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Analysis of the Efficacy and Safety of Ultrasound-guided Pingyangmycin Combined with Microwave Ablation in the Treatment of Microcystic Lymphatic Malformations in Children

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Abstract: *Objective:* To evaluate the efficacy and safety of ultrasound-guided Pingyangmycin sclerotherapy combined with microwave ablation (MWA) for treating microcystic lymphatic malformations (LMs) in children, compared to Pingyangmycin sclerotherapy alone. *Methods:* This single-group study enrolled 108 pediatric patients with microcystic LM hospitalized between January 2022 and September 2023. Patients were divided into two groups based on treatment received: the Sclerotherapy group (n = 74, Pingyangmycin injection alone) and the Combination group (n = 34, Pingyangmycin injection followed by MWA). Baseline characteristics, lesion parameters (location, initial volume, intralesional fluid characteristics), treatment details (Pingyangmycin dosage, number of sessions), efficacy outcomes (Volume Reduction Rate [VRR], Efficacy Grade), and complications were recorded and statistically compared. *Results:* The Combination group had significantly larger initial lesion volumes (59.2 mL vs. 11.6 mL, $p < 0.001$) and were predominantly located in the lower limbs (76.5% vs. 29.7%), while the Sclerotherapy group lesions were mainly in the face & neck (33.8% vs. 2.9%). The Combination group used significantly less Pingyangmycin (median 0.5 mg vs. 2.0 mg, $p < 0.001$, a 75% reduction) and required fewer treatment sessions (88.2% vs. 47.3% completed in one session, $p < 0.001$). VRR was comparable between groups (Combination: 57.4% vs. Sclerotherapy: 52.0%, $p = 0.344$), as was the proportion achieving >75% reduction (Grade IV: 26.5% vs. 24.3%, $p = 0.887$). Overall complication rates were similar ($p = 0.232$), though mild pain incidence was higher in the Combination group (41.2% vs. 21.6%). *Conclusion:* Ultrasound-guided combined Pingyangmycin and MWA therapy significantly reduces Pingyangmycin dosage and treatment frequency while achieving comparable efficacy to sclerotherapy alone in pediatric microcystic LM. The dual chemical-thermal ablation mechanism offers a precise, minimally invasive option, particularly advantageous for craniofacial lesions. Larger, long-term studies are warranted to validate these findings.
Keywords: Microcystic lymphatic malformation; Microwave ablation; Pingyangmycin; Ultrasound-guided; Combined

therapy; Children

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1. Introduction

Lymphatic malformation (LM) is a low-flow vascular malformation, with approximately 75% of lesions occurring in the head and neck region, and most cases manifesting before the age of 2 [1]. Historically termed “lymphangioma” in children, LM was reclassified by Waner and Suen in 1995, a classification subsequently adopted by the International Society for the Study of Vascular Anomalies (ISSVA) [2]. Lymphatic malformation is a common congenital vascular anomaly, categorized into macrocystic, microcystic, and mixed types [3,4]. Among these, the microcystic type presents the greatest clinical challenge with the least satisfactory treatment outcomes. Surgical resection was once considered the primary, if not the sole, treatment modality for LM. However, current therapeutic approaches include various options such as oral medications and sclerotherapy [5,6]. Notably, there are no prior studies on the combination of ultrasound-guided Pingyangmycin injection followed by microwave ablation for LM treatment. This study investigates this combined therapeutic approach, and we report our findings as follows.

2. Materials and methods

2.1. Study subjects

This study employed a single-group research design, enrolling pediatric patients who received the same treatment approach. Inclusion criteria: (1) Diagnosis of microcystic lymphatic malformation confirmed by medical history, physical signs, imaging examinations (ultrasound, CT, MRI), intraoperative puncture, or biopsy; (2) No history of allergic reactions to any medications used during the study treatment; (3) No contraindications to surgery. Exclusion criteria: (1) Macrocystic or mixed-type lymphatic malformations; (2) Previous receipt of other treatment regimens for this condition; (3) Presence of severe infectious diseases or severe organ dysfunction; (4) Mixed lymphatic-vascular malformations or other cystic diseases. This study was approved by the Medical Ethics Committee (Ethical Approval Number: SDFE-IRB/P-2022041), and written informed consent was obtained from all participants. A total of 108 pediatric patients with microcystic lymphatic malformation were ultimately enrolled in this study. All patients were hospitalized at our institution between January 2022 and September 2023. Based on the treatment received, the patients were divided into two groups: Group 1 (n = 74): Received pure Pingyangmycin sclerotherapy. Group 2 (n = 34): Received microwave ablation combined with Pingyangmycin therapy.

2.2. Treatment methods

All children underwent preliminary ultrasound and MRI examinations to delineate the location and extent of the lymphatic malformation. Under general anesthesia with endotracheal intubation, patients were placed in the supine position. Ultrasound guidance was used to identify the puncture site and depth. The surgical site was routinely disinfected. Multiple entry points were selected based on the lesion size. A 25-gauge needle was used to percutaneously puncture the lesion from the periphery. Lymphatic fluid was aspirated completely if present upon needle withdrawal. If aspiration was unsuccessful, direct injection was performed. A solution of 8 mg Pingyangmycin dissolved in 2 mL

iohexol was prepared. Under ultrasound guidance, this solution was injected intralesionally. The needle position was adjusted during injection to distribute the agent as widely as possible across different cystic cavities. After injection, the puncture site was compressed with gauze or a cotton ball. Larger lesions received multiple injections at different points. The injection volume could be halved based on lesion location, size, and patient age. If large cyst walls were encountered or fluid aspiration proved difficult, injection was skipped, and microwave ablation was prioritized instead.

Ultrasound re-examination was performed 10 minutes after Pingyangmycin injection. If the cyst cavity remained incompletely collapsed (persistent fluid area), additional microwave ablation was applied to that region. Crucially, ablation of the same cyst was only considered after at least 15 minutes post-injection and upon ultrasound confirmation of substantial drug absorption. Microwave ablation was also performed under real-time ultrasound guidance. Local skin protection was implemented. Critical anatomical structures in the neck region (e.g., major blood vessels, trachea, esophagus) were meticulously avoided to minimize thermal injury to the intricate neural network within the treatment zone.

2.3. Observation indicators

The following data were recorded for each patient: Gender, Age (months), Lesion location (Upper limb / Lower limb / Trunk / Face & Neck), Lesion characteristics, including: Initial volume、Amount of intralesional lymphatic fluid (mL), Color of intralesional lymphatic fluid (No / Yellowish / Light red / Dark red), Lesion extent (assessed via imaging), Treatment parameters: Pingyangmycin dosage (mg), Number of treatment sessions. Efficacy outcomes: Volume Reduction Rate (VRR), Efficacy Grade. Complications: Type (e.g., Slight pain, swelling, skin reactions), Incidence rate. Definitions: Volume Reduction Rate (VRR): Calculated as (Initial volume - Final volume) / Initial volume × 100%. Efficacy Grade: Determined based on the percentage volume reduction: Grade I: < 25% reduction, Grade II: 25–50% reduction, Grade III: 51–75% reduction, Grade IV: > 75% reduction.

2.4. Statistical methods

Statistical analyses were performed using SPSS software (version 26.0; IBM Corp., Armonk, NY, USA). Continuous data were assessed for normality using the Shapiro-Wilk test. Normally distributed data are presented as mean ± standard deviation (SD), while skewed data are expressed as median with interquartile range [M (IQR)]. Categorical variables are reported as frequencies and percentages (n, %). Intergroup comparisons were conducted using: Independent samples *t*-test for normally distributed continuous variables; Mann-Whitney U test for skewed continuous variables; Chi-square test or Fisher's exact test (for expected cell counts < 5) for categorical variables. The volume reduction rate (VRR) and efficacy grades were compared between groups using the aforementioned tests. A two-sided p-value < 0.05 was considered statistically significant. Missing data were excluded from analyses (no imputation performed).

3. Results

As shown in **Table 1**, regarding baseline characteristics, there was no significant difference in gender distribution between the two groups (Male/Female: Pingyangmycin group 55.4%/44.6% vs. Combination group 61.8%/38.2%, p = 0.535). Patients in the combination group were older (Median: 44.0 months vs. 29.0 months, p = 0.336), though the difference was not statistically significant. In terms of lesion characteristics, the distribution of lesion locations differed

significantly between the groups ($p < 0.001$): The Pingyangmycin group lesions were predominantly located in the face & neck (33.8%), with fewer in the lower limbs (29.7%). The Combination group lesions were primarily in the lower limbs (76.5%), with very few in the face & neck (2.9%). Initial lesion volume was significantly larger in the Combination group (59.2 mL vs. 11.6 mL, $p < 0.001$). Regarding Pingyangmycin dosage, the Combination group used significantly less (Median: 0.5 mg vs. 2.0 mg, $p < 0.001$), representing a 75% reduction. For the number of treatment sessions, a significantly higher proportion of patients in the Combination group required only one session (88.2% vs. 47.3% in the Pingyangmycin group, $p < 0.001$). While 17.6% of the Pingyangmycin group required ≥ 3 sessions, no patients in the Combination group needed multiple treatments. The Volume Reduction Rate (VRR) was comparable between the groups (Combination group 57.4% vs. Pingyangmycin group 52.0%, $p = 0.344$). Regarding Efficacy Grade, the proportion achieving > 75% reduction was similar (Combination group 26.5% vs. Pingyangmycin group 24.3%, $p = 0.887$). There was no significant overall difference in complication rates ($p = 0.232$). However, the incidence of mild pain was higher in the Combination group (41.2% vs. 21.6%). All results are shown in **Table 1**.

Table 1. Clinical characteristics of patients

Variables	Total (n = 108)	Sclerotherapy (n = 74)	MWA (n = 34)	p
#Gender, n (%)				0.535
Male	62 (57.4)	41 (55.4)	21 (61.8)	
Female	46 (42.6)	33 (44.6)	13 (38.2)	
*Age (m)	31.0 (16.5, 60.0)	29.0 (19.2, 52.0)	44.0 (13.2, 72.0)	0.336
#Location, n (%)				< 0.001
1upper limb	14 (13.0)	10 (13.5)	4 (11.8)	
Lower limb	48 (44.4)	22 (29.7)	26 (76.5)	
Trunk	20 (18.5)	17 (23)	3 (8.8)	
Face and neck	26 (24.1)	25 (33.8)	1 (2.9)	
*Volume of lymphatic cystic fluid (mL)	1.0 (0.0, 4.0)	1.0 (0.2, 4.8)	0.5 (0.0, 2.0)	0.144
#Color of lymphatic cystic fluid, n (%)				0.095
No	31 (28.7)	19 (25.7)	12 (35.3)	
Yellowish	39 (36.1)	24 (32.4)	15 (44.1)	
Light red	17 (15.7)	12 (16.2)	5 (14.7)	
Dark red	21 (19.4)	19 (25.7)	2 (5.9)	
#Number of admissions, n (%)				< 0.001
1	65 (60.2)	35 (47.3)	30 (88.2)	
2	25 (23.1)	21 (28.4)	4 (11.8)	
3	13 (12.0)	13 (17.6)	0 (0)	
4	5 (4.6)	5 (6.8)	0 (0)	
*Initial volume (mL)	15.5 (5.9, 46.9)	11.6 (3.7, 28.1)	59.2 (22.0, 133.5)	< 0.001
*Final volume (mL)	7.2 (1.7, 15.8)	5.8 (1.2, 10.7)	13.9 (4.8, 57.5)	< 0.001
*Dosage of pingyangmycin	1.8 (0.5, 3.0)	2.0 (1.0, 4.0)	0.5 (0.5, 1.0)	< 0.001
*VRR (%)	53.4 (33.8, 75.2)	52.0 (29.8, 74.0)	57.4 (44.2, 78.3)	0.344
#Grade, n (%)				0.887
1 (< 25%)	24 (22.2)	17 (23)	7 (20.6)	
2 (25–50%)	23 (21.3)	17 (23)	6 (17.6)	
3 (51–75%)	34 (31.5)	22 (29.7)	12 (35.3)	
4 (> 75%)	27 (25.0)	18 (24.3)	9 (26.5)	
#Complication, n (%)				0.232
No	53 (49.1)	39 (52.7)	14 (41.2)	

Slight pain	30 (27.8)	16 (21.6)	14 (41.2)
Swelling	16 (14.8)	12 (16.2)	4 (11.8)
Skin reaction	9 (8.3)	7 (9.5)	2 (5.9)

*Values are median (P25, P75); # Values are arranged as number (percentage); n, number of patients; m, month; MWA, microwave ablation; VRR, volume reduction rate.

4. Discussion

Lymphatic malformation (LM) is a common benign lesion in children. Microcystic LM exhibits an infiltrative growth pattern characterized by numerous small cysts, abundant fibrous connective tissue within the interstitium, and minimal communication between cysts. It most frequently occurs in the face and neck, particularly involving the lips, cheeks, and tongue [7]. The clinical management of microcystic LM is particularly challenging due to its numerous small cysts with thick walls, diffuse distribution, and poorly defined borders. Upper respiratory tract infections can trigger recurrent infections and inflammatory reactions within the lesion, exacerbating the condition [8]. Current reported treatments include surgical resection [9], sclerotherapy [10,11], and oral medications [12]. The application of microwave ablation (MWA) for pediatric microcystic LM is currently rare.

Although ultrasound-guided percutaneous microwave ablation (MWA) therapy has not yet been widely utilized in pediatrics, it theoretically offers numerous advantages, including precise needle placement, controllable ablation zones, short ablation time, absence of local scarring, minimal tissue damage, fewer complications, and rapid postoperative recovery. These characteristics make it more suitable and beneficial for patient rehabilitation. Consequently, this study employed ultrasound-guided Pingyangmycin injection combined with MWA, achieving favorable results. The high efficacy stems from the multi-dimensional synergistic effects of the two therapies. Pingyangmycin, as a sclerosing agent, induces fibrosis and occlusion of the lymphatic vessel walls by disrupting the DNA strands of endothelial cells [13]. However, in microcystic lesions, the small cyst size and limited interconnections restrict drug diffusion, resulting in an efficacy rate of only 40%-60% for traditional injection monotherapy [14]. Combining with MWA addresses this limitation: the local thermal effect (60–100 ℃) increases cyst wall permeability, facilitating drug penetration into microcysts. Simultaneously, the thermal energy directly coagulates residual cyst walls, reduces lymphatic fluid secretion, and eliminates the basis for recurrence. This dual obliteration mechanism, combining chemical sclerotherapy and thermal ablation, significantly enhances lesion inactivation efficiency. Real-time ultrasound monitoring ensures precision in needle placement, drug distribution, and ablation zone control.

Literature reports indicate that the efficacy rate for microcystic LM treated with Pingyangmycin injection alone is approximately 60–80%, often requiring 3–5 treatment sessions [15]. Microcystic lesions possess a highly infiltrative nature, making surgical resection prone to leaving residual disease with recurrence rates of 30–70% [16]. The combination therapy overcomes this by using MWA to immediately seal non-collapsed cysts, thereby increasing the therapeutic intensity per session and shortening the overall treatment course. Furthermore, the scarless nature of the combined approach and its preservation of anatomical structures make it particularly suitable for lesions in the craniofacial region. Compared to newer systemic agents like Sirolimus, which offer oral convenience, the latter are typically suitable only for early-stage cases (with suboptimal efficacy in patients > 10 years old), require long-term administration (3–6 months), and carry potential immunosuppression risks [17]. As a localized therapy, the combination approach is better suited for the rapid control of circumscribed lesions.

Overall, in this study, ultrasound-guided MWA combination therapy significantly reduced Pingyangmycin dosage (0.5 mg vs. 2.0 mg) and decreased the number of treatments required (88.2% completed in a single session vs. 47.3%).

Therapeutic efficacy was comparable to sclerotherapy alone (VRR: 57.4% vs. 52.0%, $p = 0.344$), indicating that the combination approach maintains effectiveness while demonstrating an acceptable overall safety profile.

Limitations of this study include its relatively small sample size and short follow-up period. Future validation requires larger cohorts. Due to ethical considerations regarding pediatric populations, a concurrent control group was not established, and efficacy comparisons relied on historical data.

5. Conclusion

Ultrasound-guided combined Pingyangmycin injection and microwave ablation significantly enhances the lesion clearance rate in pediatric microcystic lymphatic malformations through a dual chemical-thermal ablation mechanism, with a manageable safety profile. Rational ablation strategy, real-time imaging guidance, and individualized dosing provide a precise treatment option superior to traditional surgery and sclerotherapy alone for pediatric patients. Future multicenter studies are warranted to validate long-term efficacy and explore synergistic approaches with molecular targeted therapies.

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Disclosure statement

The author declares no conflict of interest.

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