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Efficacy analysis of vincristine, adriamycin, dexamethasone chemotherapy regimen combined with thalidomide in the treatment of multiple myeloma nephropathy and its impact on renal function factors

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Abstract: Myeloma nephropathy is a rare but challenging disease. This study aimed to evaluate the efficacy and renal functional outcomes of the VAD chemotherapy regimen and thalidomide treatment for myeloma nephropathy. From August 2022 to December 2023, a total of 94 patients were admitted to People's Hospital of Shangrao City. Patients were randomly assigned to Group C (VAD chemotherapy) and Group O (VAD chemotherapy plus thalidomide). Comparisons of renal function, treatment outcomes, and patient characteristics indicated that disease control and overall efficacy were significantly better in Group O (P<0.05). Compared with Group C, Group O also had greater reductions in serum creatinine, blood urea nitrogen, retinol-binding protein, M-protein, bone marrow plasma cells, and 24-hour proteinuria (P<0.05). Hemoglobin levels were significantly higher in Group O (P<0.05), and adverse reactions were significantly lower (P<0.05). The combination of VAD chemotherapy and thalidomide improved the therapeutic effects and renal function in myeloma nephropathy, supporting further exploration of this therapy.

Keywords: Myeloma nephropathy, VAD chemotherapy regimen, thalidomide, quantitative proteinuria, renal function.

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INTRODUCTION

Multiple myeloma (MM) is a plasma cell dysregulatory disorder originating from abnormal proliferation of plasma cells within the bone marrow, subsequently progressing to malignancy. Clinical manifestations encompass anemia, bone pain, renal impairment, hypercalcemia and immunodeficiency, increasing the susceptibility to infections, primarily impacting the bone marrow and skeletal system (Drummond *et al*., 2023). The incidence of MM accounts for approximately 1% of all cancers and with the occurrence of an aging population, it has become the second most common hematologic malignancy globally (Blue *et al*., 2023). Literature has reported that MM may be associated with various factors, including genetics, environmental factors and immunological abnormalities (Hanamura, 2022). MM nephropathy (MMN) is a common complication within MM, potentially leading to renal impairment in patients, characterized by symptoms such as proteinuria and decreased glomerular filtration rate. It is a rare but highly detrimental condition, characterized by abnormal proliferation of myeloma cells within the kidneys, resulting in renal functional impairment. Research indicates that MMN is one of the earliest complications to manifest in MM, with the most common form being the deposition of monoclonal free light chains and urinary regulatory proteins in the distal tubules, referred to as light chain cast nephropathy (Bridoux *et al*., 2021). Studies have revealed that the renal damage caused by MM results from various factors. Research has shown that MM cells secrete monoclonal immunoglobulin light chains, leading to proteinuria in patients. Approximately 80% of MM patients exhibit positive proteinuria in urinary tests (Menè *et al*., 2022). Furthermore, factors such as hypercalcemia, hyperuricemia and amyloidosis are also associated with the onset of MMN.

Chemotherapy is currently the most commonly employed approach for treating MM. While conventional treatment methodologies, including steroids and immunosuppressants, have demonstrated some efficacy in certain patients, a significant proportion still exhibits poor responses or develops resistance to conventional therapies (Xing *et al*., 2022). Complications associated with MMN are severe, with a high mortality rate primarily attributed to renal dysfunction and the exacerbation of related symptoms. Research has identified inflammation, tumor burden and immune response as crucial factors in the progression of MMN (Dimopoulos *et al*., 2023). Consequently, current treatment strategies primarily focus on mitigating inflammatory responses, controlling tumor burden and enhancing immune function. In recent years, the Vincristine, Adriamycin, Dexamethasone (VAD) chemotherapy regimen and Thalidomide have garnered significant attention as novel therapeutic approaches (Tanimura *et al*., 2020). The VAD chemotherapy regimen incorporates Vincristine, Adriamycin and Dexamethasone, which possess both anti-proliferative effects on tumor cells and immunomodulatory properties (Iijima *et al*., 2022). Thalidomide is an immunomodulatory agent

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capable of suppressing inflammatory responses and excessive activation of the immune system. Research has shown that Thalidomide can inhibit tumor growth and metastasis in patients with MM by continuously suppressing angiogenesis. Furthermore, Thalidomide exhibits potent anti-inflammatory effects, capable of inhibiting the synthesis of tumor necrosis factor-alpha (TNF-α) from activated monocytes (Ravichandran *et al*., 2023). Studies have also revealed that Thalidomide, when combined with the VAD regimen, can improve platelet factor 4 (PF4) and the median serum PF4 concentration is inversely correlated with the response in MM (Bai *et al*., 2019). Thus, it can be used to gauge the prognostic outcomes of MMN. While the VAD treatment regimen may not be as favorable as first- and second-line treatment options utilizing bortezomib, it is effective in reducing tumor burden and achieving maximal short-term efficacy (Yıkılmaz *et al*., 2020). In the majority of MM patients, symptoms of renal impairment eventually develop. Clinical observations have shown that the VAD regimen is safe for patients with renal insufficiency or renal failure. Bone marrow suppression is relatively mild, and patients tend to recover quickly after chemotherapy (Toriu *et al*., 2020). Hence, the VAD regimen represents the optimal choice for those with renal dysfunction and the need to reduce tumor burden.

The objective of this study was to evaluate the efficacy and safety of the VAD chemotherapy regimen in combination with Thalidomide for the treatment of MMN. Through a retrospective analysis of clinical data and laboratory test results from patients with MMN, it aimed to elucidate the impact of this combined treatment approach on quantitative proteinuria, renal function and other relevant indicators. This research endeavors to provide scientific evidence for the exploration of more effective treatment modalities. The findings from this study were expected to serve as crucial references for enhancing the prognosis of patients with MMN, reducing the occurrence of complications and improving overall survival rates.

MATERIALS AND METHODS

Selection criteria

This study included a cohort of 94 patients diagnosed with MMN who received treatment at People's Hospital of Shangrao City from August 2022 to December 2023. All patients were randomly rolled into Group C (control group) and Group O (observation group), with each group consisting of 47 individuals.

Inclusion criteria

Patients who were clinically diagnosed with MMN by the attending physicians, completion of the full treatment regimen, absence of contraindications to the study medications, approval of the study protocol by the institutional ethics committee and informed consent obtained from both patients and their family members.

Exclusion criteria

Patients with concomitant renal dysfunction, individuals with a history of psychiatric or psychological disorders; those with concurrent malignancies. This study had been approved by the Ethics Committee of our hospital (Approval Number: PHSC210). Prior to enrollment, all patients and their families were thoroughly informed of the research objectives, content and potential risks and signed informed consent forms indicating their voluntary participation in the study. On the basis of informed consent, patients were formally enrolled and participate in the study after sufficient communication.

Treatment plan and observation of adverse reactions

Patients in Group C underwent treatment with the VAD chemotherapy regimen, consisting of intravenous administration of the following: Vincristine sulfate infusion at a dose of 0.4mg/day for four consecutive days, intravenous infusion of Adriamycin at a dose of 10mg/day for four consecutive days, and intravenous infusion of Dexamethasone sodium phosphate administered daily at a dosage calculated based on 20mg/m² for three cycles within a 20-day period, with each cycle comprising four consecutive days of treatment. The complete treatment cycle extended over 28 days.

Patients in Group O received a combined treatment approach involving the VAD chemotherapy regimen and Thalidomide. In addition to the treatment administered to Group C, Group O received Thalidomide orally, initially at a dose of 50mg/day for one week, followed by an increase to 50mg/week after one week and then adjusted to a range of 150-200mg/day for a treatment duration of four months.

During the chemotherapy process, all patients received supportive treatments such as gastric acid suppression, gastric mucosal protection and bone marrow protection. Each patient underwent a minimum of four treatment cycles. Prior to and after chemotherapy, a dynamic monitoring and record-keeping of the patients' hematological parameters, hematopoietic capacity, and renal function were conducted. Following the completion of the chemotherapy cycles, bone marrow examinations were performed and adverse reactions (ARs) occurring during the treatment period were observed and recorded, including their incidence rates (table 1).

Outcome measures

The renal function indicators of patients in both groups were assessed before and after treatment. In the early morning, fasting venous blood samples (5mL) were collected from patients to measure parameters including serum creatinine (SCr), blood urea nitrogen (BUN), retinol-binding protein and 24-hour proteinuria. The level of SCr in patient serum was determined using enzyme-linked immunosorbent assay (ELISA), while the levels of BUN and retinol-binding protein were measured using a BS-600M biochemical analyzer. BUN levels were also

assessed using the UV-glutamate dehydrogenase method. The concentration of retinol-binding protein was determined using a retinol-binding protein assay kit (turbidimetry). The 24-hour proteinuria was detected using the pyrogallol red colorimetric method. This involved collecting the total urine output from patients over a 24-hour period, measuring the total protein in the 24-hour urine and calculating the level of 24-hour proteinuria. Hemoglobin (Hb) levels in both groups were determined using a hematology analyzer, as part of the complete blood count assessment. The number of bone marrow plasma cells in both groups was assessed by extracting hematopoietic cells from patients' bone marrow fluid, staining the slides, and observing the hematopoiesis under a microscope. The clinical treatment outcomes between the two groups were compared, and ARs following treatment were observed. ARs included infections, gastrointestinal abnormalities, bone marrow suppression, vomiting, and peripheral neuropathy, among others. During the examination, drawing blood may cause brief pain or discomfort, but it was usually mild. There may be small-scale bruising at the site of blood draw. Moreover, although the risk was extremely low, there was still a possibility of infection due to skin puncture. These detection methods were routine and relatively safe medical examinations. For most patients, the side effects of the testing process were mild and brief. However, for patients with bleeding tendencies or weakened immune function, doctors may pay special attention to avoid the occurrence of ARs.

Efficacy evaluation criteria

The treatment efficacy of patients was assessed in accordance with the Chinese MM Diagnosis and Treatment Guidelines (2022 Revised Edition). Treatment outcomes were categorized into five grades: complete remission (CR), very good partial remission (VGPR), partial remission (PR), stable disease (SD) and disease progression (PD). The overall response rate was calculated as the sum of CR, VGPR and PR, while the disease control rate included CR, VGPR, PR and SD.

STATISTICAL ANALYSIS

The data obtained were processed using SPSS 23.0. Continuous variables were recorded as mean ± standard deviation ($\bar{X}\pm s$) and compared adopting t-tests. Categorical data were denoted as percentages (%) and compared adopting chi-square ($\chi 2$) test. $P<0.05$ meant statistically significant, indicating the presence of a meaningful difference.

RESULTS

Comparison of patient general information

In fig. 1 and table 2, no significant differences were found between Group C and Group O in terms of gender, age, or disease duration ($P>0.05$). This result indicated that the study design effectively balanced the baseline characteristics between the two groups, reducing potential biases that might affect subsequent treatment outcomes. Ensuring the comparability of baseline characteristics is crucial for the validity and credibility of the study results. The similarity between the two groups at the start of the study suggested that differences in treatment efficacy were more likely attributable to the treatments rather than to baseline characteristics. This point is particularly important because factors such as gender, age, and disease duration are known potential confounders that can influence treatment outcomes, thereby providing a reliable basis for the study conclusions.

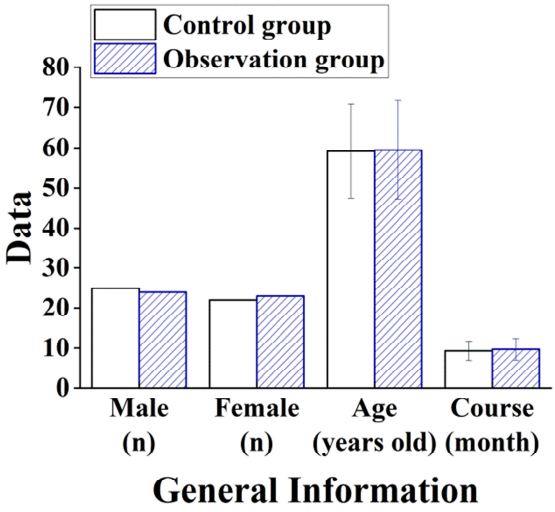


Fig. 1: Comparison of general information between groups

Comparison of treatment efficacy

In fig. 2 and tables 3 and 4, the clinical disease control rate and overall response rate of Group O (91.48% and 76.74%) after treatment were significantly higher than those of Group C (68.09% and 53.49%) ($P<0.05$). This indicated that the combination of VAD chemotherapy and thalidomide had significant advantages in improving disease control and response rates in patients with MM-related nephropathy.

Comparison of renal function factors

In fig. 3 and table 5, no significant differences were found between the two groups in serum creatinine (Scr), blood urea nitrogen (BUN), and retinol-binding protein levels before treatment ($P>0.05$), indicating no significant differences in baseline renal function. However, after treatment, both groups showed significant decreases in Scr, BUN, and retinol-binding protein levels ($P<0.05$), with Group O showing significantly greater improvements than Group C ($P<0.05$). This result indicated that the combination of VAD chemotherapy and thalidomide not only performed well in disease control but also had significant advantages in protecting or improving renal function.

Table 1: Treatment medication information

Name	Producer	National medicine permission number
Vincristine (VCR)	Guangzhou Baiyunshan Hanfang Modern Pharmaceutical Co., Ltd	H44023474
Adriamycin	Shenzhen Main Luck Pharmaceutical Co., Ltd	H10930105
Dexamethasone sodium phosphate	Shijiazhuang Pharmaceutical Group Ouyi Pharmaceutical Co., Ltd	H20052358
Thalidomide	Changzhou Pharmaceutical Factory Co., Ltd	H32026129

Table 2: Comparison of general data of patients

General information	Group C (n=47)	Group O (n=47)
Male (example)	25	24
Female (example)	22	23
Age (years old)	59.13±11.69	59.47±12.32
Course of disease (month)	9.28±2.46	9.69±2.74

Table 3: Comparison of therapeutic effects of patients

Therapeutic effect	Group C (n=47)	Group O (n=47)
CR (example)	6	12
VGCR (example)	6	9
PR (example)	11	12
SD (example)	9	10
PD (example)	15	4

Table 4: Comparison of the effective rates of patients

Effective rate of treatment	Group C (n=47)	Group O (n=47)
Total effective rate	23 (53.49%)	33 (76.74%)*
Disease control rate	32 (68.09%)	43 (91.48%)*

Note: *P<0.05 vs. Group C.

Table 5: Comparison of renal function factors in patients

Renal function factor	Group C (n=47) Pre-treatment	Post-treatment	**Group O (n=47) Pre-treatment**	**Post-treatment**
Scr (umol/L)	311.96±51.84	94.84±23.73*	319.73±52.67	74.52±20.62*#
BUN (mmol/L)	17.95±2.86	15.24±1.83*	17.93±2.93	10.14±1.27*#
Retinol-binding protein (mg/L)	248.52±47.83	147.24±32.85*	239.75±45.97	87.29±20.17*#

Note: *P<0.05 vs. pre-treatment; #P<0.05 vs. Group C.

Table 6: Comparison of 24-hour proteinuria in patients

24h Poteinuria level	Group C (n=47)	Group O (n=47)
Before treatment (g/24h)	5.02±1.12	4.98±1.13
After treatment (g/24h)	2.92±0.73*	0.94±0.42*#

Note: *P<0.05 vs. pre-treatment; #P<0.05 vs. Group C.

Table 7: Comparison of Hb levels in patients

Hb level	Group C (n=47)	Group O (n=47)
Before treatment (g/L)	73.24±14.27	74.31±14.62
After treatment (g/L)	80.76±15.28*	99.68±16.72*#

Note: *P<0.05 vs. pre-treatment; #P<0.05 vs. Group C.

Table 8: Comparison between the number of plasma cells in bone marrow and the level of M protein in patients

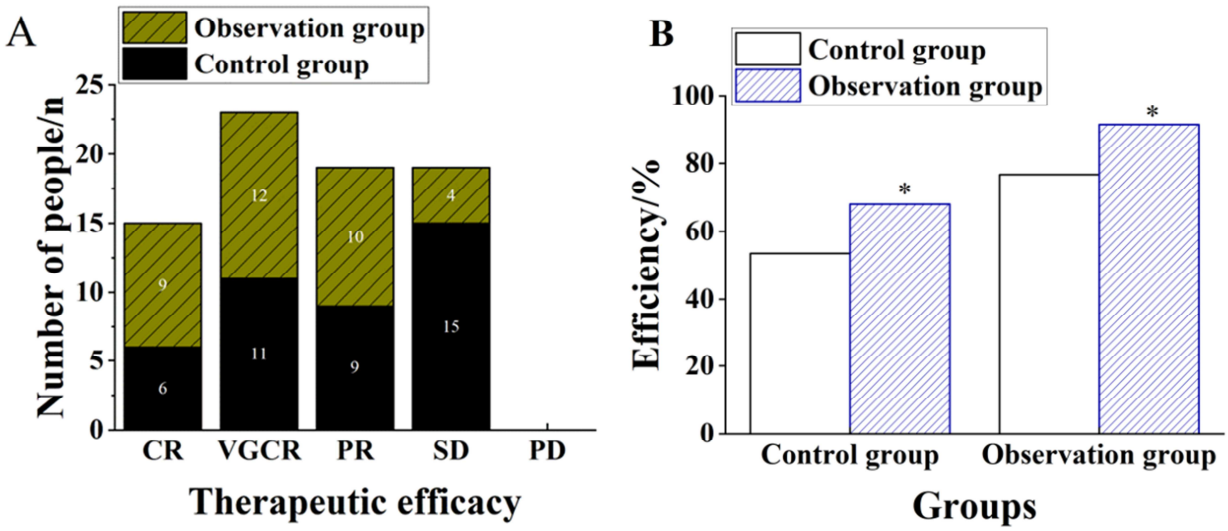
Number of plasma cells in bone marrow and M protein level	Group C (n=47)		Group O (n=47)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Number of plasma cells in bone marrow (%)	59.95±14.57	11.27±3.62*	59.24±13.72	5.16±2.86*#
M protein level (g/L)	56.73±13.24	15.29±4.73*	54.97±13.18	24.97±6.58*#

Note: *P<0.05 vs. pre-treatment; #P<0.05 vs. Group C.

Table 9: Comparison of ARs of patients

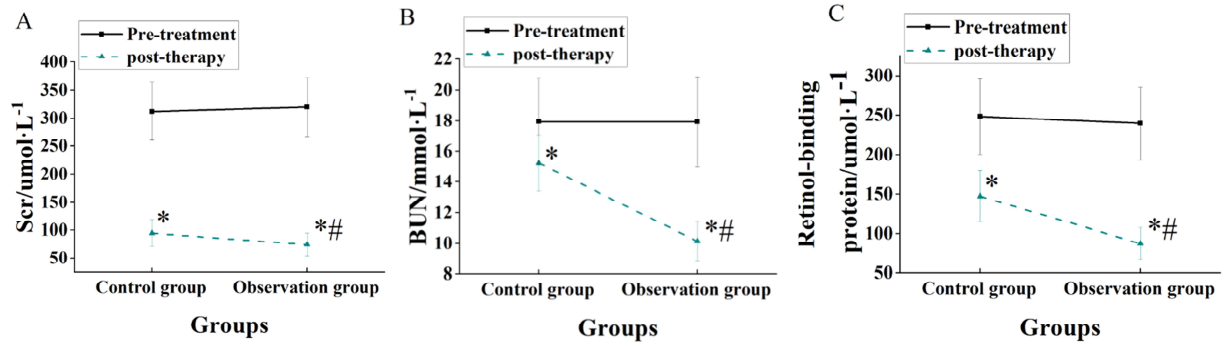
ARs	Group C (n=47)	Group O (n=47)
Infection (case)	7	4
Abnormal digestive system (case)	3	3
Bone marrow suppression (case)	6	6
Vomiting (case)	13	0
Peripheral neuropathy (case)	4	1
AR rate	33 (70.21%)	15 (31.91%)*

Note: *P<0.05 vs. Group C.



(A represents the number of patients, B represents disease control rate and treatment efficiency.) Note: *P<0.05 vs. Group C.

Fig. 2: Comparison of treatment efficacy between two groups of patients

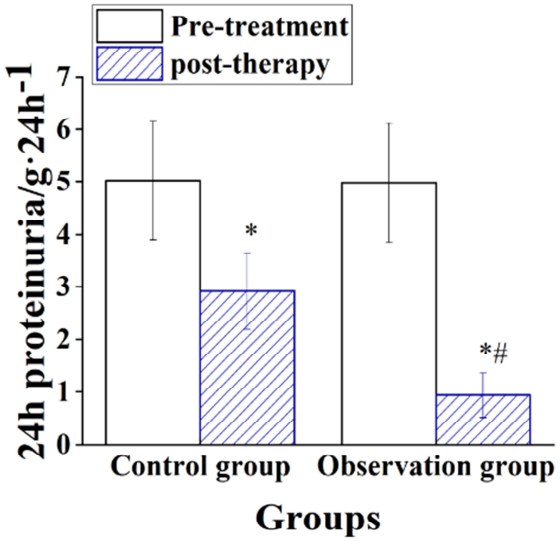


(A is Scr, B is BUN and C is retinol binding protein.) Note: *P<0.05 vs. pre-treatment; #P<0.05 vs. Group C.

Fig. 3: Comparison of renal function factors

Comparison of 24-hour proteinuria

In the comparison of 24-hour proteinuria levels shown in fig. 4 and table 6, no significant differences were found between the two groups before treatment (P>0.05), indicating similar baseline severity of renal impairment. However, after treatment, the 24-hour proteinuria levels in both groups decreased significantly, with Group O showing a significantly greater reduction compared to Group C (P<0.05). This result indicated that the combination of VAD chemotherapy and thalidomide was more effective in reducing renal damage.



Note: *P<0.05 vs. pre-treatment; #P<0.05 vs. Group C.

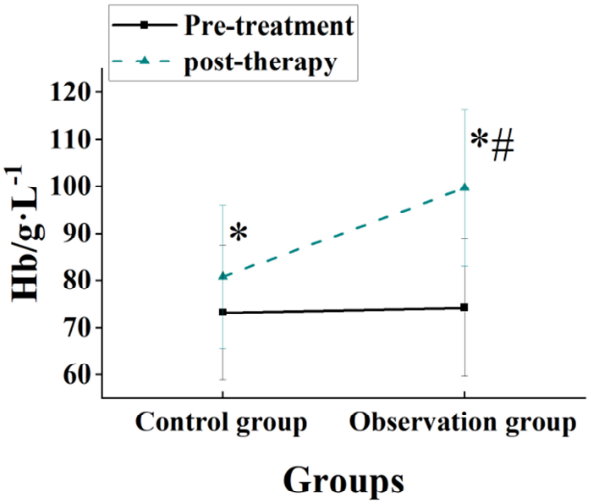
Fig. 4: Comparison of 24-hour proteinuria levels between groups.

Comparison of hemoglobin levels

In the comparison of hemoglobin (Hb) levels shown in fig. 5 and table 7, no significant differences were found between the two groups before treatment (P>0.05), indicating similar baseline anemia status. After treatment, Hb levels in both groups were significantly increased (P<0.05), with the increase in Group O being significantly greater than that in Group C (P<0.05). This result indicated that the combination of VAD chemotherapy and thalidomide had a significant effect on improving anemia, with more pronounced effects observed in Group O.

Comparison of the number of bone marrow plasma cells and the level of m protein

In the comparison of the number of bone marrow plasma cells and the level of M protein in fig. 6 and table 8, no significant difference was found between the two groups before treatment (P>0.05), indicating that the baseline disease severity of the two groups was similar. After treatment, the number of bone marrow plasma cells and the level of M protein in both groups decreased significantly (P<0.05), with the reduction in Group O being significantly greater than that in Group C (P<0.05). These results indicated that the VAD chemotherapy regimen combined with thalidomide significantly reduced the number of bone marrow plasma cells and the level of M protein, with the effect in Group O being more pronounced.



Note: *P<0.05 vs. pre-treatment; #P<0.05 vs. Group C.

Fig. 5: Comparison of Hb levels between groups.

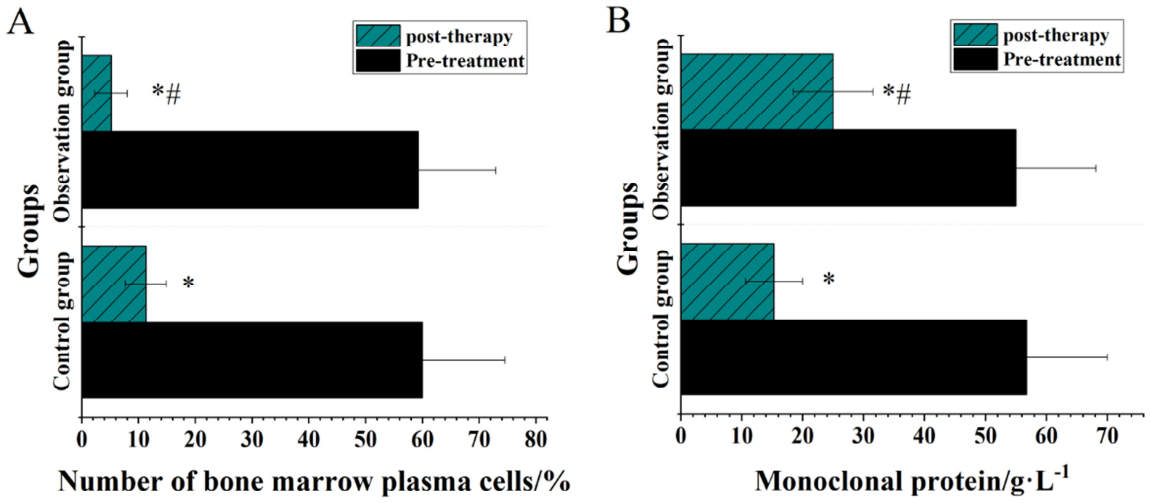
Comparison of ARS

In fig. 7 and table 9, seven cases of infection, three cases of gastrointestinal abnormalities, six cases of myelosuppression, thirteen cases of vomiting, and four cases of peripheral neuropathy were reported in Group C, while four cases of infection, three cases of gastrointestinal abnormalities, six cases of myelosuppression, zero cases of vomiting, and one case of peripheral neuropathy were reported in Group O. The overall incidence rate of adverse reactions in Group O (31.91%) was significantly lower than that in Group C (70.21%). These results indicated that the VAD chemotherapy regimen combined with thalidomide significantly reduced the incidence rate of adverse reactions, especially in vomiting and peripheral neuropathy.

DISCUSSION

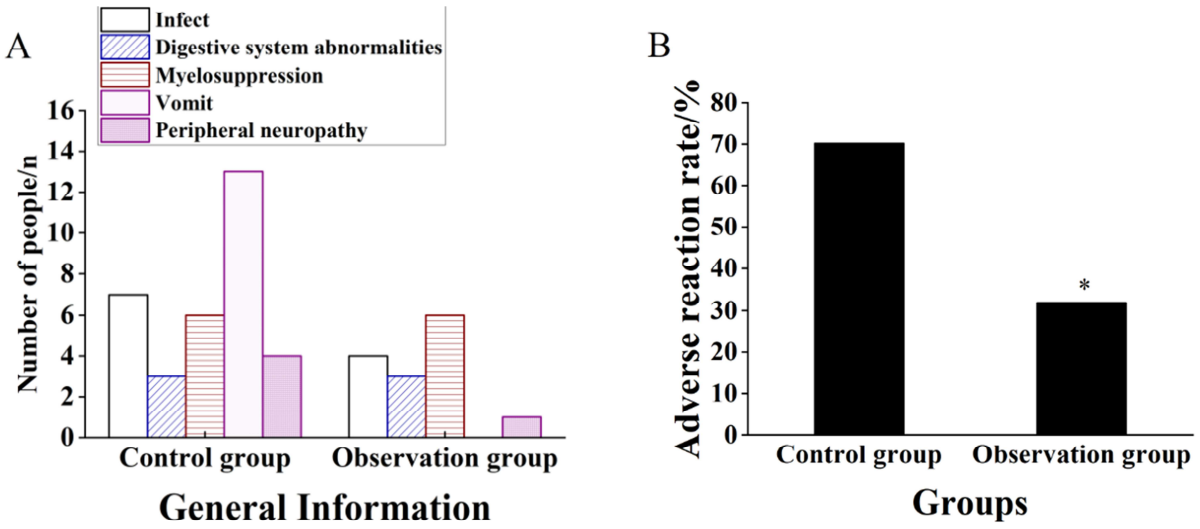
This study was designed to evaluate the efficacy of VAD chemotherapy combined with thalidomide in treating MMN. The results demonstrated that the combination regimen significantly outperformed the VAD chemotherapy alone in multiple clinical indices, including disease control, renal function, improvement of anemia, and the incidence rate of adverse reactions.

The clinical disease control rate (91.48%) and overall response rate (76.74%) in Group O (the group treated with VAD chemotherapy combined with thalidomide) were significantly higher than those in Group C (68.09% and 53.49%), indicating that the combination regimen had a significant advantage in improving disease control and response rate in MMN patients (P<0.05).



(A represents the number of bone marrow plasma cells and B represents the level of M protein.) Note: *P<0.05 vs. pre-treatment; #P<0.05 vs. Group C.

Fig. 6: Comparison of the number of bone marrow plasma cells and the level of M protein between groups



(A represents the number of ARs, B represents the rate of ARs.) Note: *P<0.05 vs. Group C.

Fig. 7: Comparison of AR rates between groups

These findings were consistent with previous studies, suggesting that thalidomide, through its immunomodulatory and anti-angiogenic effects, enhanced the efficacy of VAD chemotherapy, thereby more effectively inhibiting the proliferation of myeloma cells and improving clinical outcomes (Villa *et al*., 2022). The increase in the overall response rate also indicated that the addition of thalidomide enabled more patients to have a positive response to treatment, potentially prolonging remission and providing a better prognosis. Moreover, the results also showed that the combination therapy had more advantages in long-term management than the chemotherapy alone, further supporting the potential role of thalidomide in the treatment of MM.

After treatment, the levels of Scr, BUN and retinol-binding protein in both groups decreased significantly (P<0.05), but the improvement in Group O was significantly greater than that in Group C (P<0.05). These results indicate that the VAD chemotherapy regimen combined with thalidomide can significantly protect and improve renal function while controlling the disease. The immunomodulatory effects of thalidomide may help reduce renal inflammation and slow the progression of kidney damage (Zhang *et al*., 2023). Moreover, the combination therapy may more effectively control the proliferation of myeloma cells, thereby reducing the renal burden and improving renal function (Peng *et al*., 2023). For MMN patients, maintaining and improving renal

function is crucial for enhancing quality of life and long-term survival (Ojo *et al*., 2022), making this finding particularly important.

In the comparison of 24-hour proteinuria, a significant decrease was observed in both groups after treatment ($P<0.05$), with the reduction in Group O being significantly greater than that in Group C ($P<0.05$). Proteinuria, a key indicator of renal damage, typically implies an improvement in renal filtration function when its level decreases (Shi *et al*., 2022). The significant reduction in proteinuria in Group O indicates that the VAD chemotherapy regimen combined with thalidomide is more effective in alleviating renal damage (Kuno *et al*., 2023). Thalidomide may promote the recovery and improvement of renal function by inhibiting inflammatory responses and reducing the progression of tubulointerstitial fibrosis (Zaffanello *et al*., 2022). Moreover, the significant decrease in proteinuria may also be associated with the reduction of tumor burden, suggesting a decrease in the pathological impact on the kidneys (Miki *et al*., 2023).

In the comparison of Hb levels, the Hb levels in both groups were significantly increased after treatment ($P<0.05$), and the increase in Group O was significantly greater than that in Group C ($P<0.05$). These results indicate that the VAD chemotherapy regimen combined with thalidomide has a significant effect on improving anemia, with a more pronounced effect in Group O. Anemia is a common complication in patients with MM-related renal disease, mainly due to the suppression of normal hematopoietic function by myeloma cells and the reduction of red blood cell production caused by renal dysfunction (Wang *et al*., 2022; Yong *et al*., 2021). Thalidomide may promote red blood cell production by improving the bone marrow microenvironment and reducing the suppression of normal hematopoietic cells by myeloma cells (Weng *et al*., 2021). Moreover, the immunomodulatory effects of thalidomide may further support the recovery of bone marrow hematopoiesis by reducing the release of inflammatory mediators (Xu *et al*., 2022). These findings are consistent with the literature on thalidomide's role in improving bone marrow function and alleviating anemia (Syed, 2023), providing strong support for its application in the treatment of MMN.

More adverse reaction events, including infections, gastrointestinal abnormalities, myelosuppression, vomiting, and peripheral neuropathy, were reported in Group C. The overall incidence rate of adverse reactions in Group O was significantly lower than that in Group C (31.91% vs. 70.21%), especially in terms of vomiting and peripheral neuropathy ($P<0.05$). These results indicate that the VAD chemotherapy regimen combined with thalidomide significantly reduced the incidence rate of adverse reactions. The immunomodulatory effects of thalidomide may have mitigated the side effects of chemotherapeutic agents, thereby improving treatment tolerability and patient compliance. Thalidomide not only enhances therapeutic efficacy but also potentially alleviates the side effects of chemotherapeutic drugs, making treatment more tolerable for patients and contributing to improved long-term therapeutic outcomes.
This study has demonstrated that the VAD chemotherapy regimen combined with thalidomide has significant therapeutic advantages in the treatment of MMN patients. It can effectively control the disease and improve the response rate, as well as enhance renal function and hematological indices such as anemia, while reducing the incidence of adverse reactions. The addition of thalidomide to the treatment regimen not only enhances the efficacy of chemotherapy but also improves patient tolerance and quality of life, potentially having a positive impact on long-term prognosis.

CONCLUSION

This study has demonstrated that the VAD chemotherapy regimen combined with thalidomide is superior to VAD chemotherapy alone in the treatment of MMN patients, showing higher disease control rates and overall response rates. After treatment, patients in Group O exhibited significant improvements in renal function, including notable decreases in Scr, BUN, retinol-binding protein, bone marrow plasma cell count, M protein levels and 24-hour proteinuria, as well as a significant increase in Hb levels. Additionally, the incidence of adverse reactions in Group O was lower than that in Group C, with particularly significant improvements in vomiting and peripheral neuropathy.

One year after the experiment, patients in Group O maintained better disease control and renal function, experienced relief from anemia and enjoyed a higher quality of life. In contrast, patients in Group C experienced a decline in renal function and relapse of some symptoms. Although the sample size of this study was small and did not explore the effects of different doses and treatment durations, the results indicate that the long-term efficacy of VAD chemotherapy combined with thalidomide is superior to that of VAD chemotherapy alone in MMN patients. Future research should expand the sample size and further investigate the long-term safety of thalidomide.

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