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通道弯数与长度对静脉曲张泡沫硬化疗法的泡沫稳定性影响实验研究

白逃萍¹, 刘雨秋^{1,2}, 蒋文涛¹, 李亚兰¹

(1. 四川大学生物力学省重点实验室, 成都 610065; 2. 北京航空航天大学生物与医学工程学院, 北京 100191)

摘要:目的 研究通道弯数与长度对静脉曲张泡沫硬化疗法的泡沫稳定性影响。方法 设置3组实验: 实验组1通道弯数不同(A、B、C组弯数分别为1、2、3)、实验组2(对照组)通道总长度不同(A、B、C组总长度分别为2、6、10)、实验组3通道长短比例不同(A、B、C组长短边比值分别为1:1、5:1、9:1)。选用5 mL注射器, 液气比1:4, 并在室温环境下进行CO₂和空气的Tessari法制备泡沫实验。每组实验全程摄像, 设置重复实验5次, 通过视频回放方式获取析水时间、半衰期、析水率曲线等数据。结果 实验组2中, CO₂泡沫除析水率40%和80%, A组与B组、C组都具有显著性差异。空气泡沫中, 析水率20%和50%的B组与A组具有显著性差异; 所有析水率下, C组与A组具有显著性差异。通道总长度对CO₂泡沫的影响更为显著。通道总长度越长, 泡沫越稳定。实验组1与对照组对比, CO₂泡沫的实验组1析水率曲线明显高于对照组, 而空气泡沫出现重合和交叉, 差异不明显。实验组3和对照组对比, CO₂泡沫实验组3的曲线明显高于对照组, 而空气泡沫只在析水达到100%时, 实验组明显高于对照组。通道长短比例的影响在CO₂泡沫中较为明显。半衰期在CO₂泡沫中存在较大影响。结论 制备泡沫的通道弯数增强了泡沫的稳定性, 通道总长度增加对泡沫稳定性具有积极意义, 而通道长短比例对泡沫稳定性的影响较大。研究结果对于临床制备泡沫以及其他泡沫的稳定性研究具有一定意义。

关键词: 通道弯数; 通道长度; 泡沫稳定性; 泡沫半衰期; 静脉曲张

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Effects of Channel Bend Number and Length on Foam Stability of Varicose Vein Foam Sclerotherapy: An Experimental Study

BAI Taoping¹, LIU Yuqiu^{1,2}, JIANG Wentao¹, LI Yalan¹

(1. Provincial Key Laboratory of Biomechanical Engineering, Sichuan University, Chengdu 610065, China;

2. School of Biological Science and Medical Engineering, Beihang University, Beijing 100191, China)

Abstract: **Objective** To study the effect of channel bend number and length on foam stability of varicose vein foam sclerotherapy. **Methods** Three groups of experiments were set up: experimental group 1 with different channel turns (channel turn of subgroup A, B, C was 1, 2, 3, respectively), experimental group 2 (control group) with different channel total lengths (total length of subgroup A, B, C was 2, 6, 10, respectively), experimental group 3 with different channel length ratios (ratio of long and short sides for subgroup A, B, C was 1:1, 5:1, 9:1, respectively). A 5 mL syringe was used, the liquid-gas ratio was 1:4, and the Tessari method of

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通信作者: 蒋文涛, 教授, E-mail: scubme_jwt@outlook.com

CO₂ and air was used to prepare foam experiments at room temperature. The whole process of experiments on each group was photographed, and the experiment was repeated 5 times. Data such as water separation time, half-life, and water separation rate curve were obtained by video playback. **Results** In experimental group 2, the water removal rate of CO₂ foam was 40% and 80%, and there were significant differences between subgroup A, subgroup B and subgroup C. In air foam, there is a significant difference between subgroup B and subgroup A with a water separation rate of 20% and 50%; for all water separation rates, subgroup C and subgroup A had a significant difference. The total length of the channel had a more significant impact on the CO₂ foam. The longer the total length of the channel, the more stable the foam would be. Compared with control group, the CO₂ foam in experimental group 1 had a significantly higher water separation rate curve than that in the control group, while the air foam overlapped and crossed, and the difference was not obvious. Compared with the control group, the curve of the CO₂ foam in experimental group 3 was significantly higher than that in control group, while the air foam was only significantly higher than that in control group when the water separation reached 100%. The influence of the channel length ratio was more obvious in CO₂ foam. The half-life had a greater impact in CO₂ foam. **Conclusions** The number of channel turns used to prepare the foam enhances stability of the foam. The increase in total length of the channel has a positive effect on stability of the foam, and the ratio of the channel length has a greater influence on stability of the foam. The results have certain significance for clinical preparation of foams and the stability research of other foams.

Key words: channel bend; channel length; foam stability; foam half-life; varicose veins

下肢静脉曲张发病率约为 40%，而泡沫硬化疗法是静脉曲张治疗的微创疗法之一。泡沫硬化剂的制备通常是将液态硬化剂（如聚多卡醇、鱼肝油酸钠等）按一定体积比与气体（如空气、CO₂、CO₂/O₂ 等）混合形成均匀稳定的泡沫，再将泡沫注入曲张静脉，使其纤维条索化，同时堵塞血液形成闭塞^[1-2]。泡沫硬化疗法以操作简单、微创、炎症反应低且疗效可观等优点逐渐被患者认可^[3-5]。然而泡沫硬化疗法仍存在如肺动脉栓塞和深部静脉血栓（0.6%~3.2%）、视觉障碍（1.5%）、静脉炎（4.7%）等问题^[6-7]。原因是衰变后的泡沫形成液体硬化剂和气体，进入人体其他部位，而泡沫衰变与泡沫稳定性十分相关^[8-10]。学者们针对介入疗法的生物材料属性进行大量相关的研究^[11-13]。泡沫硬化疗法作为介入疗法，泡沫稳定性一直是泡沫硬化疗法重点关注的问题之一^[14-17]。泡沫稳定性是泡沫衰变速度的表征，主要指标有泡沫析水率曲线（析水率与时间的函数）、半衰期（析出 50% 液体所消耗的时间）、析水时间（出现肉眼可见液体的时间）等。

Tessari 法是目前制备泡沫的常用方法之一，将两支注射器通过狭小通道相连后来回推注，由此形成均匀的微泡沫^[18-20]。研究者对制备方式、推注速度、药物、气体种类等进行大量实验，获得

了一些特定的结果^[21-34]。但泡沫在特定药物和气体类型下的稳定性却很难再提高。Tessari 法中狭小通道是形成泡沫的关键，狭小通道具有一定长度和弯曲，对气泡膜的破碎和气液混合具有重要作用，但关于通道的相关研究却鲜有报道。本文通过实验测试，获得通道弯数和长度对泡沫稳定性的影响规律，为临床制备更稳定的泡沫硬化剂提供依据和思路。

1 材料和方法

Tessari 法制备泡沫硬化剂时，利用两个注射器与中间三通阀垂直相连，来回推注形成稳定均匀的泡沫。本实验将中间三通阀形式改进，探讨三通阀的弯数对泡沫稳定性的影响。5 mL 注射器抽取 1 mL 油酸钠注射液（0.05 g/mL，上海信谊金朱药业有限公司），另一支抽取 4 mL 二氧化碳（CO₂）/室内空气，通过图 1 所示分组进行连接制备泡沫。制备好的泡沫静置于水平面上，黑色背板前，使用摄像机（CX900E，SONY 公司，日本）进行全程摄像。

实验分组：设置 3 组不同三通阀组合的微通道，分别为实验组 1、实验组 2（对照组）、实验组 3（见表 1）。实验组 1 通道弯数不同（A、B、C 组弯数分别为 1、2、3）、实验组 2（对照组）通道总长度不同

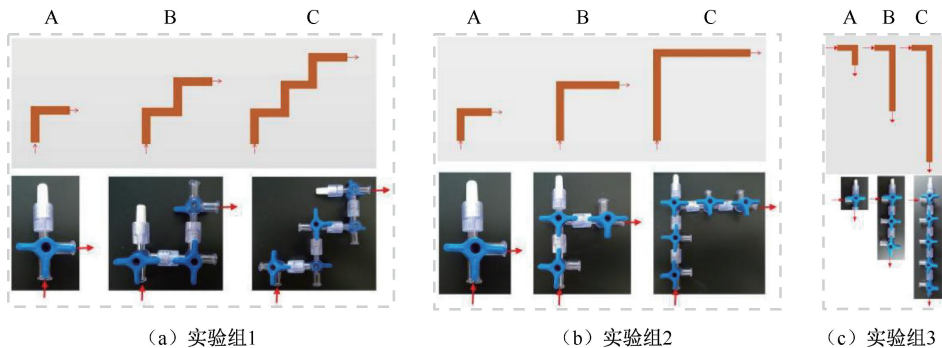


图1 实验分组设计

Fig. 1 Experimental grouping design (a) Experimental group 1, (b) Experimental group 2, (c) Experimental group 3

(A、B、C组总长度分别为2、6、10)、实验组3通道长短比例不同(A、B、C组长短边比值分别为1:1、5:1、9:1)通过实验组1与对照组的对比,可以获得弯数对泡沫稳定性的影响规律;通过实验组3与对照组的对比,可以获得不同通道长短比例对泡沫稳定性的影响规律。组2自身作为实验组2获得总长度对泡沫稳定性影响规律。

表1 实验分组

Tab. 1 Experiment grouping

分组	序号	弯数	总长度	长短边比值
实验组 1	A	1	2	—
	B	2	6	—
	C	3	10	—
实验组 2	A	1	2	1:1
	B	1	6	1:1
	C	1	10	1:1
实验组 3	A	1	2	1:1
	B	1	6	5:1
	C	1	10	9:1

注:总长度指单边三通长度倍数。

数据采集通过回放录像的形式,获得泡沫析水率曲线、半衰期、析水时间等参数,并利用SPSS 25.0进行统计学分析。

2 结果

从实验组2泡沫的析水过程总体曲线可以看出,析水率越大衰变时间越长,衰变速度越来越慢(见图2)。随着析水率的升高,标准误差越来越大。每种析水率下,A组到B组再到C组的衰变时间越来越长。在CO₂制备的泡沫中,析水率20%~100%的B组与A组都具有显著性差异($P < 0.01$);析水

率20%和100%下,C组与A组具有显著性差异($P < 0.01$);析水率50%和60%下,B组与A组具有显著性差异($P < 0.05$);析水率40%和80%下,C组与A组无显著性差异;所有析水率下,B组与C组无显著性差异。而在空气制备的泡沫中,析水率20%和50%的B与A都具有显著性差异($P < 0.05$),其他析水率下B与A无显著性差异;析水率20%、40%和100%下,C组与A组具有显著性差异($P < 0.05$);析水率50%、60%和80%下,C组与A组具有显著性差异($P < 0.01$);所有析水率下,B组与C组无显著性差异。由此可见,CO₂制备的泡沫通道总长度的影响更为显著。通道总长度越长,泡沫析水时间越长,泡沫越稳定。

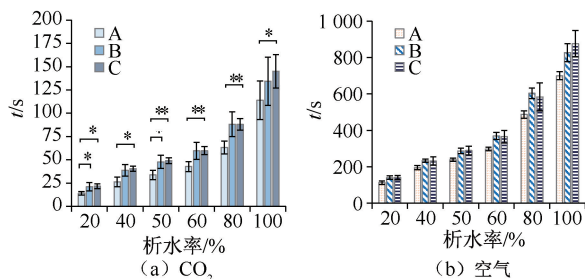
图2 实验组2析水结果(* $P < 0.05$, ** $P < 0.01$)

Fig. 2 Results of water separation for experimental group 2

(a) CO₂, (b) Air

实验组1与对照组对比结果表明,整体析水率曲线呈现逐渐上升趋势,析水过程越来越慢。在B、C组的对比中,CO₂制备的泡沫出现实验组1析水率曲线明显高于对照组,而空气制备的泡沫实验组1与对照组曲线出现重合和交叉,在考虑标准差的情况下差异不明显(见图3)。

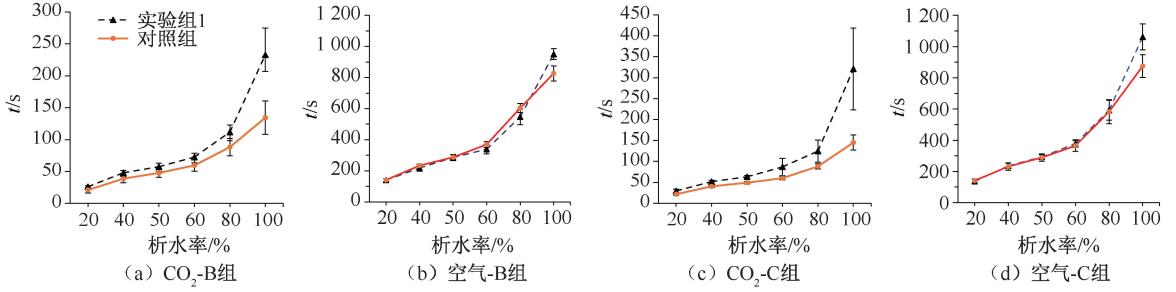


图3 实验组1与对照组对比结果

Fig. 3 Comparison results between experimental group 1 and control group (a) CO₂-B group, (b) Air-B group, (c) CO₂-C group, (d) Air-C group

实验组3和对照组的对比结果表明,析水率曲线都呈现逐渐上升的趋势,说明析水过程越来越慢。CO₂制备的泡沫,在B组和C组的对比中,实验组3的曲线明显高于对照组,而空气制备的泡沫在析水率80%之前都无明显差

异;而析水达到100%时,实验组明显高于对照组(见图4)。由此可见,通道的长短比例对泡沫稳定性的影响在CO₂制备的泡沫中较为明显,但在空气制备的泡沫中也存在析水总时间的影响。

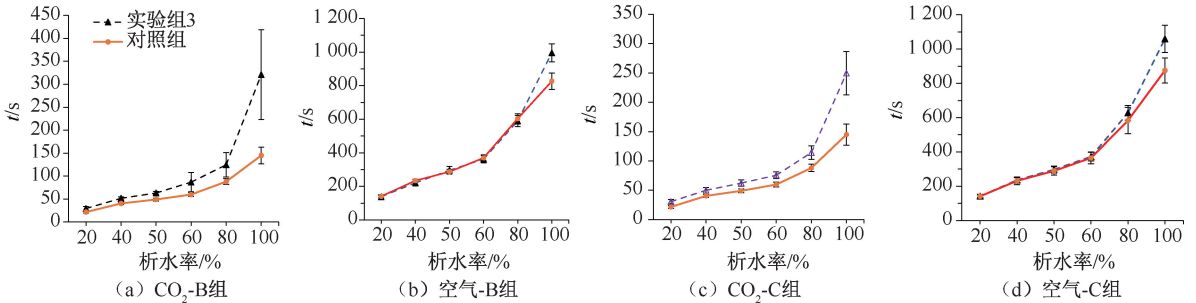


图4 实验组3与对照组对比结果

Fig. 4 Comparison results between experimental group 3 and control group (a) CO₂-B group, (b) Air-B group, (c) CO₂-C group, (d) Air-C group

实验组1和对照组以及实验组3和对照组半衰期的对比结果表明,CO₂制备的泡沫中,实验组1的B组和对照组的B组存在显著性差异($P < 0.05$);实验组1的C组和对照组的C组存在显著性差异($P < 0.01$);实验组3的B组和对照组的B组无显著性差异($P > 0.05$);实验组3的C组和对照组的C组存在显著性差异($P < 0.01$)。但在空气制备的泡沫中,半衰期都无显著性差异($P > 0.05$),且空气泡沫比CO₂泡沫半衰期更大(见图5)。由此可见,通道弯数及长度比例对CO₂制备的泡沫影响更明显,对空气制备的泡沫影响不明显。

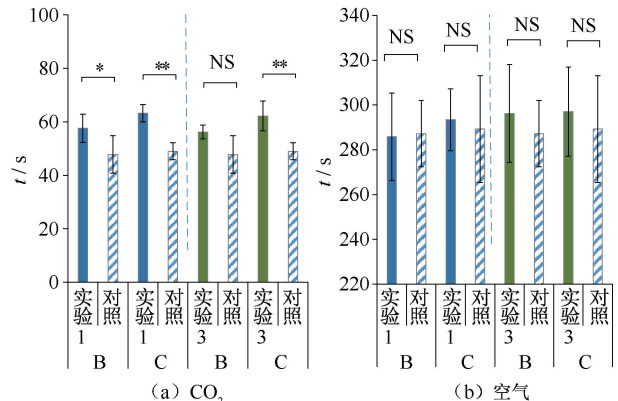


图5 半衰期对比结果

Fig. 5 Half-life comparison results (a) CO₂, (b) Air

注: * $P < 0.05$, ** $P < 0.01$; NS, $P > 0.05$

3 讨论

Tessari 法制备泡沫主要原理是使气液流体来回通过狭窄通道和垂直通道,不断形成涡流和打碎气泡,最终获得均匀的泡沫。因此,泡沫的形成中,狭窄通道的长度以及垂直弯曲通道的个数对泡沫的影响具有重要作用,本文通过设计 3 个实验,获取通道长度及弯数对泡沫稳定性的影响规律,指导临床制备更稳定的泡沫硬化剂。

本文结果表明,实验组 2 通道总长度的增加,泡沫衰变减缓,泡沫稳定性增强,狭窄三通阀的通道总长度在泡沫形成中具有积极的作用(见图 2)。对比实验组 1 和对照组排除通道总长度改变的影响,实验组 1 的 B 组和 C 组的通道弯数增加,泡沫的稳定性增强(见图 3)。管道流动中,直管和弯管产生流场有很大区别,弯数会引起弯数的增加对流体在通道内的流场改变显著,产生更明显的气泡破碎,使得泡沫更均匀,增强稳定性。同时,弯曲的通道会引起压强的分布改变,较高的压力使得气液混合驱动力更大。本文发现,CO₂ 制备的泡沫对于通道弯数的影响更为敏感。CO₂ 和空气的差异可能是因为 CO₂ 的可溶解性。空气泡沫比 CO₂ 泡沫更稳定,溶解的气体改变了溶液的表面张力和气液比例,表面张力会引起泡沫衰变过程中气体扩散和曲面张力引起的排液速度改变,从而改变稳定性,气液比改变了泡沫的干湿程度,影响泡沫排液快慢。本文还发现,通道长短比例的改变对泡沫稳定性具有积极的影响(见图 4)。通道长度的不对称性比通道弯数对泡沫的影响更为显著,在空气泡沫的总衰变时间中具有一定的积极作用。泡沫总长度一致的情况下(实验组 3 和对照组),不同通道长短比例的改变,会引起流体在通道内来回流动的不对称性,有益于气液破碎和混合,从而使得泡沫的混合更为均匀,泡沫稳定性增强。

本研究揭示了通道弯数和通道总长度及长度比例的不同对泡沫稳定性影响的规律,对于制备更稳定的泡沫具有实际意义。同时,对制备泡沫通道的设计和其他类似改进装置的设计具有指导意义。

4 结论

制备泡沫的通道弯数增强了泡沫的稳定性,通道总长度的增加对泡沫稳定性具有积极意义,而通道长短比例对泡沫稳定性的影响较大。本实验仅测试了 3 种弯数、总长度和长短比例,所获的结论具有一定的局限性。但该结论对于临床制备泡沫,以及其他泡沫的稳定性研究具有一定意义,同时可指导相关泡沫制备装置的设计。

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