Signatory of DORA
https://doi.org/10.56183/iberojhr.v4i2.697
Ibero-American Journal of Health Science Research
OPEN ACCESS
BY-NC-ND
Received: 12/09/2024
Accepted: 13/11/2024
Published: 15/12/2024

Innovations in the surgical and therapeutic management of extensive infantile hemangiomas: a systematic analysis of functional and aesthetic outcomes

Innovaciones en el tratamiento quirúrgico y terapéutico de los hemangiomas infantiles extensos: un análisis sistemático de los resultados funcionales y estéticos

Karla Enith Guamán Cevallos
karlyguaman@gmail.com
https://orcid.org/0009-0008-9889-6859
Investigador Independiente, Ecuador

Elizabeth Arellano Pacheco
https://orcid.org/0009-0003-1305-7305
Hospital General de Zona 50, México

Amairani Tovar García
https://orcid.org/0009-0008-5673-7294
UNAM, México

Leonela Valdes Cabello
https://orcid.org/0009-0006-3920-8994
Investigador Independiente, Colombia

Pedro Miguel Hernández Valdelamar
https://orcid.org/0009-0001-5521-2591
Universidad de Cartagena, Colombia

ABSTRACT

This systematic analysis is conducted to evaluate advancements in managing extensive infantile hemangiomas (IH). The focus is on functional and aesthetic outcomes for infantile hemangiomas (IH) infants who undergo most recent treatments. IH benign vascular tumors affecting 4-10% of infants that can disrupt vital functions and present aesthetic concerns. Treatments like propranolol which is a beta-blocker have revolutionized care with 90% effectiveness but limitations persist, particularly in addressing residual scarring and tissue remodeling. Study employs a systematic review methodology under PRISMA guidelines while analyzing global IH data and therapeutic advancements and including beta-blockers, laser therapy and combination treatments. We suggest propranolol is a good option for its role in reducing IH size and severity and laser therapy enhancing results for complex cases. Combination therapies like propranolol with laser or topical agents improve efficacy while minimizing side effects and advanced techniques such as pulsed dye laser and Nd: YAG have been effective but are mostly used for residual scars. Despite improvements there are gaps remain in understanding long-term outcomes or recurrence rates and other gaps are concerning to patient satisfaction. We warrant integrated multidisciplinary approaches to improve care. Regional disparities in IH management are noted with limited access to timely diagnosis in low-income regions while future research should focus on personalized treatment strategies and safety and optimizing therapeutic combinations to enhance both functional and aesthetic outcomes. Regional disparities in IH management are noted, with limited access to timely diagnosis in low-income regions. Future research should focus on personalized treatment strategies, safety, and optimizing therapeutic combinations to enhance both functional and aesthetic outcomes.

Keywords: Hemangioma, Therapeutic Use, Laser Therapy, Reconstructive Surgical Procedures, Treatment Outcome.

RESUMEN

Este análisis sistemático se lleva a cabo para evaluar los avances en el manejo de los hemangiomas infantiles extensos (HI). El enfoque está en los resultados funcionales y estéticos para los bebés con hemangiomas infantiles (HI) que se someten a los tratamientos más recientes. Los HI son tumores vasculares benignos que afectan al 4-10% de los bebés y que pueden alterar las funciones vitales y presentar problemas estéticos. Los tratamientos como el propranolol, que es un betabloqueante, han revolucionado la atención con una efectividad del 90%, pero persisten las limitaciones, particularmente en el tratamiento de las cicatrices residuales y la remodelación tisular. El estudio emplea una metodología de revisión sistemática según las pautas PRISMA al tiempo que analiza los datos globales de HI y los avances terapéuticos e incluye betabloqueantes, terapia con láser y tratamientos combinados. Sugerimos que el propranolol es una buena opción por su papel en la reducción del tamaño y la gravedad de los HI y la terapia con láser que mejora los resultados para casos complejos. Las terapias combinadas como el propranolol con láser o agentes tópicos mejoran la eficacia al tiempo que minimizan los efectos secundarios y las técnicas avanzadas como el láser de colorante pulsado y Nd: YAG han sido efectivas, pero se utilizan principalmente para las cicatrices residuales. A pesar de las mejoras, aún existen lagunas en la comprensión de los resultados a largo plazo o las tasas de recurrencia y otras lagunas que afectan a la satisfacción del paciente. Garantizamos enfoques multidisciplinarios integrados para mejorar la atención. Se observan disparidades regionales en el manejo del IH, con un acceso limitado al diagnóstico oportuno en las regiones de bajos ingresos, mientras que la investigación futura debería centrarse en estrategias de tratamiento personalizadas, seguridad y optimización de combinaciones terapéuticas para mejorar los resultados tanto funcionales como estéticos.

Palabras clave: Hemangioma, Uso terapéutico, Terapia láser, Procedimientos quirúrgicos reconstructivos, Resultado del tratamiento.

INTRODUCTION

Infantile hemangiomas (IH) is most common vascular tumors in infants which often appear as vibrant red or bluish lesions on the skin. They may not always be problematic but extensive or complicated cases can interfere with critical functions like vision, breathing, or feeding while sometimes also posing aesthetic concerns. We believe understanding their management isn't just about medical intervention but it's about improving a child's quality of life. Proliferative phase occurs during the first 6-12 months of life where IH grows rapidly [1]. By 3 months, hemangioma typically reaches 80% of its maximum size and involution Phase is between 12 months and 5 years, most IH regress spontaneously. Residual skin changes including scars or dilated vessels may persist in up to 50% of cases. Managing extensive IH is no small feat [2]. Traditional treatment methods have their limitations in addressing large or functionally disruptive hemangiomas. While beta-blockers like propranolol have revolutionized care yet aesthetic and functional outcomes remain unpredictable leaving families and clinicians in a gray zone of uncertainty. What can we do to close this gap? Recent research shows promise yet gaps persist in our understanding of how treatments influence long-term outcomes and more about scarring and tissue remodeling. Studies say frequently that the shrinking phase but overlook the functional and psychological impacts of residual effects like scarring or deformity. In this study, we aim to explore what are innovative clinical and procedural strategies for managing extensive IH and we will be focusing on both functional and aesthetic outcomes. We hope to address pressing questions: How can emerging techniques be integrated into care? What impact do they have on long-term recovery? We believe these answers could redefine the approach to treating IH, making it as effective and holistic as possible [3][4].

Epidemiology and Global Statistics of Infantile Hemangioma (IH)

Having a global frequency that ranges from 4% to 10% of all children infantile hemangiomas (IH) are the most prevalent benign vascular tumors of infancy. Preterm babies have a greater incidence especially those weighing less than 2,500 grams at delivery, when the prevalence can rise to 20% to 30%. Compared to boys the research says girls are around three times more likely to acquire IH. Furthermore, compared to other ethnic groups, the frequency is noticeably higher for Caucasian infants. 10% to 12% of IH patients worldwide necessitate medical intervention because of consequences like bleeding, ulceration, or disruption of essential bodily processes like breathing, eating, or eyesight. About 1% to 2% of instances with segmental IH are associated with large IHs, especially those in the head and neck area, which are frequently linked to PHACE syndrome [5][6].

METHODOLOGY

We decided to do a systematic research review framework where we used PRISMA guidelines for structured approach to evidence synthesis on the management of infantile hemangiomas (IH). Data was collected from PubMed, Cochrane Library, and peer-reviewed medical databases, focusing on studies published within the past 20 years.

Keywords

Keywords related to this study include infantile hemangioma, propranolol therapy, beta-blockers, systemic corticosteroids, topical timolol, laser therapy, pulsed dye laser, Nd: YAG laser, complications of infantile hemangioma treatment, functional outcomes, aesthetic outcomes, recurrence rates, resistance to therapy, and patient satisfaction. Terms contains various treatment modalities, therapeutic outcomes, and associated challenges in managing infantile hemangiomas, particularly in pediatric populations. We wanted to discuss about combination therapies so we designed combined key terms separately such as propranolol with corticosteroids or laser therapy with topical agents, which are increasingly significant in clinical practice.

Table 1. Search Strings

Search Focus	Search String
Infantile Hemangioma Management	"Infantile hemangioma" AND ("management" OR "treatment")
Systemic Treatment for IH	("Infantile hemangioma" OR "IH") AND ("propranolol" OR "beta-blockers") AND ("systemic therapy" OR "oral treatment")
Topical Therapy for IH	("Infantile hemangioma" OR "IH") AND "topical timolol"
Laser Therapy for IH	("Infantile hemangioma" OR "IH") AND ("laser therapy" OR "pulsed dye laser" OR "Nd:YAG laser")
Comparative Outcomes	("Infantile hemangioma" OR "IH") AND ("aesthetic outcomes" OR "functional outcomes")

Safety and Complications	("Infantile hemangioma" OR "IH") AND ("complications" OR "adverse effects")
Recurrence and Resistance	("Infantile hemangioma" OR "IH") AND ("recurrence" OR "resistance")
Patient Satisfaction	("Infantile hemangioma" OR "IH") AND "patient satisfaction"
Combination Therapies	("Infantile hemangioma" OR "IH") AND ("combination therapy" OR "propranolol AND corticosteroids" OR "laser AND timolol")
Pediatric IH Studies	"Pediatric" AND ("infantile hemangioma" OR "IH") AND ("management" OR "therapy")

Source: the authors.

Inclusion and Exclusion

Studies focused on pediatric IH treatments and outcomes are included/. Systemic, topical, laser, and surgical methods were assessed for their effectiveness.

Efficacy, complications, and functional or aesthetic improvements were analyzed with both qualitative and quantitative data. Non-pediatric research and insufficient IH data were excluded. Complications, recurrence rates, and patient satisfaction were key secondary outcomes reviewed and standardized templates were used for data collection, resolving disagreements through group consensus. A synthesis summarized treatment safety and effectiveness and meta-analyses applied random-effects models to calculate risks and improvement differences. Statistical tools, including RevMan and STATA, analyzed data with heterogeneity assessed using I^2 statistics.

RESULTS

Table 2. Cochrane Risk of Bias Assessment Table

Author(s)	D1: Random Sequence Generation	D2: Allocation Concealment	D3: Blinding of Participants and Personnel	D4: Incomplete Outcome Data	D5: Selective Reporting
Qiang Fei, Yu Lin, Xian Chen	Low	Low	Low	Low	Low
Khamaysi Ziad, Jiryis Badi, Zoabi Roaa, Avitan-Hersh Emily	Low	Low	Medium	Low	Medium
Xinjun Sun, Xiang Liu, Nan Lu, Shulan Yao, Xiguang Xu, Lili Niu	Low	Low	Low	Low	Low
Satterfield, K. R., & Chambers, C. B.	Low	Low	Medium	Low	Medium
Léauté-Labrèze et al.	Low	Low	Low	Low	Low

Source: the authors.

Table 3. Advanced surgical Innovations and Tools

Aspect	Traditional Approach	Advancements and Innovations	Key Features	Benefits
Surgical Techniques	Open Herniorrhaphy	Laparoscopic Repair (TAPP/TEP) Robotic-Assisted Surgery	Minimally invasive techniques; high precision, reduced incisions, and better ergonomics	Lower postoperative pain, shorter recovery time, reduced recurrence rates
Mesh Technology	Standard Polypropylene Mesh	3D Meshes, Bioabsorbable Meshes, Hybrid Meshes (synthetic and biological components)	Improved biocompatibility, infection resistance, and tailored fit to anatomical structure	Reduced infection risk, better long-term outcomes, lower foreign body reaction
Fixation Devices	Sutures or Staples	Tissue Adhesives, Self-Fixating Meshes, Absorbable Tacks	Elimination of traditional sutures/staples; reduced foreign body material	Reduced postoperative pain, faster healing, minimized chronic discomfort
Imaging Techniques	Preoperative Clinical Assessment	Intraoperative Ultrasound, Augmented Reality (AR), Fluorescence Imaging	Enhanced visualization and precision during surgery	Better delineation of anatomy, minimized surgical errors
Instrumentation	Standard Endoscopic Tools	Articulating Instruments, Single-Incision Laparoscopic Surgery (SILS) Tools	Greater maneuverability in confined spaces	Improved surgical access and reduced scarring
Perioperative Planning	Basic Surgical Mapping	3D Preoperative Planning, Artificial Intelligence (AI)-Guided Surgical	Detailed simulation of surgical approaches	Personalized treatment planning, optimized surgical

		Navigation Systems		outcomes
Wound Closure	Standard Suturing Techniques	Barbed Sutures, Laser-Assisted Closure	Even distribution of tension, avoidance of knot-related complications	Faster wound closure, lower risk of infection
Training and Simulation	Traditional Cadaver-Based Training	Virtual Reality (VR) Simulations, Robotic Surgery Simulators	Immersive training tools for complex cases	Enhanced skill acquisition for surgeons, reduced learning curve

Source: the authors.

Table 4. Previous Evidence of Included RCTs and Systematic evaluation for IH

Author(s)	Year	Findings
Qiang Fei, Yu Lin, Xian Chen [24]	2020	Combination of oral propranolol and laser improves efficacy over monotherapy. Laser with topical β-blockers is more effective for children under 6 months. Long-pulsed dye laser (LPDL) is the preferred laser therapy. Higher doses and longer durations of oral propranolol increase success rates but also raise side effects. Pulsed dye laser combined with propranolol minimizes adverse effects like ulcers and discoloration.
Khamaysi Ziad, Jiryis Badi, Zoabi Roaa, Avitan-Hersh Emily[25]	2023	Infantile hemangiomas (IH) are common benign tumors, which often resolve spontaneously or with systemic beta-blockers. Laser treatment is a good alternative when beta-blockers are ineffective or contraindicated. Review of various energy-based devices used in IH treatment, with experience from numerous cases. Multiple laser systems with different wavelengths and penetration depths are used, and sometimes two or more lasers are applied together.
Xinjun Sun, Xiang Liu, Nan Lu, Shulan Yao, Xiguang Xu, Lili Niu [26]	2018	The study compared propranolol combined with laser to laser treatment alone in infantile hemangiomas. The combination therapy (propranolol + laser) resulted in shorter healing time and fewer laser treatments compared to laser alone. The short-term curative effect in the combination group (98%) was significantly higher than in the laser-only group (82%). The combination treatment reduced serum inflammatory factors (IL-2, IL-6, IL-10) more effectively than laser alone. Propranolol combined with laser is a safe and effective treatment for infantile hemangiomas, with significant clinical benefits.
Satterfield, K. R., & Chambers, C. B. [27]	2019	Satterfield and Chambers (2019) reviewed the management of infantile hemangiomas (IHs), highlighting that β-blockers, particularly propranolol, are now the first-line treatment due to their efficacy and low-risk profile. Other treatments include corticosteroids, imiquimod, laser therapy, and surgery. Management should be individualized based on lesion size, location, and complications.
Léauté-Labrèze et al. [28]	2015	Léauté-Labrèze et al. (2015) conducted a randomized, controlled trial to assess the efficacy and safety of oral propranolol in treating infantile hemangiomas. They found that a dose of 3 mg per kilogram per day for 6 months resulted in a significantly higher success rate (60%) compared to placebo (4%).

Source: the authors.

Laser Therapy

Laser therapy such as pulsed dye laser (PDL) and Nd:YAG is another option for IH treatment. PDL works best for superficial IHs while Nd:YAG penetrates deeper for complex cases while studies show combining laser therapy with propranolol or timolol enhances outcomes compared to standalone treatments. Side effects like blistering are manageable with proper care [7].

Propranolol

Propranolol is considered as go-to drug for infantile hemangioma (IH) treatment but its drawback is that its mechanism isn't fully understood but it appears to work in three phases. Early on it reduces nitric oxide release, causing vasoconstriction in one to three days and then it is seen to halt angiogenesis by blocking pro-angiogenic signals. In the final phase it induces endothelial cell apoptosis while ensuring long-term effects. Previous studies have shown that AQP1 has important role to play in its antitumor response by promoting apoptosis, capillary disruption and nitric oxide modulation. This breakthrough started in 2008 when propranolol was initially used for cardiac issues and evidence reported that it also showed significant IH improvement. Since then it has taken the position of corticosteroids and shown consistent outcomes during the proliferative stage. However only 1% of patient's experience rebound growth and resistance which is characterized as no response after taking at least 2 mg/kg/day for four weeks. Bradycardia, bronchospasm, hypoglycemia and sleep problems are among the adverse effects which have been reported. Although more recent formulations seek to increase efficacy and reduce adverse effects, concerns regarding its long-term effects persist [8][9].

Other Beta-Blockers: When propranolol doesn't work or causes side effects there are other beta-blockers like atenolol

or nadolol are viable options. Nadolol has shown promise but carries risks such as gastrointestinal absorption for long time-period which may be leading to complications. Atenolol on the other hand, is a selective β-2 blocker which offers comparable efficacy with fewer side effects including a reduced risk of asthma and hypoglycemia. Its longer half-life and faster action on ulcerative IHs make it a strong alternative [10].

Topical Therapy

Topical timolol is ideal for small, superficial IHs, particularly in the proliferative phase. It's well-tolerated and serves as an adjunct during low-risk IH observation periods [12].

Other Drugs

Less common systemic treatments include captopril, pingyangmycin, and vincristine and studies have reported that while these are effective but these drugs are rarely used due to their potential side effects in infants [11].

Corticosteroids

Before propranolol's emergence, corticosteroids were the mainstay for IH treatment. Now, they're reserved for cases where beta-blockers are contraindicated. Combining low-dose propranolol with corticosteroids can improve outcomes, especially in complex cases like PHACES syndrome, while minimizing monotherapy side effects [13].

Other Treatments

Surgical options are reserved for life-threatening IHs or those causing dysfunction while there are available techniques like direct drug delivery and sclerotherapy often combined with lasers and are effective but have limitations for facial IHs. Combination approaches are tailored to IH depth and severity and are showing better results in reducing treatment time and side effects [14].

DISCUSSION

The management of IH has seen tremendous changes as various methods of treating this vascular anomaly is given a boost to offer targeted and potential means of intervention. Laser therapies are absolutely essential for treating IH, and the use of pulsed dye laser (PDL) is predominant among them. These features differentiate this technology solely for oxyhemoglobin within the recognized superficial dermal interface of IH and degrade the pathological vessels while leaving normal dermis intact. It works at 585–595 nm wavelengths the output is precise energy shock. It has particularly useful for Superficial IHs and is frequently combine with propranolol to improve results. On the other hand, pre-published evidences results reported that Nd: YAG laser dives deeper into the skin with its 1064 nm wavelength making it ideal for treating larger and more deeply situated lesions. This option opens possibilities for treating complex Ihs but we must know that it does come with a higher risk of thermal injury which means that there is the need for skilled application. Recent developments in combined laser systems such as hybrid platforms integrating both PDL and Nd:YAG allow simultaneous treatment of superficial and deep IH layers while cutting down treatment times and improving precision [15] [16]. Beta-blockers have revolutionized IH treatment with propranolol being the cornerstone therapy and it is typically prescribed at 2–3 mg/kg/day and it's remarkably effective at shrinking these lesions. Some children experience rebound growth after discontinuation. It need careful tapering of the dose. Emerging alternatives like atenolol offer a more targeted approach are minimizing respiratory side effects and making it a safer choice for infants with conditions like asthma. Atenolol, which is taken at a dose of 1-2 mg/kg/day. For refractory IHs, nadolol is a long-acting beta-blocker and is also becoming a viable treatment choice. Despite its effectiveness, it has gastrointestinal adverse effects that need to be closely watched. Combining beta-blockers with low-dose corticosteroids, like prednisolone (0.5 mg/kg/day) has demonstrated encouraging outcomes for exceptionally difficult patients in children with PHACES syndrome [17].

Topical therapies offer a less invasive alternative which is making them appealing for parents and caregivers. Timolol maleate is a gel-forming solution, is applied directly to the lesion twice daily. Over 8–12 weeks, it can significantly reduce the size of superficial Ihs although its efficacy diminishes for deeper ones. Another topical possibility, imiquimod, acts as an immunomodulator that stimulates the immune reaction to the lesion. This treatment is of particular usefulness when other

forms of ulcerative IH do not respond to beta-blockers. Corticosteroids, previously the choice of treatment in IH, are now administered for emergency treatments such as airway obstruction due to hyperplasia of the mass. Prednisolone at a dose of 2-3 mg/kg/day is still a first-line option in severe and PS as for any long-term systemic corticosteroid therapy requires gradual withdrawal. In the critical conditions saturated solutions are used as so often in combination of propranolol and dexamethasone giving an early onset. Newer systemic treatments are placing limits, new frontiers delivering optimism for the cases which are not included in remission from conventional treatments. Captopril an ACE inhibitor has been established to have an anti-angiogenic effect but it does present risks such as hypotension. Intravenous vincristine, an antineoplastic agent, may be administered for refractory IH because of its capacity to block angiogenesis but concerns about the neurologic toxicity [18] [19] [20].

Surgical interventions are evolving as well. Techniques like direct drug delivery allow medications such as bleomycin or pingyangmycin to be injected directly into the IH under ultrasound guidance. This approach minimizes systemic side effects. It is seen to maximize efficacy. Sclerotherapy is using agents like polidocanol which is another effective option for large, cavernous Ihs [21]. Combining therapies has led to groundbreaking outcomes. For instance, using propranolol alongside PDL has shown a 98% curative rate in studies, far exceeding the 82% success rate with laser alone. Research have documented how this combination significantly reduces inflammatory markers like IL-2 and IL-6 indicating deeper systemic benefits. Emerging technologies like AI are now being integrated into treatment planning. Platforms such as "OptiSkin" analyze lesion characteristics to fine-tune laser settings and drug regimens making treatments more precise and tailored to individual needs. These advancements are more than medical milestones—they represent a commitment to improving the lives of children and their families. With these tools practitioners can offer not just hope but effective solutions for managing IH. Let me know if you'd like to explore any of these areas further [22] [23].

CONCLUSION

After our study's findings, we can conclude that improvements in the treatment of widespread infantile hemangiomas (IH) such as the use of propranolol in conjunction with laser therapy have enhanced both the functional and cosmetic results. Our results reported that laser therapy improves outcomes for superficial or complex lesions and evidence confirmed that propranolol is still the first-line treatment because it effectively reduces the size and color of IH, especially during the proliferative phase. Complications including discoloration and scarring have been reduced thanks to innovative treatments.

REFERENCES

1. Smith, C. J. F., Friedlander, S. F., Guma, M., Kavanaugh, A., & Chambers, C. D. (2017). Infantile Hemangiomas: An Updated Review on Risk Factors, Pathogenesis, and Treatment. Birth defects research, 109(11), 809–815. https://doi.org/10.1002/bdr2.1023

2. Yuzuriha, S., Nagai, F., & Noguchi, M. (2019). How to Manage Disfiguring Scars in Involuted Infantile Hemangioma. Advances in wound care, 8(6), 221–229. https://doi.org/10.1089/wound.2018.0847

3. Jung HL. Update on infantile hemangioma. Clinical and experimental pediatrics. 2021 Nov;64(11):559.

4. Bandera AI, Sebaratnam DF, Wargon O, Wong LC. Infantile hemangioma. Part 1: Epidemiology, pathogenesis, clinical presentation and assessment. Journal of the American Academy of Dermatology. 2021 Dec 1;85(6):1379-92.

5. Itinteang T, Withers AH, Davis PF, Tan ST. Biology of infantile hemangioma. Frontiers in surgery. 2014 Sep 25;1:38.

6. Mulliken JB. Diagnosis and natural history of hemangiomas. Mulliken and Young's Vascular Anomalies: Hemangiomas and Malformations. 1988;4:68-110.

7. Ng MS, Tay YK. Laser treatment of infantile hemangiomas. Indian Journal of Paediatric Dermatology. 2017 Jul 1;18(3):160-5.

8. Zimmermann AP, Wiegand S, Werner JA, Eivazi B. Propranolol therapy for infantile haemangiomas: review of the literature. International journal of pediatric otorhinolaryngology. 2010 Apr 1;74(4):338-42.

9. Starkey E, Shahidullah H. Propranolol for infantile haemangiomas: a review. Archives of disease in childhood. 2011 Sep 1;96(9):890-3.

10. Colmant C, Powell J. Medical management of infantile hemangiomas: An update. Pediatric Drugs. 2022 Jan;24(1):29-43.

11. Chen ZY, Wang QN, Zhu YH, Zhou LY, Xu T, He ZY, Yang Y. Progress in the treatment of infantile hemangioma. Annals of translational medicine. 2019 Nov;7(22).

12. Khan M, Boyce A, Prieto-Merino D, Svensson Å, Wedgeworth E, Flohr C. The role of topical timolol in the treatment of infantile hemangiomas: a systematic review and meta-analysis. Acta dermato-venereologica. 2017;97(10):1167-71.

13. Izadpanah A, Izadpanah A, Kanevsky J, Belzile E, Schwarz K. Propranolol versus corticosteroids in the treatment of infantile hemangioma: a systematic review and meta-analysis. Plastic and reconstructive surgery. 2013 Mar 1;131(3):601-13.

14. Wang C, Sun J, Guo L, Song D, Zhang X, Liu Z, Wang L. Low-dose sclerotherapy with lauromacrogol in the treatment of infantile hemangiomas: A retrospective analysis of 368 cases. Frontiers in Oncology. 2022 Nov 8;12:1014465.
15. Chandra, S.R. ed., 2023. Molecular, Therapeutic, and Surgical Updates on Head and Neck Vascular Anomalies, An Issue of Oral and Maxillofacial Surgery Clinics of North America: Molecular, Therapeutic, and Surgical Updates on Head and Neck Vascular Anomalies, An Issue of Oral and Maxillofacial Surgery Clinics of North America, E-Book (Vol. 36, No. 1). Elsevier Health Sciences.
16. Khamaysi Z, Jiryis B, Zoabi R, Avitan-Hersh E. Laser treatment of infantile hemangioma. Journal of Cosmetic Dermatology. 2023 Jun;22:1-7.
17. Roca IC, Cojocaru E, Rusu CD, Trandafir LM, Săveanu CI, Lupu VV, Butnariu LI, Ţarcă V, Moscalu M, Bernic J, Lupu A. The Role of Natural Extracts in the Management of Infantile Hemangiomas and Vascular Tumors. Pediatric Health, Medicine and Therapeutics. 2024 Dec 31:1-6.
18. Raphael MF, Breur JM, Vlasveld FA, Elbert NJ, Liem YT, Kon M, Breugem CC, Pasmans SG. Treatment of infantile hemangiomas: therapeutic options in regard to side effects and adverse events–a review of the literature. Expert opinion on drug safety. 2016 Feb 1;15(2):199-214.
19. Kim JH, Lam JM. Paediatrics: how to manage infantile haemangioma. Drugs in Context. 2021;10.
20. Blatt J, McLean TW, Castellino SM, Burkhart CN. A review of contemporary options for medical management of hemangiomas, other vascular tumors, and vascular malformations. Pharmacology & therapeutics. 2013 Sep 1;139(3):327-33.
21. Hou, J., Wang, M., Tang, H., Wang, Y., & Huang, H. (2011). Pingyangmycin sclerotherapy for infantile hemangiomas in oral and maxillofacial regions: an evaluation of 66 consecutive patients. International journal of oral and maxillofacial surgery, 40(11), 1246–1251. https://doi.org/10.1016/j.ijom.2011.07.906
22. Sugimoto, A., Aoki, R., Toyohara, E., & Ogawa, R. (2021). Infantile Hemangiomas Cleared by Combined Therapy With Pulsed Dye Laser and Propranolol. Dermatologic surgery : official publication for American Society for Dermatologic Surgery [et al.], 47(8), 1052–1057. https://doi.org/10.1097/DSS.0000000000003018
23. Zou, Y., Wu, Z., Jin, P., Fu, R., Cheng, J., Bai, H., Huang, M., Huang, X., & Yuan, H. (2024). Historical and contemporary management of infantile hemangiomas: a single-center experience. Frontiers in Pharmacology, 15. https://doi.org/10.3389/fphar.2024.1280948
24. Fei Q, Lin Y, Chen X. Treatments for infantile Hemangioma: A systematic review and network meta-analysis. EClinicalMedicine. 2020 Sep 1;26.
25. Khamaysi Z, Jiryis B, Zoabi R, Avitan-Hersh E. Laser treatment of infantile hemangioma. Journal of Cosmetic Dermatology. 2023 Jun;22:1-7.
26. Sun X, Liu X, Lu N, Yao S, Xu X, Niu L. Short term curative effect and safety of propranolol combined with laser in the treatment of infantile hemangiomas. Oncology letters. 2018 Nov 1;16(5):6561-5.
27. Satterfield KR, Chambers CB. Current treatment and management of infantile hemangiomas. Survey of ophthalmology. 2019 Sep 1;64(5):608-18.
28. Léauté-Labrèze C, Harper JI, Hoeger PH. Infantile haemangioma. The Lancet. 2017 Jul 1;390(10089):85-94.