MEDS Clinical Medicine (2024)
Clausius Scientific Press, Canada

DOI: 10.23977/medsc.2024.050504
ISSN 2616-1907 Vol. 5 Num. 5

Research progress in the treatment of chronic subdural hematomas by embolisation of the middle meningeal artery

Liu Lei[1,a], Zhang Yi[2,*]

[1]*Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, 712000, China*
[2]*Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, 712000, China*
[a]*1057300146@qq.com*
[*]*Corresponding author: SXgg1129@163.com*

Keywords: Chronic subdural hematoma, middle meningeal artery embolization, research progress, review

Abstract: CSDH is one of the common diseases in neurosurgery, and currently surgical treatment is the preferred treatment option for symptomatic CSDH, but the high rate of postoperative recurrence is still a major drawback of surgical treatment; in recent years, some studies have proved that the method of blocking the source of hematoma by EMMA is effective in the treatment of CSDH; therefore, this paper presents an overview of anatomical-pathophysiological bases, indications, and contraindications for the treatment of CSDH by EMMA, research progress of clinical embolization materials and embolization efficacy are reviewed.

1. Introduction

Chronic subdural hematoma (CSDH) is one of the most common neurosurgical disorders, which is a chronic and complex disease. Statistical data prove that the incidence of CSDH ranges from 1.7 to 20.6 per 100,000 people in the population, and in the elderly population, the incidence is as high as 58 per 100,000 people[1,2]. In recent years, due to the aging of the population and the use of anticoagulant drugs, the incidence of CSDH has been increasing year by year. The main choices of drug therapy for CSDH are atorvastatin, dexamethasone, tranexamic acid, and angiotensin converting enzyme inhibitors (ACEIs). However, for patients with obvious clinical symptoms, the first-line treatment is still surgery, and the main surgical methods include cranial drilling and flushing drainage, cranial hematoma removal and neuroendoscopic surgery. However, these modalities have a high recurrence rate, up to 30%[3]. Therefore, researchers are constantly seeking other methods in the hope of reducing the recurrence rate, and through a large number of basic and clinical studies, researchers have found that middle meningeal artery embolization (EMMA) can be used for the treatment of recurrent and high-risk CSDH. Therefore, this paper provides a review and analysis of the research progress of EMMA for the treatment of CSDH. Research progress is reviewed and analyzed.

2. Main text

2.1. Anatomic-pathophysiologic basis of EMMA for CSDH treatment

The subdural cavity was first thought to be a physiological natural cavity similar to the thoracic cavity, but later under the observation of electron microscope, it was found that the subdural cavity is composed of a layer of flat fibroblasts, which connect the dura mater with the arachnoid membrane and are also known as dura mater edge cell layer , which is not easy to be destroyed naturally, but under the action of external forces and other factors, this layer is relatively weak in comparison with the arachnoid membrane and dura mater, and can be easily torn away. However, under the influence of external forces and other factors, this layer is easy to be torn apart due to its relative weakness compared to the arachnoid and dura mater[4]. The dura mater is not easily damaged by external forces or other factors. When the body is subjected to external forces, the dura mater marginal cell layer and the surrounding pontine veins are torn, blood and tissue fluids continue to ooze out, inflammatory reactions are activated, fibroblasts proliferate and inflammatory cells continue to accumulate, and neovascularization continues to form, and after these reactions, the outer membrane structure that encases the hematoma is formed. However, the microstructure under the microscope showed that the new capillaries were characterized by wide inner diameters, fragile endothelial cell layers, and incomplete basement membranes, which resulted in high vascular permeability, and the hematoma was further enlarged due to the continuous infiltration of blood into the hematoma cavity. At the same time, in the process of inflammatory reaction, various signaling pathways were activated, the local coagulation function of hematoma was abnormal, leading to hyperfibrinolytic system, and it was difficult for the enlarged hematoma to form a thrombus, which continued to tear the marginal cell layer of the dura mater and the bridging vein, forming a vicious circle, and then the hematoma volume was further expanded to form a compression effect, leading to a series of clinical symptoms such as headache, dizziness, mild hemiparesis and even change of consciousness[5]. The result is headache, dizziness, mild hemiparesis and even altered consciousness.

Therefore, from the viewpoint of the anatomic-pathophysiologic mechanism of CSDH, blocking the blood source of the hematoma is one of the ways to address the persistent enlargement of the hematoma from the etiologic point of view.Shapiro et al.[6] demonstrated that, on post contrast imaging, the capillary vessels in normal subjects have a fine diameter and are difficult to image, but in patients with CSDH there is a patchy enhancement of the vascular epithelium on angiography on the side of the hematoma.Santiago et al. [7] showed that when N-butyl cyanoacrylate (n-BCA) glue was injected into the anterior portion of the left middle meningeal artery (MMA) during the treatment of patients with CSDH, the hematoma showed a filamentous linear staining close to the left cerebral hemisphere, which was connected to the MMA by branches. Tempaku et al.[8] showed that polyvinyl alcohol (PVA) particles dissolved in a contrast reagent were used for embolization of the MMA, and the later use of computed tomography (CT) of the head showed contrast leakage in the hematoma. Based on the above theories and studies, EMMA provides a new therapeutic idea and method for the fundamental treatment of CSDH, which makes up for the shortcomings of the high postoperative recurrence rate of drilling and drainage, and can also be used to assist in the treatment of recurrent CSDH.

2.2. Indications and contraindications of EMMA for the treatment of CSDH

Combined with the results of related studies and case studies reported in the literature in recent years, the following conditions can be considered as indications for EMMA: 1) EMMA can be considered for patients with mild clinical symptoms who have failed to respond to conservative treatment[9] .A meta-analysis by Ironside et al. showed that the recurrence and surgical rescue rates

of EMMA treatment were significantly lower than those of conventional treatment in five related studies with 902 patients. 2) EMMA can be used as an adjunctive treatment for refractory CSDH, organized CSDH and recurrent CSDH, HaiDaoXuan et al. [10] reported a case in which EMMA was applied prior to surgery for organized CSDH involvement; Additionally, Yokoya et al.[11] conducted a study involving two patients with organized CSDH who received EMMA treatment before surgical intervention; the results indicated that there was no recurrence, thereby offering new possibilities and methodologies for managing organized CSDH; a retrospective analysis of high-risk recurrent CSDH included 23 patients with high-risk recurrent CSDH, in which 11 patients were treated with conventional surgery as the control group and 12 patients were treated with EMMA intervention. The final results showed that there was no significant difference in the efficiency between the two groups, but the recurrence rate of the observation group was significantly lower than that of the control group[12]. The recurrence rate of the observation group was significantly lower than that of the control group. Another clinical study on the use of EMMA in the treatment of recurrent CSDH showed that 17 recurrent patients included in the study had no recurrence and no complications after EMMA treatment[13]. 3) Abnormal coagulation or patients who are receiving and cannot stop anticoagulant and antiplatelet medications; several studies have shown that EMMA has advantages over traditional surgery in treating CSDH patients with abnormal coagulation[14-16]. 4) Patients with many underlying diseases who have failed or failed conservative treatment and cannot tolerate conventional surgery.

There are contraindications to EMMA intervention, mainly as follows: 1) allergy to contrast or embolizing agents; 2) severe renal insufficiency; 3) abnormal structural development of the MMA or dangerous anastomotic branches with adjacent important blood vessels; normal MMA originates from the maxillary artery, but developmental abnormalities that lead to an abnormal origin of the MMA can lead to embolization of the main blood supply arteries of the brain and lead to cerebral infarction. When the MMA anastomoses with the blood-supplying arteries of the ophthalmic and facial nerves, it can lead to blindness and facial paralysis due to accidental embolization[17]. The MMA can lead to blindness, facial paralysis, etc.

2.3. Embolization material selection for CSDH treatment by EMMA

Currently, the embolic materials commonly used in clinical practice are mainly categorized into solid embolic materials and liquid embolic materials. Solid embolic materials are mainly PVA particles, gelatin sponge particles, detachable spring coils and so on; the most commonly used are PVA particles , the earliest use of which can be traced back to 1974, with a particle size of 45-1,180 μm, which stay distally by aggregating in the vascular system[18]. The advantages and disadvantages of PVA particle embolization are as follows; first, PVA particles are more commonly used in clinical practice and require less skill on the part of the operator than liquid material embolization; second, the use of large particles prevents penetration of dangerous internal and external carotid artery anastomoses; however, injection of PVA particles requires the use of a larger-diameter microcatheter, which can result in the spasm or occlusion of important vascular branches of the MMA; and third, PVA material is difficult to visualize on X-ray. In addition, it is difficult for PVA material to be visualized under X-ray, which is not conducive to the observation of embolization by the operator during the procedure and may affect the embolization effect; solid embolization material may theoretically have the possibility of recurrence of the disease due to the prolonged degradation of the material by absorption, but there are few reports of recurrence of the disease due to this reason for PVA material; lastly, the absence of pain reaction when injecting the material and the low price of the material are the important advantages of the PVA particles[19,20]. Finally, the lack of pain associated with injection and the low cost of PVA particles are important advantages. Liquid

embolization materials mainly include Onyx , n-BCA, anhydrous ethanol, etc.; Onyx uses dimethyl sulfoxide (DMSO) as a solvent and tantalum powder, vinyl vinyl alcohol composition of the mixture, n-BCA is a kind of synthetic glue, containing ethyl iodine oil and tantalum powder, due to the addition of tantalum powder so that the two embolization materials are easy to develop under fluoroscopy, more conducive to the operator to observe embolization situation; in addition, Onyx and n-BCA can be used for the injection of PVA particles. Onyx, n-BCA and other liquid embolic agents are not easily absorbed, and permanent embolization can be achieved; compared with the PVA material, Onyx can be infused with a microcatheter with a finer diameter, so it can be in the small distal branches of the MMA, making embolization more refined. On the other hand, n-BCA material can be used in conjunction with Ethiopian alcohol and 5% glucose aqueous solution to promote better penetration of n-BCA, which is more favorable for patients with proximal MMA tortuosity. At the same time, the disadvantages of liquid embolization materials are also obvious. Onyx and n-BCA have the common disadvantage of being expensive compared with PVA; DMSO contained in Onyx is vasotoxic, and will stimulate the blood vessels to produce a painful reaction during infusion, so it is necessary to be performed under general anesthesia; n-BCA is a kind of synthetic glue, which has a high degree of adhesion, so that if it is not withdrawn from the catheter in a timely manner, it may be adhered to the vessel wall by the catheter. If the catheter is not withdrawn in time, the catheter may be adhered to the blood vessel wall, therefore, the operator's skills are more demanding[19]. Therefore, the operator's technique is more demanding.

Regarding the results of trials comparing the clinical effectiveness of embolic materials, a meta-analysis evaluating the effect of PVA, Onyx, and n-BCA embolic agents on embolization outcomes showed that there were no statistically significant differences between the three embolic agents in terms of recurrence rate (P=0.71), the need for surgical salvage (P=0.89), or postoperative complications (P=0.48)[19]. Another retrospective study compared the liquid embolic agent group (101 cases, 76.5%) with the granular embolic material group (31 cases, 23.5%) and showed that there was no statistically significant difference in the rate of hematoma clearance (P=0.753)) and retreatment (P=0.197) within 90 days in patients[21] . Various embolization materials have their own advantages and disadvantages, and there are few studies on the selection of embolization materials, and the selection of specific materials for embolization still requires a large amount of comparative data from studies to determine the most appropriate embolization materials.

2.4. Clinical efficacy of EMMA in the treatment of CSDH

Aggipothu et al.[22] A retrospective study was conducted to analyze the postoperative outcome of 29 patients treated with EMMA procedure for CSDH, which showed complete resolution of hematoma in 25 patients, significant reduction of bilateral hematoma in 3 patients, and 1 patient died from complications related to renal failure and aspiration pneumonia. Orscelik et al.[23] conducted a single-center retrospective study of patients with CSDH who underwent MMA embolization, which included 209 successful EMMAs (PVA as the primary embolic agent) in 144 patients with CSDH, and showed that the median maximum width of the hematoma was 12 mm and 3 mm before the intervention and at the last follow-up, respectively, and that 72.8% of the patients had a greater than 50% improvement after the procedure. Tan Yun et al.[12] retrospectively analyzed 23 patients with CSDH treated with EMMA between March 2020 and March 2022, in which 23 cases of embolization were treated as the observation group, 20 patients with unilateral recurrence, 3 patients with bilateral recurrence, and traditional treatment as the control group, and the results showed that the recurrence rate of the observation group was significantly lower than that of the control group, and there was a statistically significant difference, and there was no statistically significant difference in the comparison of the treatment effectiveness rate. A study observed the therapeutic effect of EMMA in

17 patients with multiple recurrences of CSDH, and the results showed that none of the 17 patients who had undergone EMMA had relapsed during the follow-up period (4-60 weeks), and no significant complications occurred[13]. Kan et al.[3] evaluated the treatment outcome of 154 patients treated with embolization for CSDH and showed improvement in subdural hematoma thickness in 90% of patients at the late 90-day follow-up; more than 70% of patients had a reduction in hematoma thickness of more than 50% at the last 1 follow-up visit.

3. Conclusion and outlook

With the deepening of population aging, the number of patients with CSDH is gradually increasing, and traditional treatment has a certain recurrence rate in the clinic, and the increase in the number of morbidities makes the number of recurrences also increasing. With the continuous progress of medicine, the research on the etiology and pathophysiological mechanisms of CSDH is becoming more and more in-depth, EMMA as an emerging treatment is expected to reduce the recurrence rate, improve the prognosis of patients, and at the same time provide a new option for patients who cannot tolerate traditional surgery. To date, many studies in the literature have demonstrated the safety and efficacy of EMMA, but there is still a lack of evidence-based data to support the selection of surgical procedures, control of indications, and choice of embolization materials, which has prevented the formation of a complete clinical guideline to guide treatment for the time being. Through continuous research, EMMA is expected to become the first-line treatment for symptomatic CSDH.

References

[1] FEGHALI J, YANG W, HUANG J. Updates in chronic subdural hematoma: epidemiology, etiology, pathogenesis, treatment, and outcome [J]. World neurosurgery, 2020, 141: 339-345.

[2] OU Y, DONG J, WU L, et al. The clinical characteristics, treatment, and outcomes of chronic subdural hematoma in young patients [J]. World Neurosurgery, 2019, 125: e1241-e1246.

[3] KAN P, MARAGKOS G A, SRIVATSAN A, et al. Middle meningeal artery embolization for chronic subdural hematoma: a multi-center experience of 154 consecutive embolizations [J]. Neurosurgery, 2021, 88(2): 268-277.

[4] TAMURA R, SATO M, YOSHIDA K, et al. History and current progress of chronic subdural hematoma [J]. J Neurol Sci, 2021, 429: 118066.

[5] HU Kai, ZHANG Hua. Advances in the pathogenesis and treatment of chronic subdural hematoma [J]. Journal of Clinical Neurosurgery, 2024, 21(01): 102-5+9.

[6] SHAPIRO M, WALKER M, CARROLL K T, et al. Neuroanatomy of cranial dural vessels: implications for subdural hematoma embolization [J]. Journal of NeuroInterventional Surgery, 2021, 13(5): 471-477.

[7] SANTIAGO R B, JASTRZEBSKI C, DAKWAR E, et al. Middle meningeal artery embolization for chronic subdural hematoma-pathophysiology and radiological findings [J]. World Neurosurgery: X, 2024, 23: 100296.

[8] TEMPAKU A, YAMAUCHI S, IKEDA H, et al. Usefulness of interventional embolization of the middle meningeal artery for recurrent chronic subdural hematoma: Five cases and a review of the literature [J]. Interv Neuroradiol, 2015, 21(3): 366-371.

[9] IRONSIDE N, NGUYEN C, DO Q, et al. Middle meningeal artery embolization for chronic subdural hematoma: a systematic review and meta-analysis [J]. Journal of neurointerventional surgery, 2021, 13(10): 951-957.

[10] XUAN H D, MINH T P, VAN H D, et al. Preoperative middle meningeal artery embolization in the treatment of organized chronic subdural hematoma [J]. Radiol Case Rep, 2024, 19(8): 3569-3573.

[11] YOKOYA S, NISHII S, TAKEZAWA H, et al. Organized Chronic Subdural Hematoma Treated with Middle Meningeal Artery Embolization and Small Craniotomy. Two Case Reports [J]. Asian J Neurosurg, 2020, 15(2): 421-424.

[12] TAN Yun, SONG Yi, WU Yao, et al. Standardized middle meningeal artery embolization for high-risk recurrent chronic subdural hematoma [J]. China Standardization, 2023, (24): 290-293.

[13] ZHENG He, XIA Xiaolong, ZHANG Meibiao, et al. Middle meningeal artery embolization for recurrent chronic subdural hematoma in 17 cases [J]. Zhejiang Surgery of Trauma, 2023, 28(11): 2042-2045.

[14] HIRAI S, ONO J, ODAKI M, et al. Embolization of the Middle Meningeal Artery for Refractory Chronic Subdural Haematoma. Usefulness for Patients under Anticoagulant Therapy [J]. Interv Neuroradiol, 2004, 10 Suppl 2(Suppl 2): 101-104.

[15] MORDEN F T C, CABALLERO C G, ABELLA M, et al. Middle meningeal artery embolization for symptomatic

chronic subdural hematoma in the setting of severe transfusion-refractory thrombocytopenia: a case study and review of the literature [J]. Surg Neurol Int, 2023, 14: 223.
[16] YAJIMA H, KANAYA H, OGINO M, et al. Middle meningeal artery embolization for chronic subdural hematoma with high risk of recurrence: a single institution experience [J]. Clin Neurol Neurosurg, 2020, 197: 106097.
[17] SHAPIRO M, WALKER M, CARROLL K T, et al. Neuroanatomy of cranial dural vessels: implications for subdural hematoma embolization [J]. J Neurointerv Surg, 2021, 13(5): 471-477.
[18] VAIDYA S, TOZER K R, CHEN J. An overview of embolic agents [J]. Semin Intervent Radiol, 2008, 25(3): 204-215.
[19] ELLENS N R, SCHARTZ D, KOHLI G, et al. Safety and efficacy comparison of embolic agents for middle meningeal artery embolization for chronic subdural hematoma [J]. J Cerebrovasc Endovasc Neurosurg, 2024, 26(1): 11-22.
[20] FIORELLA D, HIRSCH J A, ARTHUR A S. Embolization of the middle meningeal artery for the treatment of chronic subdural hematoma: considerations for pragmatic trial design [J]. J Neurointerv Surg, 2021, 13(4): 295-297.
[21] SCOVILLE J, JOYCE E, TAUSSKY P, et al. Primary middle meningeal artery embolization for non-acute subdural hematoma: a multi-institutional retrospective review of particle versus liquid embolic agents [J]. Neurosurgery, 2020, 67.
[22] AGGIPOTHU B, DEEPALAM S, BADACHI S, et al. Middle Meningeal Artery Embolization for the Management of Chronic Subdural Hematoma [J]. Cureus, 2023, 15(10): e47293.
[23] ORSCELIK A, SENOL Y C, BILGIN C, et al. Middle meningeal artery embolization without surgical evacuation for chronic subdural hematoma: a single- center experience of 209 cases [J]. Front Neurol, 2023, 14: 1222131.