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加味八珍汤联合 PFNA 术治疗老年股骨转子间骨折患者的临床效果 及对血液流变学指标的影响 *

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摘要 目的:研究加味八珍汤联合股骨近端防旋髓内钉(Proximal Femoral Nail Antirotation, PFNA)对老年股骨转子间骨折患者的临床效果及对术后隐性失血和血液流变学的影响。**方法:**选择 2014 年 3 月至 2017 年 3 月我院收治的 68 例接受 PFNA 治疗的转子间骨折者,将其随机平均分为观察组(34 例,术后口服加味八珍汤颗粒 7 天)、对照组(34 例)。对比两组总失血量、隐性失血量、隐性失血比例、血液流变学指标(血浆粘度及全血粘度低、中、高切)、不良反应等。**结果:**(1) 两组各剔除 2 例,94.12%(64/68)的受试者完成研究。(2) 两组总失血量相当,差异无统计学意义($P>0.05$);与对照组相比,观察组隐性失血量及隐性失血发生率均显著降低($P<0.05$)。(3) 治疗前,两组血浆粘度及低、中、高切全血粘度比较差异无统计学意义($P>0.05$);治疗后,两组血浆粘度及低、中、高切全血粘度均显著低于本组治疗前($P<0.05$),且观察组以上指标均明显低于对照组($P<0.05$)。(4) 观察组发生肌间静脉血栓 1 例,无药物过敏及毒副反应;对照组发生 1 例深静脉血栓、4 例肌间静脉血栓。观察组不良反应率为 3.125%,显著低于对照组(15.625%, $P<0.05$)。**结论:**加味八珍汤既可显著减少老年股骨转子间骨折患者 PFNA 术后隐性失血,又能改善血流动力学、减少并发症。

关键词:股骨转子间骨折;加味八珍汤;隐性失血;血粘度;静脉血栓

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A Study on the Effect of Jiawei Bazhen Decoction Combined with PFNA on the Hemorheology of Elderly Patients with Intertrochanteric Fracture of Femur*

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ABSTRACT Objective: To study the clinical efficacy of Jiawei Bazhen Decoction combined with proximal femoral nail antirotation (PFNA) in the treatment of elderly patients with femoral intertrochanteric fracture and its effect on the postoperative hidden blood loss and hemorheology. **Methods:** From March 2014 to March 2017, 68 cases of intertrochanteric fractures treated by PFNA in our hospital were randomly divided into the observation groups (34 cases, oral Jiawei Bazhen Tang granules for 7 days after operation) and the control group (34 cases). The total blood loss, recessive blood loss, proportion of recessive blood loss, blood rheology indexes (plasma viscosity and whole blood viscosity low, medium and high cut) and incidence of adverse reactions were compared between the two groups. **Results:** (1) Two cases were excluded from each group, and 94.12% (64/68) of the subjects completed the study. (2) No significant difference was found in the total blood loss between two groups ($P>0.05$); the amount of implicit blood loss and the incidence of implicit blood loss in the observation group were significantly lower than those of the control group ($P<0.05$). (3) Before treatment, there was no statistically significant difference in the plasma viscosity and low, medium and high cut whole blood viscosity between the two groups ($P>0.05$); after treatment, the plasma viscosity and low, medium and high cut whole blood viscosity of both groups were significantly lower than those before treatment ($P<0.05$), and the above indicators in the observation group were significantly lower than those in the control group ($P<0.05$). (4) One case of intramuscular venous thrombosis was found in the observation group without drug allergy and toxic and side effects; one case of deep vein thrombosis and 4 cases of intermuscular venous thrombosis were found in the control group. The adverse reaction rate in the observation group was 3.125%, which was significantly lower than that in the control group (15.625%, $P<0.05$). **Conclusion:** Jiawei Bazhen Decoction can not only significantly reduce the postoperative PFNA hidden blood loss in elderly patients with intertrochanteric fractures, but also improve the hemodynamics and safety.

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前言

股骨转子间骨折在髋部、全身骨折中的比例分别为(31%~51%)、2%，其发病率随着道路交通建筑事业的飞速发展和老龄化进程的持续加快在近年来呈上升趋势，股骨近端防旋髓内钉(Proximal Femoral Nail Antirotation, PFNA)作为其主要治疗方式目前虽应用较多，但围术期失血不可避免，平均失血量在700 mL以上，不仅加重心脏负担、增加心脑不良事件风险，而且可导致切口愈合不良、深静脉血栓形成等并发症^[1-4]。进一步研究显示隐性失血占总失血量的90%以上^[5-8]。祖国医学将老年股骨转子间PFNA术后患者的隐形失血归属于“血虚”范畴，同时，气血联系紧密，即“气行则血行”、“气为血之母，血为气之帅”。而加味八珍汤立意为气血双补，在补气的同时，进行补血，在纠正骨科围手术期隐形失血、改善体内血液循环等方面运用广泛^[9,10]，但用于干预老年股骨转子间骨折患者PFNA术后隐性失血尚未见相关报道。基于此，本研究主要探讨了加味八珍汤对老年股骨转子间骨折患者PFNA术后隐性失血的影

响，以期为临床治疗提供更多的参考依据。

1 资料与方法

1.1 选择标准

纳入标准：⁽¹⁾ 经CT等影像学资料确诊的新鲜、闭合、单侧、转子间骨折；⁽²⁾ 年龄≥60岁、对本研究知情并签署同意书。排除标准：⁽¹⁾ 陈旧性、病理性、开放性骨折或合并神经精神类疾病等无法正常研究；⁽²⁾ 多发骨折、围术期输注血制品，或合并消化道出血、血液病、免疫病，长期营养不良，或持续免疫抑制剂、激素服用等可能影响观察指标者。剔除标准：死亡、治疗依从性差、主动退出等未完成研究者。

1.2 一般资料

选取2014年3月至2017年3月就诊于我院的转子间骨折者68例，依据随机平均原则分为观察组(34例)、对照组(34例)。两组的性别、年龄、身体质量指数、受伤至手术时间、Evans分型、侧别、致伤原因等基线资料均衡性良好($P>0.05$)，具有可比性，见表1。

表1 两组基线资料的对比

Table 1 Comparison of baseline data between two groups

Datas	Observation group (34 cases)	Control group (34 cases)	t/ χ^2	P
Gender (male / female)	12/22	13/21	1.697	0.495
Age (year)	78.35±5.08	79.05±5.03	1.053	0.566
Body mass index (kg/m ²)	23.44±3.11	23.21±3.22	1.152	0.412
Time from injury to operation (d)	1.52±0.51	1.59±0.53	1.368	0.384
Evans typing (I / II / III / IV)	8/12/10/4	8/12/11/3	1.447	0.368
Side (left / right)	12/22	13/21	1.024	0.557
Cause of injury (fall / crash)	20/14	19/15	1.475	0.365

1.3 治疗方法

两组均由同一高年资主任医师主刀完成PFNA治疗：麻醉达成后，取仰卧位，垫高患臀，C臂机、骨科牵引床辅助下复位骨折，大转子顶端取5 cm纵切口，打入导针后扩髓，插入适宜PFNA主钉，顺瞄准器旋入螺旋刀及远端锁钉，透视满意后，拧入钉螺帽，术后常规抗感染、抗凝、指导患者功能锻炼。观察组自术后第1天起口服加味八珍汤颗粒(四川新绿色药业科技发展有限公司生产)，药物组成：白术、赤芍、熟地各12克，茯苓、川芎、当归各9克，丹参、桃仁、人参、红花各6克，炙甘草3克。沸水冲至400 mL，分早晚两次饭前口服，规范治疗7天。术后第1、3、7天复查血常规、肝肾功能等指标。

1.4 观察指标

1.4.1 失血指标 参照Gross线性方程^[11]，计算总失血量、隐性失血量、隐性失血比例(隐性失血量/总失血量)。

1.4.2 血液流变学指标 于治疗前(入院当天)、治疗后(术后第7天)抗凝管收集晨起空腹8小时、安静半小时左侧肘静脉血

5 mL/管，混匀后经全自动血液流变学分析仪(型号：MVIS-2035；重庆天海医疗设备有限公司生产)检测血浆黏度及全血黏度低、中、高切。所有操作由我院同两名具有副高级职称的高年资技师、严格按说明书独立完成检测。

1.4.3 不良反应的发生情况 包括药物过敏、毒副反应及静脉血栓等并发症。

1.5 统计学处理

统计学分析经SPSS20.0完成，不良反应等计数资料用百分率(%)表示，两组间比较采用卡方检验；血浆黏度等计量资料用(均数±标准差)表示，组间、组内比较采用独立样本t检验、配对t检验，以 $P<0.05$ 为有统计学差异性的标准。

2 结果

2.1 研究完成情况

观察组1例治疗依从性差，对照组1例突发大面积心肌梗死抢救无效死亡，两组各1例主动退出研究，均剔除，94.12%

(64/68)的受试者完成研究。

2.2 两组术后失血情况的对比

两组总失血量比较差异无统计学意义($P>0.05$)；观察组隐性失血量、隐性失血比例均显著低于对照组($P<0.05$)，见表2。

表2 两组术后失血情况的对比($\bar{x}\pm s$)
Table 2 Comparison of the incidence of blood loss between the two groups after operation($\bar{x}\pm s$)

Groups	Cases	Total blood loss (mL)	Occult blood loss (mL)	Ratio of occult blood loss (%)
Observation group	32	898.39±101.04	592.14±69.01	65.88±10.25
Control group	32	901.73±109.92	820.14±95.01	91.33±6.59
t Between groups	-	1.022	8.954	10.874
P	-	0.169	0.018	0.011

2.3 两组治疗前后血流变学指标的对比

治疗前，两组血浆粘度及低、中、高切全血粘度比较差异无统计学意义($P>0.05$)；治疗后，两组血浆粘度及低、中、高切全血

黏度均显著低于本组治疗前($P<0.05$)，且观察组以上指标均明显低于对照组($P<0.05$)，见表3。

表3 两组血浆粘度对比情况(mPa os)
Table 3 Comparison of plasma viscosity between the two groups(mPa os)

Groups	Cases	plasma viscosity		t In group	P
		Before treatment	After treatment		
Observation group	32	1.9544±0.1255	1.1258±0.3255	7.247	0.029
Control group	32	1.9602±0.1279	1.4047±0.3111	5.242	0.037
t Between groups	-	1.247	6.354	-	-
P	-	0.151	0.032	-	-

3 讨论

隐性失血对老年粗隆间骨折术后康复具有很大危害^[12-15]。而导致隐性失血发生发展的因素可能有^[16-20]：(1)转子间区以松质骨为主，周围肌肉组织丰厚，局部血运充沛，骨折及医源性手术操作出血可大量进入髓腔、肌肉等组织间隙内；(2)骨折暴力、手术等创伤可导致机体局部缺血缺氧，导致氧自由基大量形成，后者与红细胞膜上脂肪酸发生脂质过氧化反应，从而降低细胞膜通透性，麻醉、创伤应激、手术应激可降低红细胞变形能力，增加红细胞破裂风险，诱发溶血反应。另外，未洗涤红细胞的过滤亦可发生溶血；(3)补液、活血化瘀药物等所致的毛细血管床异常开放，可使围术期血液进入组织腔隙，不参与体循环。这均可导致大量隐性失血，诱发心脑不良事件，不利于患者病程恢复。相关研究表明^[21-25]，PFNA术后隐性失血影响因素较多，大致可分为骨折类型、年龄、体重等术前因素，麻醉方式、手术方式等术中因素，抗凝药等术后因素。对此，目前已进行了术前营养改善、术中微创化、尽量缩短手术操作时间、不放置引流管、术后冰敷及氨甲环酸静滴等流程优化改措，但止血效果并不理想，隐形失血这个问题仍在困扰临床因此，寻求有效的止血策略仍重要临床意义。

近年来，中医药辅助治疗改善手术失血的疗效正逐渐得到重视。中医并无隐性失血的确切记载，依据中医理论，可将其归为“血证”范畴。老年人脾胃功能衰退明显，气血生化无源，肝肾逐步亏虚，加之慢性劳损积累，进一步消耗气血。另外，骨折多由跌扑损伤所致，患者经络受损、血液离经而行，而骨折愈合

本质为“瘀去、新生、骨和”的过程。再则中医流传“气为血之帅，血为气之母；无气者血瘀，无血者气衰”之说；《素问》中讲：人之所有，唯血与气也；《难经》曰：气主响之，血主濡之。因此，老年转子间骨折隐性失血为本虚标实证，其治疗当以补气血为主，以化瘀活血为辅。本研究所用加味八珍汤源自《瑞竹堂经验方》，全方由补气为主的四君子汤、补血为主的四物汤及丹参、红花、桃仁等活血类药物构成。该方以熟地、人参为君，人参味甘性温，善补元气，复脉固脱，补脾、益肺、安神、生津功著，气足可固摄血液循经而行，气旺则精血生化有源；熟地补血，有通血脉、生精血、长肌肉、填骨髓之功，且血足可濡养气，避免气随血脱。中焦脾胃为气血生化之源，故而同时应行益气健脾治疗，白术性燥温味苦，可燥湿健脾、益气利水；茯苓归脾经，可利水、行气、化湿。当归活血补血，行中有补，补中有动，有“血中之圣药、血中之气药”之称；白芍味酸苦性甘寒，可养血和营、敛阴止汗、平肝止痛，以上四药共为臣。佐以丹参、红花、桃仁、川芎，祛风活血行气，使补气血的同时而不滞，血随气行。甘草为使调和，共奏补益气血、祛瘀活血之效。李冀等研究后指出^[26,27]，八珍汤内富含多糖、总皂苷、叶酸、维生素、磷脂、氨基酸及微量元素，可抑制超氧阴离子生成，增强超氧化物歧化酶活动，从而延长红细胞寿命，这对提高机体免疫力、改善血液流变性、改善造血有重要意义。药理研究同样表明^[28-33]，人参中的多糖、皂苷等可促进有丝分裂，加速蛋白质、RNA、DNA合成，刺激造血；当归多糖、熟地多糖可提高红细胞c3b受体表达率，加速集落刺激因子生成，促进红细胞生成及血红蛋白合成，抑制机体非特异性免疫反应^[34-38]；白术对红系祖细胞生成有显著促进作用；茯苓

可明显升高胞内2,3二磷酸甘油含量；桃仁中的苦杏仁甙,川芎中的生物碱、挥发油,红花中的红花黄色素,丹参富含的酮类物质,有显著的抗凝、降低红细胞聚集率和血液粘度。

本研究中,两组总失血量接近,且以隐性失血为主,与既往报道一致^[5]。而观察组隐性失血及其占比低于对照组,与吴绍宾等^[39-40]的研究吻合,提示加味八珍汤可显著改善骨科大手术后隐性失血,我们推测这与加味八珍汤气血双补,能加快骨折术后“瘀去、新生、骨和”的过程有关。本研究观察组治疗后血浆粘度及全血粘度低、中、高切及并发症率低于对照组,这与马士超等研究相类似^[41],提示加味八珍汤可能通过改善血流动力学进而减少血栓形成,这均有助于患者病情恢复,这与加味八珍汤既能补血,又能活血化瘀有关。本研究的样本量偏少,且来源医院单一,且随访时间仅有一周,未进行长期跟踪随访,以及未对加味八珍汤中的有效成分进行研究。因此,我们下一步将针对加味八珍汤干预老年股骨转子间PFNA术后患者进行大样本的研究,纳入凝血功能等指标,进行长期随访,并开展药理学试验,研究加味八珍汤中的有效成分。

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