing the tumor cells. Furthermore, cisplatin has the effect of increasing sensitivity to radiotherapy^[8]. Cisplatin has a good effect on systemic sub-clinical metastases and local recurrence in the simultaneous treatment regimen of radiation and chemotherapy. Therefore, it is commonly used in simultaneous radiotherapy treatment regimens. Although cisplatin conventional chemotherapy combined with a radiotherapy regimen can increase the efficacy, it also improves the toxicity and side effects and promotes patient compliance.

Metronomic chemotherapy involves administering lower doses of drugs but increasing the dose frequency. When combined with radiotherapy, it can synergistically target vascular endothelial cells. In addition, metronomic chemotherapy reduces the expression of pro-angiogenic growth factors, promotes the normalization of the tumor vasculature, increases the blood supply to the tumor tissue, and promotes the improvement of the sensitivity of radiotherapy^[9]. The dosage is generally about 1/10–1/3 of the dose of conventional chemotherapy. In this study, the control group implemented cisplatin conventional chemotherapy combined with a radiotherapy program, while the observation group adopted cisplatin metronomic chemotherapy combined with a radiotherapy program. Results showed that the clinical remission rate between both groups was not significant, indicating that cisplatin metronomic chemotherapy instead of conventional chemotherapy methods can also achieve similar chemotherapeutic effects. Results showed that the incidence of various adverse reactions in the observation group was lower than that in the control group, and the treatment compliance was higher as compared to that of the control group. This is because anti-angiogenic chemotherapy can promote the improvement of the microcirculation status of the tumor tissues, and the anti-angiogenic effect is ideal^[10]. The low-dose sustained drug delivery method can reduce the incidence of adverse reactions and increase patient compliance with treatment. While the disease progresses, the patient's cellular immune function gradually decreases. This study showed that the NK cell activity of patients in the observation group was higher after treatment, and the levels of CD3, CD4, and CD4/CD8 cells were also higher than those of the control group ($P < 0.05$). This shows that the overall effect of metronomic chemotherapy is more ideal than that of conventional chemotherapy.

5. Conclusion

In the treatment of stage II–IV nasopharyngeal carcinoma, the therapeutic effect of cisplatin metronomic chemotherapy combined with radiotherapy showed considerable results, where adverse reactions were reduced, and had a high application value.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Li B, Liu J, Zhu Q, et al., 2023, Effect of Capecitabine Metronomic Chemotherapy in Locally Advanced Nasopharyngeal Carcinoma Patients with Persistently Elevated Plasma EBV DNA after Radical Synchronous Radiotherapy. *Chinese Journal of Practical Diagnosis and Therapy*, 37(3): 265–268.
- [2] Xi Y, Hua P, Jiang F, et al., 2023, The Value of Delta Imaging Histology in Predicting the Efficacy of Induction Chemotherapy Combined with Simultaneous Radiotherapy in Nasopharyngeal Carcinoma. *Journal of Clinical Radiology*, 42(2): 216–221.
- [3] Xuan X, Lu C, Tang J, et al., 2023, Recent Efficacy of Synchronized Radiotherapy Combined with Compound Bitter Ginseng Injection for Nasopharyngeal Carcinoma and Its Effect on The Levels of Immune Factors, MIP-3 α , and sCD44. *China Hospital Drug Evaluation and Analysis*, 23(5): 524–527.
- [4] Wang C, Chen L, Qin S, 2023, Observation on the Efficacy of Teraplizumab Combined with Simultaneous Radiotherapy in The Treatment of Intermediate and Advanced Nasopharyngeal Carcinoma. *Zhongnan Journal of Medical Science*, 51(1): 114–116.
- [5] Zhong Q, Nie Q, Wu R, et al., 2023, Effect of Nituzumab Combined with Simultaneous Radiotherapy in The Treatment of Nasopharyngeal Carcinoma and Its Effect on Serum Tumor Markers. *China Medical Innovation*, 20(30): 1–5.
- [6] Wang W, Zhang Z, Li Y, et al., 2022, Correlation of ERCC1 Gene Expression in Circulating Tumor Cells with Radiotherapy Efficacy and Prognosis in Nasopharyngeal Carcinoma Patients. *Chinese Journal of Gerontology*, 42(13): 3166–3170.
- [7] Hu D, Chen Z, Lin Y, et al., 2023, Construction of Risk Factors and Prediction Model for Poor Prognosis of Locally Advanced Nasopharyngeal Carcinoma Treated with IMRT-Based Synchronous Radiotherapy Regimen. *China Otorhinolaryngology-Head and Neck Surgery*, 30(3): 148–151.
- [8] Luo H, Zhong Y, Luo Q, et al., 2022, Relationship Between the Combined Use of Proton Pump Inhibitors and The Occurrence of Acute Kidney Injury During Cisplatin-Synchronized Radiotherapy in Nasopharyngeal Carcinoma Patients. *Shandong Medicine*, 62(29): 28–31.
- [9] Li Ying, Wang Xiaohua, Chen Lin, 2023, Evaluation Value of DCE-MRI Combined with 3D-pCASL Parameters on The Recent Efficacy of Radiotherapy for Nasopharyngeal Carcinoma. *Chinese Journal of CT and MRI*, 21(12): 45–47.
- [10] Li D, Wang X, Lu X, 2022, Analysis of Factors Affecting Neutropenia Caused by Paclitaxel Combined with Platinum-Based Simultaneous Radiotherapy for Nasopharyngeal Carcinoma and Evaluation of The Rationality of Preventive Medication. *China Pharmaceutical Industry*, 31(24): 111–115.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.