

Original Article

Enhanced efficacy and safety of combining Aidi injection with megestrol acetate for endometrial cancer treatment

Qinglin Li¹, Jiaxin Li¹, Chunjuan Zhang²

¹Xinyang Vocational and Technical College, Xinyang 464000, Henan, China; ²Department of Obstetrics, Luoyang Central Hospital, Luoyang 471000, Henan, China

Received April 23, 2025; Accepted September 8, 2025; Epub September 15, 2025; Published September 30, 2025

Abstract: Purpose: To evaluate the therapeutic efficacy of Aidi injection combined with megestrol acetate (MA) in patients with endometrial cancer (EC) and to investigate its effects on serum biomarkers, including human epididymis protein 4 (HE4), carcinoembryonic antigen (CEA), and cancer antigen 125 (CA125). Methods: A retrospective analysis was conducted on 120 EC patients treated at Luoyang Central Hospital between January 2023 and January 2024. Patients were categorized into two groups based on their treatment regimen: the MA group (n=60) that received chemotherapy combined with oral MA, and the Aidi group (n=60) that received additional Aidi injection alongside the regimen used in the MA group. Clinical outcomes assessed included overall treatment efficacy, maximum lesion size, survival status, tumor marker levels, serological indicators, and adverse reaction rates (ARR). Results: The Aidi group demonstrated superior outcomes compared to the MA group, with significantly higher objective response rates (ORR) and disease control rates (DCR) ($P<0.05$). Additionally, the Aidi group demonstrated a greater reduction of maximum lesion diameter ($P<0.001$), improved quality of life ($P<0.001$), and lower serum concentrations of HE4, CEA, and CA125 ($P<0.001$). In addition, levels of connective tissue growth factor (CTGF), angiopoietin-2 (Ang-2), prolactin (PRL), and ARR were significantly reduced ($P<0.05$). Conclusion: Aidi injection combined with MA provided a promising therapeutic strategy for EC. This regimen effectively inhibited tumor progression, improved quality of life, and decreased serum tumor marker levels (HE4, CEA, and CA125), supporting its potential for broader clinical application.

Keywords: Aidi injection, megestrol acetate, endometrial cancer

Introduction

Endometrial cancer (EC) has emerged as one of the most common gynecologic malignancies worldwide, with clinical presentation varying markedly between early and advanced stages. In the early phase, patients often exhibit non-specific symptoms such as irregular vaginal bleeding or discharge, frequently leading to delayed diagnosis [1]. As the disease progresses, more severe manifestations - including palpable abdominal masses, persistent lower abdominal pain, and systemic symptoms like unexplained weight loss - become apparent, substantially complicating treatment and worsening prognosis [2-4]. Current therapeutic approaches for advanced EC typically involve multimodal strategies integrating surgery with

adjuvant therapies such as chemotherapy, radiotherapy, and hormone therapy, all aimed at improving survival rates and quality of life [5].

The global burden of EC has risen substantially since 2010. According to World Health Organization (WHO) statistics, both incidence and disease-related mortality have continued to increase, showing a need for early detection and timely intervention. Conventional diagnostic methods rely on imaging techniques [transvaginal ultrasound, Computed Tomography (CT), or Magnetic Resonance Imaging (MRI)] and histopathologic examination of endometrial biopsy. However, these approaches often have limited sensitivity, particularly for early-stage disease [6-9]. In clinical practice, serum tumor markers have shown increasing clinical

relevance for diagnosis and monitoring. Among them, human epididymis protein 4 (HE4), carcinoembryonic antigen (CEA), and cancer antigen 125 (CA125) are most widely utilized. Particularly, CA125 has demonstrated strong clinical utility due to its high sensitivity in EC detection and its established role in assessing treatment response and monitoring disease progression [10, 11].

For the pharmacologic management of EC, megestrol acetate (MA) has long been recognized as an effective hormonal therapeutic agent. As a synthetic progestin, MA exerts direct anti-tumor effects on endometrial tissue and provides significant palliative benefits by stimulating appetite and alleviating the debilitating chemotherapy-related side effects, thereby improving patients' nutritional status and treatment tolerance [8-10]. Parallel to these conventional approaches, traditional Chinese medicine (TCM) has been increasingly incorporated into comprehensive cancer care regimens. Aidi injection, a standardized TCM preparation derived from multiple herbal extracts, has shown promising oncological applications. Modern pharmacological studies revealed that Aidi injection inhibits tumor growth and enhances chemosensitivity, and may exert synergistic effects when combined with agents such as MA. These mechanisms are often described within the TCM framework as heat-clearing and detoxification [12-15].

To systematically evaluate the clinical efficacy of this integrative regimen and its effect on key serum biomarkers, we conducted a retrospective analysis of 120 EC patients treated at Luoyang Central Hospital between January 2023 and January 2024. This study specifically assessed the therapeutic benefits of Aidi injection combined with MA and monitored dynamic changes in serum HE4, CEA and CA125 levels throughout the treatment course. Our findings provide valuable insight into the role of this novel combination therapy might play in optimizing EC management.

Patients and methods

Case selection

A total of 120 EC patients admitted to Luoyang Central Hospital between January 2023 and January 2024 were retrospectively selected.

Patients who received chemotherapy combined with oral MA were defined as the MA Group (n=60), while those who additionally received Aidi injection were defined as the Aidi Group (n=60). This study was approved by the Ethics Committee of Luoyang Central Hospital.

Inclusion criteria: (1) availability of complete clinical data; (2) histopathological confirmation of EC [16]; (3) age ≥ 18 years; (4) estimated survival time >3 months [17]; (5) advanced clinical stages (III-IV).

Exclusion criteria: (1) psychiatric disorders affecting communication or treatment adherence; (2) presence with other significant organic diseases that might affect treatment outcomes or patient safety; (3) contraindications to chemotherapy, such as severe cardiac, hepatic, or renal dysfunction [18]; (4) receipt of TCM treatment within three months prior to hospital admission [19]; (5) unmeasurable lesions on standard imaging; (6) history of severe allergy to any study drug components; (7) pregnancy or lactation.

Intervention method

Patients in the MA group received chemotherapy combined with oral MA. On this basis, patients in the Aidi group were additionally treated with Aidi injection. The regimens were as follows: (1) MA treatment: patients orally took 160 mg of MA tablets [manufactured: Qingdao GuoHai Biological Pharmaceutical Co., Ltd.; National Medical Products Administration (NMPA) Approval No. H20010074] once a day. (2) Aidi injection treatment: 50 mg of Aidi injection liquid (manufactured: Guizhou Yibai Pharmaceutical Co., Ltd.; NMPA Approval No. Z52020236) was mixed with 400 ml of normal saline and then injected intravenously once a day for consecutively 2 weeks in each chemotherapy cycle. Both groups underwent three cycles of treatment, with each cycle lasting three weeks.

Data collection

Transvaginal ultrasound was performed before treatment. Routine transvaginal ultrasound was performed using a GE Voluson E8 color Doppler ultrasound instrument (manufactured: GE Healthcare) with an EV3-10B intracavitary probe with a frequency between 3.0

Table 1. General information in the two groups

Group	Aidi group (n=60)	MA group (n=60)	X ² /t	P
Age (years old)				
Range	32-74	33-74		
Mean age	50.37±6.18	51.23±6.22	0.759	0.449
BMI (kg/m ²)				
Range	18-26	18-26		
Mean BMI	21.85±3.22	21.31±3.24	0.905	0.367
Clinical stage				
III	30	31	0.033	0.855
IV	30	29		
Histological type			0.171	0.918
Adenocarcinoma	11	12		
Clear cell carcinoma	19	17		
Seros carcinoma	30	31		

Note: MA: Megestrol Acetate; BMI: Body Mass Index.

MHZ and 10 mhz. After bladder emptying, patients were placed in the lithotomy position. Two-dimensional ultrasound was used to evaluate endometrial structure, intrauterine lesion size, internal echo, and depth of myometrial invasion. Color Doppler flow imaging (CDFI) was used to assess vascularity in multiple sections, and the resistance index (RI) value was recorded. Due to the retrospective design, archived serum samples were used for non-routine serological assays.

Primary indicators: Overall efficacy. According to WHO evaluation standards for efficacy, treatment response was categorized into complete remission (CR), partial remission (PR), stable disease (SD), and progressive disease (PD). Objective remission rate (ORR) was calculated as CR+PR, and the disease control rate (DCR) was calculated as CR+PR+SD [20, 21].

Secondary indicators: (1) Maximum lesion diameter. Lesion size was compared before and after treatment. (2) Living status. Daily food intake, body weight, and Karnofsky Performance Scale (KPS) score [22] were evaluated after treatment, with higher KPS scores indicating better physical condition. (3) Tumor marker levels. Serum levels of HE4, CEA, and CA125 were compared before and after treatment. Fasting blood samples (5 mL) were collected in the morning and centrifuged at 3000 r/min for 10 minutes using a low-temperature high-speed centrifuge (TGL-20M, Hunan Xiangxi

Scientific Instrument Factory, China). The concentrations of HE4, CEA, and CA125 were measured using enzyme-linked immunosorbent assay (ELISA) kits (HE4: ab240688, CEA: ab264604, and CA125: ab274402; Abcam, UK), according to the manufacturers' instructions. (4) Serological indicators. The serum levels of connective tissue growth factor (CTGF), angiopoietin-2 (Ang-2), and prolactin (PRL) were measured using ELISA kits (CTGF: ab261851; Ang-2: ab-99971; PRL: ab309317; R&D Systems, USA), according to the manufacturers' instructions. (5) Adverse reaction rate

(ARR). Adverse reactions, including myelosuppression, alopecia, gastrointestinal reaction, cardiac dysfunction, and hepatic or renal impairment, were recorded, and the incidence was compared between the two groups.

Statistical analysis

All statistical analyses were conducted using SPSS 20.0 software. Data visualization was with GraphPad Prism 7 (GraphPad Software, San Diego, USA). Categorical variables (n, %) were analyzed using the Chi-square test, while continuous variables (mean ± standard deviation) were compared using independent-sample t-tests. A *P*-value <0.05 was considered significant.

Results

Comparison of baseline data before treatment

Baseline data of the two groups were obtained from the hospital medical record system and compared. As shown in **Table 1**, there were no significant differences between the two groups in terms of age, BMI, clinical stage, or histologic type (*P*>0.05).

Comparison of transvaginal ultrasound images before treatment

A comparison of transvaginal ultrasound image characteristics between the two groups prior to treatment revealed no significant differences

Table 2. Comparison of baseline characteristics of transvaginal ultrasound images between the two groups [n (%)]

Group	Aidi group (n=60)	MA group (n=60)	X ²	P
Shape			0.141	0.707
Irregularity	38 (63.33%)	36 (60%)		
Agglomerate	22 (36.67%)	24 (40%)		
Boundary			0.208	0.648
Sharpness	11 (18.33%)	13 (21.67%)		
Obscure	49 (81.67%)	47 (78.33%)		
Blood flow signal			0.175	0.916
No	4 (6.67%)	4 (6.67%)		
Abundant	39 (65%)	41 (68.33%)		
Not abundant	17 (28.33%)	15 (25%)		
Lesion diameter			0.164	0.685
≥2 cm	42 (70%)	44 (73.33%)		
<2 cm	18 (30%)	16 (26.67%)		
RI			0.333	0.564
≤0.4	38 (63.33%)	41 (68.33%)		
>0.4	22 (36.67%)	19 (31.67%)		
Echo			0.141	0.707
Low	36 (60%)	38 (63.33%)		
Uneven	24 (40%)	22 (36.67%)		
Intimal thickness			0.04	0.841
≥1.5 cm	43 (71.67%)	42 (70%)		
<1.5 cm	17 (28.33%)	18 (30%)		
Muscle infiltration			0.341	0.843
None	4 (6.67%)	5 (8.33%)		
Shallow	25 (41.67%)	27 (45%)		
Deep	31 (51.67%)	28 (46.67%)		

Note: MA: Megestrol Acetate; RI: Resistance Index.

across most variables (**Table 2**). Specifically, there was no significant difference in lesion shape (P=0.707), boundary clarity (P=0.648), blood flow signal (P=0.916), lesion diameter (P=0.685), resistance index (RI) value (P=0.564), echo uniformity (P=0.707), intimal thickness (P=0.841), or muscle infiltration depth (P=0.843). For instance, irregular shapes were detected in 38 cases (63.33%) in the Aidi group compared to 36 cases (60%) in the MA group. Similarly, abundant blood flow signals were observed in 39 patients (65%) in the Aidi group compared to 41 patients (68.33%) in the MA group.

Comparison of overall efficacy

As shown in **Table 3**, significant differences were observed between the two groups in

terms of PD rates (P=0.032), ORR (P=0.003), and DCR (P=0.032). The Aidi group demonstrated a significantly higher ORR and DCR, along with a lower PD rate compared to the MA group. However, no significant differences were found in CR, PR, or SD rates between the two groups (all P>0.05). These results suggest that the treatment in the Aidi group was more effective in achieving better response outcomes and controlling disease progression compared to the MA group.

Comparison of maximum lesion diameter

Before treatment, no significant difference was observed in maximum lesion diameter between the Aidi group (2.75±0.46 cm) and the MA group (2.69±0.52 cm) (t=0.681, P=0.497), indicating comparable baseline tumor sizes.

After treatment, however, the Aidi group exhibited a significantly smaller mean lesion diameter (1.88±0.31 cm) compared with the MA group

(2.23±0.36 cm) (t=5.864, P<0.001). These results suggest that the addition of Aidi injection to the treatment produced a more pronounced reduction in lesion size than MA alone. See **Figure 1**.

Comparison of living status

As shown in **Figure 2**, significant differences were observed between the two groups in daily food intake (t=4.474, P<0.001), body weight (t=6.066, P<0.001), and KPS scores (t=6.483, P<0.001), with the Aidi group showing higher daily food intake, greater body weight, and higher KPS scores compared to the MA group. These findings indicate that the overall health status of Aidi group was better.

Table 3. Comparison of treatment response between the two groups [n (%)]

Group	CR	PR	SD	PD	ORR	DCR
Aidi group	18 (30.0)	26 (43.3)	12 (20.0)	4 (6.7)	44 (73.3)	56 (93.3)
MA group	12 (20.0)	16 (26.7)	20 (33.3)	12 (30.0)	28 (46.7)	48 (80.0)
χ^2	1.600	3.663	2.727	4.615	8.889	4.615
P	0.206	0.056	0.099	0.032	0.003	0.032

Note: MA: Megestrol Acetate; CR: Complete Remission; PR: Partial Remission; SD: Stable Disease; PD: Progressive Disease; ORR: Objective Remission Rate; DCR: Disease Control Rate.

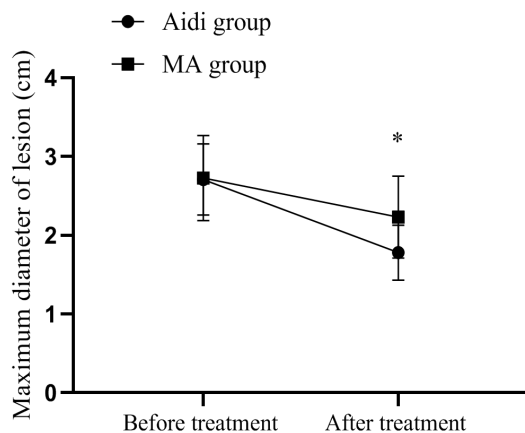


Figure 1. Comparison of maximum lesion diameter between the two groups ($\bar{x} \pm s$, cm). Note: MA: Megestrol Acetate; * $P < 0.001$, compared with the MA group.

Comparison of tumor marker levels

As shown in **Table 4**, there were no significant differences between the two groups in baseline levels of HE4 ($P=0.822$), CEA ($P=0.810$), or CA125 ($P=0.586$). After treatment, however, the Aidi group exhibited significantly lower levels of HE4 ($t=5.357$, $P<0.001$), CEA ($t=7.605$, $P<0.001$), and CA125 ($t=5.686$, $P<0.001$) compared to the MA group. These results indicate that while baseline tumor marker levels were comparable, the addition of Aidi injection resulted in a more pronounced reduction, suggesting superior efficacy in decreasing tumor marker levels.

Comparison of serological indicators

As shown in **Table 5**, no significant differences were observed between the two groups in any of the baseline serological indicators, including CTGF ($P=0.842$), Ang-2 ($P=0.911$), and PRL ($P=0.604$). After treatment, however, the Aidi group exhibited significantly lower levels of CTGF ($t=3.786$, $P<0.001$), Ang-2 ($t=5.566$,

$P<0.001$), and PRL ($t=3.002$, $P=0.003$) compared to the MA group. These results indicate that while baseline serological indicators were similar between the two groups, the addition of Aidi injection led to a more pronounced reduction in these markers, suggesting superior efficacy in modulating these serological indicators. Monitoring these markers over time may therefore provide valuable insight into treatment response.

Comparison of ARR

As shown in **Table 6**, the incidence of adverse reactions was significantly lower in the Aidi group than in the MA group. Specifically, cases of myelosuppression were 8 in Aidi group and 22 in MA group ($\chi^2=8.711$, $P=0.003$); alopecia was reported in 10 patients in the Aidi group versus 26 in the MA group ($\chi^2=10.159$, $P=0.001$). Gastrointestinal reactions, 14 versus 30 ($\chi^2=9.187$, $P=0.002$); cardiac dysfunction, 6 versus 20 ($\chi^2=9.624$, $P=0.002$); hepatic or renal dysfunction, 8 versus 24 ($\chi^2=10.909$, $P=0.001$). The total incidence of adverse reactions was also significantly lower in the Aidi group compared with the MA group ($\chi^2=18.809$, $P<0.001$). These findings suggest that the addition of Aidi injection not only enhanced therapeutic efficacy but also improved treatment tolerability by reducing adverse effects.

Discussion

Endometrial cancer (EC) is a common gynecological malignancy with multifactorial etiology, involving risk factors such as age, obesity, and endometrial hyperplasia, yet no uniform conclusions have been formed established regarding its pathogenesis. In recent years, the incidence of EC has steadily increased in parallel with environmental changes and lifestyle shifts, affecting women's physical and psychological well-being [23-25]. Current management strat-

Efficacy and safety of Aidi injection

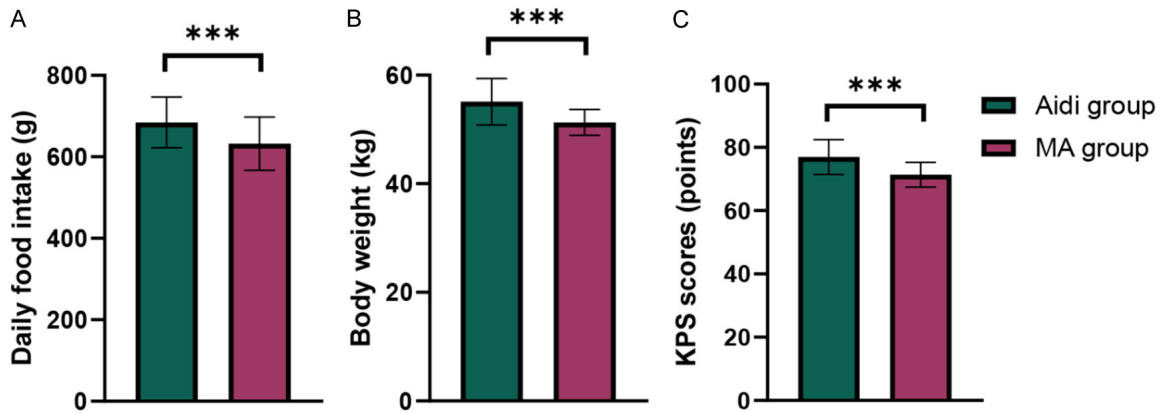


Figure 2. Comparison of living status between the two groups. A: Daily food intake (g); B: Body weight (kg); C: KPS scores (points). Note: MA: Megestrol Acetate; KPS: Karnofsky Performance Scale. *: P<0.001 for Aidi group compared to MA group.

Table 4. Tumor marker levels between the two groups before and after treatment ($\bar{x} \pm s$)

Group	HE4 (pmol/L)		CEA (ng/mL)		CA125 (kU/L)	
	Before	After	Before	After	Before	After
Aidi group	183.91±21.04	145.32±15.68	45.12±5.94	18.11±4.33	33.68±7.12	20.65±5.20
MA group	184.79±21.58	162.21±18.72	44.87±5.43	24.65±5.08	32.98±6.84	26.14±5.37
t	0.226	5.357	0.241	7.605	0.546	5.686
P	0.822	<0.001	0.810	<0.001	0.586	<0.001

Note: MA: Megestrol Acetate; HE4: Human Epididymis Protein 4; CEA: Carcinoembryonic Antigen; CA125: Cancer Antigen 125.

Table 5. Serological indicators between the two groups before and after treatment ($\bar{x} \pm s$)

Group	CTGF (μg/L)		Ang-2 (μg/L)		PRL (μg/L)	
	Before	After	Before	After	Before	After
Aidi group	135.62±18.49	94.76±10.05	1.47±0.35	0.41±0.12	33.61±5.98	18.27±3.12
MA group	134.95±18.37	102.58±12.44	1.46±0.33	0.58±0.19	34.14±5.07	20.09±3.51
t	0.200	3.786	0.112	5.566	0.520	3.002
P	0.842	< 0.001	0.911	< 0.001	0.604	0.003

Note: MA: Megestrol Acetate; CTGF: Lower Connective Tissue Growth Factor; Ang-2: Angiopoietin-2; PRL: prolactin.

Table 6. Adverse reaction rates in the two groups ($\bar{x} \pm s$)

Group	Aidi group	MA group	X ²	P
Myelosuppression	8	22	8.711	0.003
Alopecia	10	26	10.159	0.001
Gastrointestinal reaction	14	30	9.187	0.002
Cardiac dysfunction	6	20	9.624	0.002
Hepatic or renal dysfunction	8	24	10.909	0.001
Total incidence rate	26 (43.33%)	49 (81.67%)	18.809	<0.001

Note: MA: Megestrol Acetate.

egies primarily include surgery and chemoradiotherapy, while adjuvant treatments such as

hormone therapy and TCM treatments have also shown therapeutic benefits. MA, a widely

used progestogen, not only promotes apoptosis and suppresses proliferation of tumor cells but also provides supportive benefits during chemotherapy by alleviating toxic side effects and helping to maintain patients' quality of life.

Although Western medicine achieves disease-oriented therapeutic effects, it may not fully address the systemic condition of patients. TCM, by contrast, emphasizes holistic regulation and has been increasingly applied as an adjunct to EC treatment. In TCM theory, EC is often attributed to heat, toxin and blood stasis, and the treatment principles therefore focus on invigorating Qi and detoxifying to improve the astringent condition of Qi and blood in patients. Aidi injection contains components such as cantharidin (from blister beetle) and astragalus (Mongolian milkvetch root), has demonstrated antitumor activity and the ability to improve host condition in EC patients. Modern pharmacology believes that Aidi injection may induce tumor cell apoptosis, enhance bone marrow protection, maintain platelet counts within normal ranges, and increase tolerance to chemotherapy, thereby exerting synergistic effects when combined with MA [26, 27]. Taken together, these mechanisms highlight the potential of integrative regimens to enhance treatment efficacy and improve patient outcome.

In this retrospective study, the Aidi group achieved significantly higher ORR and DCR and more favorable outcomes in maximum lesion diameter and quality-of-life indicators, compared to the MA group, indicating that combining Aidi injection with MA provides superior therapeutic benefits over MA alone. Gao et al. also reported that patients receiving Aidi injection and MA had significantly higher KPS scores than those treated with MA alone [28], consistent with the present results. With increasing attention on the quality of life of cancer patients, strategies that not only prolong survival but also optimize functional status are becoming an important task in clinical medical treatment. In this context, Aidi injection shows promising potential for broader clinical application, given its ability to improve systemic condition and enhance patient quality of life.

Serum tumor markers are widely used for tumor identification and treatment evaluation. The study results showed that the levels of serum HE4, CEA, and CA125 in the Aidi group were

significantly lower than those of the MA group. Among these markers, HE4 is closely related to the occurrence and progression of EC. Previous studies have shown that HE4 levels are significantly elevated in EC patients compared with healthy individuals and increase with disease progression, making HE4 a valuable indicator for prognosis evaluation. CEA is widely used in the detection of multiple tumors and may improve diagnostic accuracy when combined with HE4. CA125, while less sensitive for EC, remains useful for monitoring treatment response and disease status. The reductions in HE4, CEA, and CA125 observed in this study suggest effective disease control, reduced tumor burden, and inhibition of tumor proliferation, highlighting the therapeutic benefit of combining Aidi injection with MA.

Serum biomarkers such as CTGF, Ang-2, and PRL play important roles in tumor progression and host immune regulation. CTGF is implicated in fibrosis and tumor metastasis, while Ang-2 promotes angiogenesis, facilitating tumor growth and invasion [29, 30]. Elevated PRL level have also been reported in patients with endometrial cancer compared with healthy individuals [31]. This study showed no significant difference in baseline CTGF, Ang-2, or PRL levels between the two groups. After treatment, all three markers were significantly lower in the Aidi group compared to the MA group. These results suggest that Aidi injection not only enhances cellular immunity, but also effectively inhibits tumor-related pathways, including angiogenesis, fibrosis, and hormone-mediated tumor progression. The observed reduction in these serologic measures further supports the multifaceted therapeutic benefits of Aidi injection, including enhancing antitumor immunity and reducing the risk of tumor progression and metastasis.

Despite the promising results of this study, which demonstrate significant benefits of combining Aidi injection with MA in improving overall outcomes and reducing tumor marker levels in patients with EC, several limitations should be acknowledged. First, as a retrospective study, the study is subject to potential selection bias due to the absence of randomized allocation. Second, while the combination therapy yielded favorable short-term outcomes, the lack of long-term follow-up data precludes a

definitive assessment of its effect on survival. Third, this study did not investigate the molecular mechanisms underlying the effects of Aidi injection, restricting a deeper understanding of its biological effects.

Future research should include prospective randomized controlled trials to validate these findings and assess the long-term efficacy of the combined use of Aidi injection and MA, particularly in relation to patient survival and quality of life. Moreover, mechanistic studies are warranted to elucidate the anti-tumor properties of Aidi injection, especially its regulation of tumor-related factors such as CTGF, Ang-2, and PRL. As our understanding of the active components and mechanisms of TCM deepens, this could facilitate the development of more effective integrative treatment approaches, providing better therapeutic options for EC patients.

Conclusion

The combination of Aidi injection and megestrol acetate demonstrates significant clinical efficacy in treating endometrial cancer by synergistically inhibiting tumor growth while improving patients' quality of life. This regimen shows superior advantages over monotherapy, including reduced adverse effects, better treatment tolerance, and significant reductions in serum tumor markers (HE4, CEA, CA125). These findings strongly support the broader clinical use of this combination therapy in standardized treatment protocols for EC.

Disclosure of conflict of interest

None.

Address correspondence to: Qinglin Li, Xinyang Vocational and Technical College, 24th Street, Yangshan New District, Xinyang 464000, Henan, China. E-mail: liqinglin@xyvtc.edu.cn

References

- [1] Sbarra M, Lupinelli M, Brook OR, Venkatesan AM and Nougaret S. Imaging of endometrial cancer. *Radiol Clin North Am* 2023; 61: 609-625.
- [2] Bilir E, Kacperczyk-Bartnik J, Bizzarri N and Kahramanoğlu İ. Current practice with operative hysteroscopy for fertility preservation in endometrial cancer and endometrial premalignancies. *Arch Gynecol Obstet* 2024; 309: 2267-2278.
- [3] Mounien L, Nakamura K, Chigr F and Maekawa F. Editorial: the roles of micro-RNAs in neuroendocrine systems. *Front Endocrinol (Lausanne)* 2024; 15: 1349804.
- [4] Maqsood Q, Sumrin A, Saleem Y, Wajid A and Mahnoor M. Exosomes in cancer: diagnostic and therapeutic applications. *Clin Med Insights Oncol* 2024; 18: 11795549231215966.
- [5] Mahdi H, Chelariu-Raicu A and Slomovitz BM. Immunotherapy in endometrial cancer. *Int J Gynecol Cancer* 2023; 33: 351-357.
- [6] Marnitz S and Schömig-Markiefka B. The PORTEC-3 trial for high-risk endometrial cancer: impact of molecular classification on prognosis and benefit from adjuvant therapy. *Strahlenther Onkol* 2021; 197: 266-268.
- [7] Malentacchi F, Turrini I, Sorbi F, Progetto E, Castiglione F, Vergoni F, Amunni G, Fambrini M, Petraglia F, Noci I and Pillozzi S. Identification of a gene panel for endometrioid endometrial cancer: a possible prognostic value? *Reprod Sci* 2020; 27: 592-598.
- [8] Oberndorfer F, Moling S, Hagelkruys LA, Grimm C, Polterauer S, Sturdza A, Aust S, Reinthaller A, Müllauer L and Schwameis R. Risk reclassification of patients with endometrial cancer based on tumor molecular profiling: first real world data. *J Pers Med* 2021; 11: 48.
- [9] Pados G, Zouzoulas D and Tsolakidis D. Recent management of endometrial cancer: a narrative review of the literature. *Front Med (Lausanne)* 2023; 10: 1244634.
- [10] Cuesta-Guardiola T, Carretero AQ, Martinez-Martinez J, Cuñarro-López Y, Pereira-Sánchez A, Fernández-Corona A and de Leon-Luis JA. Identification and characterization of endometrial carcinoma with tumor markers HE4 and CA125 in serum and endometrial tissue samples. *J Turk Ger Gynecol Assoc* 2021; 22: 161-167.
- [11] Kozakiewicz B, Chądzyńska M, Dmoch-Gajzler E and Stefaniak M. Monitoring the treatment outcome in endometrial cancer patients by CEA and TATI. *Tumour Biol* 2016; 37: 9367-9374.
- [12] Scaletta G, Dinoi G, Capozzi V, Cianci S, Pelligra S, Ergasti R, Fagotti A, Scambia G and Fanfani F. Comparison of minimally invasive surgery with laparotomic approach in the treatment of high risk endometrial cancer: a systematic review. *Eur J Surg Oncol* 2020; 46: 782-788.
- [13] Asth L, Iglesias LP, De Oliveira AC, Moraes MFD and Moreira FA. Exploiting cannabinoid and vanilloid mechanisms for epilepsy treatment. *Epilepsy Behav* 2021; 121: 106832.

- [14] Cianci S, Rosati A, Capozzi VA, Tarascio M, Uccella S, Palumbo M and Caruso S. Quality of life and sexual functioning of patient affected by endometrial cancer. *Minerva Med* 2021; 112: 81-95.
- [15] Shen Y, Shi R, Zhao R and Wang H. Clinical application of liquid biopsy in endometrial carcinoma. *Med Oncol* 2023; 40: 92.
- [16] Kitson SJ, Lindsay J, Sivalingam VN, Lunt M, Ryan NAJ, Edmondson RJ, Rutter MK and Crosbie EJ. The unrecognized burden of cardiovascular risk factors in women newly diagnosed with endometrial cancer: a prospective case control study. *Gynecol Oncol* 2018; 148: 154-160.
- [17] Yamashita H, Nakayama K, Ishikawa M, Nakamura K, Ishibashi T, Sanuki K, Ono R, Sasamori H, Minamoto T, Iida K, Sultana R, Ishikawa N and Kyo S. Microsatellite instability is a biomarker for immune checkpoint inhibitors in endometrial cancer. *Oncotarget* 2017; 9: 5652-5664.
- [18] Gockley AA, Kolin DL, Awtrey CS, Lindeman NI, Matulonis UA and Konstantinopoulos PA. Durable response in a woman with recurrent low-grade endometrioid endometrial cancer and a germline BRCA2 mutation treated with a PARP inhibitor. *Gynecol Oncol* 2018; 150: 219-226.
- [19] Konings GF, Cornel KM, Xanthoulea S, Delvoux B, Skowron MA, Kooreman L, Koskimies P, Krakstad C, Salvesen HB, van Kuijk K, Schroorders YJ, Vooijs M, Groot AJ, Bongers MY, Kruitwagen RF and Romano A. Blocking 17 β -hydroxysteroid dehydrogenase type 1 in endometrial cancer: a potential novel endocrine therapeutic approach. *J Pathol* 2018; 244: 203-214.
- [20] Pergialiotis V, Panagiotopoulos M, Koutras A, Daras A, Ntounis T, Liotos M, Daskalakis G and Thomakos N. The impact of positive peritoneal cytology on the survival rates of early-stage-disease endometrial cancer patients: systematic review and meta-analysis. *Medicina (Kaunas)* 2024; 60: 733.
- [21] Mills A, Zadeh S, Sloan E, Chinn Z, Modesitt SC and Ring KL. Indoleamine 2,3-dioxygenase in endometrial cancer: a targetable mechanism of immune resistance in mismatch repair-deficient and intact endometrial carcinomas. *Mod Pathol* 2018; 31: 1282-1290.
- [22] Kawachi A, Shimazu T, Budhathoki S, Sawada N, Yamaji T, Iwasaki M, Inoue M and Tsugane S; JPHC Study Group. Association of BMI and height with the risk of endometrial cancer, overall and by histological subtype: a population-based prospective cohort study in Japan. *Eur J Cancer Prev* 2019; 28: 196-202.
- [23] Kamizaki K, Minami Y and Nishita M. Role of the Ror family receptors in Wnt5a signaling. *In Vitro Cell Dev Biol Anim* 2024; 60: 489-501.
- [24] Passarelli A, Pisano C, Cecere SC, Di Napoli M, Rossetti S, Tambaro R, Ventriglia J, Gherardi F, Iannacone E, Venanzio SS, Fiore F, Bartoletti M, Scognamiglio G, Califano D and Pignata S. Targeting immunometabolism mediated by the IDO1 pathway: a new mechanism of immune resistance in endometrial cancer. *Front Immunol* 2022; 13: 953115.
- [25] Altındağ SD, Yiğit S and Şen S. Is microcystic, elongated, and fragmented pattern of myometrial invasion in endometrioid endometrial carcinoma associated with survival? *Turk J Med Sci* 2022; 52: 1569-1579.
- [26] Yuan L, Chen Y, Li X, Jin H and Shi J. Predictive models for overall survival in breast cancer patients with a second primary malignancy: a real-world study in Shanghai, China. *BMC Womens Health* 2022; 22: 498.
- [27] Concin N, Creutzberg CL, Vergote I, Cibula D, Mirza MR, Marnitz S, Ledermann JA, Bosse T, Chargari C, Fagotti A, Fotopoulou C, González-Martín A, Lax SF, Lorusso D, Marth C, Morice P, Nout RA, O'Donnell DE, Querleu D, Raspollini MR, Sehouli J, Sturdza AE, Taylor A, Westermann AM, Wimberger P, Colombo N, Planchamp F and Matias-Guiu X. ESGO/ESTRO/ESP Guidelines for the management of patients with endometrial carcinoma. *Virchows Arch* 2021; 478: 153-190.
- [28] Gao X, Li Q, Qu Y, Zhang J, Xing Y and Li S. Effect of combination of Traditional Chinese Medicine with Western Medicine on Endometrial Carcinoma and its influence on ultrasound, MRI, tumor markers HE4 and CA125. *Evid Based Complement Alternat Med* 2021; 2021: 6053406.
- [29] Li XT, Li JY, Zeng GC, Lu L, Jarrett MJ, Zhao Y, Yao QZ, Chen X and Yu KJ. Overexpression of connective tissue growth factor is associated with tumor progression and unfavorable prognosis in endometrial cancer. *Cancer Biomark* 2019; 25: 295-302.
- [30] Kozłowski M, Borzyszkowska D, Mirko J, Turoń-Skrzypińska A, Piotrowska K, Tołoczko-Grabarek A, Kwiatkowski S, Tarnowski M, Rotter I and Cymbaluk-Płoska A. Preoperative serum levels of PDGF-AB, PDGF-BB, TGF- α , EGF and ANG-2 in the diagnosis of endometrial cancer. *Cancers (Basel)* 2023; 15: 4815.
- [31] Standing D, Dandawate P and Anant S. Prolactin receptor signaling: a novel target for cancer treatment - Exploring anti-PRLR signaling strategies. *Front Endocrinol (Lausanne)* 2022; 13: 1112987.