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# 吻合器痔上黏膜环切术联合地奥司明对混合痔患者肛肠动力学及血清炎症因子的影响\*

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**摘要 目的:**探讨吻合器痔上黏膜环切术(PPH)联合地奥司明对混合痔患者肛肠动力学及血清炎症因子的影响。**方法:**选择2018年5月~2021年5月期间我院收治的混合痔患者115例,随机分为2组:对照组(57例)、观察组(58例),对照组给予PPH治疗,观察组给予PPH联合地奥司明治疗,比较两组疗效、症状评分、肛肠动力学指标及血清炎症因子水平,记录随访期间复发情况。**结果:**观察组的临床总有效率较对照组高( $P<0.05$ )。观察组术后3个月的直肠感觉阈、直肠耐受量高于对照组,直肠-肛管压力差低于对照组( $P<0.05$ )。观察组术后7d的血清C反应蛋白(CRP)、肿瘤坏死因子- $\alpha$ (TNF- $\alpha$ )和白介素-6(IL-6)水平均低于对照组( $P<0.05$ )。观察组术后3个月的肛周出血评分、肛缘水肿评分、肛周瘙痒评分均低于对照组( $P<0.05$ )。观察组的复发率较对照组更低( $P<0.05$ )。**结论:**混合痔患者在PPH术后给予地奥司明治疗,可明显改善术后症状和机体肛肠动力学,并降低血清炎症因子水平,同时还可减少复发率,临床疗效值得肯定。

**关键词:**吻合器痔上黏膜环切术;地奥司明;混合痔;肛肠动力学;炎症因子

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## Effects of Procedure for Prolapse and Hemorrhoids Combined with Diosmin on Anorectal Dynamics and Serum Inflammatory Factors in Patients with Mixed Hemorrhoids\*

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**ABSTRACT Objective:** To investigate the effects of procedure for prolapse and hemorrhoids (PPH) combined with Diosmin on anorectal dynamics and serum inflammatory factors in patients with mixed hemorrhoids. **Methods:** 115 patients with mixed hemorrhoids treated in our hospital from May 2018 to May 2021 were selected, patients were randomly divided into two groups: the control group (57 cases) and the observation group (58 cases). The control group was treated with PPH, and the observation group was treated with PPH combined with Diosmin. The curative effect, symptom score, anorectal dynamics indexes and serum inflammatory factor levels of the two groups were compared, and the recurrence during the follow-up period was recorded. **Results:** The total clinical effective rate of the observation group was higher than that of the control group ( $P<0.05$ ). 3 months after operation, the rectal sensory threshold and rectal tolerance of the observation group were higher than those of the control group, and the rectal-anal resting pressure difference was lower than that of the control group ( $P<0.05$ ). 7 days after operation, the levels of C-reactive protein (CRP), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6) of the observation group were lower than those of the control group ( $P<0.05$ ). 3 months after operation, the scores of perianal bleeding, pruritus and edema of the observation group were lower than those of the control group ( $P<0.05$ ). The recurrence rate of the observation group was lower than that of the control group ( $P<0.05$ ). **Conclusion:** Diosmin treatment in patients with mixed hemorrhoids after PPH can significantly improve postoperative symptoms and anorectal dynamics, which can reduce the level of inflammatory factors, but also reduce the recurrence rate, the clinical efficacy is worthy of affirmation.

**Key words:** Procedure for prolapse and hemorrhoids; Diosmin; Mixed hemorrhoids; Anorectal dynamics; Inflammatory factors

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### 前言

混合痔是由内痔和相应部位的外痔融合而成,多以青壮年发病为主,临床主要表现为肛门肿块脱出,并伴有肛门坠胀

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感<sup>[1,2]</sup>。吻合器痔上黏膜环切术(PPH)是一种新型治疗痔术式,目前常用于混合痔的治疗,效果确切<sup>[3,4]</sup>。但部分患者术后仍会出现肛缘水肿、肛周出血及瘙痒等并发症,不利于患者术后恢复,导致患者康复时间延长<sup>[5]</sup>。地奥司明是一种增强静脉张力性药物和血管保护剂,近年来将其用于混合痔的术后治疗中取得了较好的疗效<sup>[6,7]</sup>。但有关其用于混合痔患者术后的具体作用机制尚不十分明确,鉴于此,本研究采用 PPH 联合地奥司明的方案治疗混合痔,以期明确其对患者血清炎症因子水平和肛肠动力学的影响。

## 1 资料与方法

### 1.1 一般资料

纳入标准:(1)混合痔诊断标准参考《痔临床诊治指南》<sup>[8]</sup>,符合手术指征;(2)病情程度为Ⅲ、Ⅳ度混合痔患者;(3)签署研究知情同意书。排除标准:(1)结直肠肿瘤者;(2)合并其他肛门疾病者;(3)合并糖尿病等影响治疗效果的疾病者;(4)妊娠或哺乳期妇女;(5)合并严重心、肝、肾、脑血管疾病或凝血功能障碍者;(6)依从性较差,未及时复诊者。依据上述纳入排除标准选择 2018 年 5 月~2021 年 5 月期间我院收治的混合痔患者 115 例,随机分为 2 组:对照组(57 例)、观察组(58 例)。其中对照组男 36 例,女 21 例;病情程度:Ⅲ度 32 例,Ⅳ度 25 例;平均年龄(38.62±3.47)岁;平均体质指数(23.51±1.34)kg/m<sup>2</sup>。观察组男 34 例,女 24 例;病情程度:Ⅲ度 30 例,Ⅳ度 28 例;平均年龄(39.17±4.26)岁;平均体质指数(23.22±1.19)kg/m<sup>2</sup>。对照组、观察组一般资料组间对比无差异( $P>0.05$ )。本研究方案得到我院伦理委员会审查批准。

### 1.2 治疗方法

所有患者均采用 PPH 术式治疗混合痔,取截石位,术中行肛周神经阻滞麻醉联合静脉辅助麻醉,采用聚维酮碘对患者肛管、直肠以及女性阴道内进行消毒,插入肛窥器,缓慢扩肛至 4 指以上,采用 4 点法(一般取 3、6、9、12 点方向)固定肛管扩张器,小心将肛门镜缝扎器导入,于肛门镜下在齿状线上方 4~5 cm 处黏膜及其下层做荷包缝合,确保缝合线越过内痔上缘,置入吻合器收紧荷包,使用勾线器从吻合器侧孔将可吸收缝线导出,持续牵引,顺时针旋转吻合器退出。吻合完成后在闭

合状态下持续 30 s,检查切除组织是否完整、吻合线位置及肛管内出血情况。若吻合口有出血,于出血部位呈"8"字形进行缝合。如肛缘有残余外痔,则采用血管钳钳夹后切除。特别严重脱垂患者在第一道荷包线下方 1~2 cm 处再行二道荷包缝合,从而完成手术操作。观察组患者在 PPH 治疗基础上联合使用地奥司明片(国药准字 H20058471,南京正大天晴制药有限公司,规格:片剂,每片含地奥司明 0.45 g)治疗,口服,2 片/次,2 次/d,分别于每日午餐和晚餐时服用,连续服用 7 d。

### 1.3 疗效依据<sup>[8]</sup>

以创面愈合,混合痔痔体基本消失为痊愈的标准。创面部分愈合,肉芽生长形态良好,混合痔痔体体积缩小幅度 $\geq 50\%$ 为好转。而混合痔痔体体积缩小幅度 $< 50\%$ ,创面未愈合,甚至出现溃烂则为无效,总有效率=痊愈率+好转率<sup>[8]</sup>。

### 1.4 观察指标

(1)术后随访 3 个月,随访形式为门诊复查,记录两组肛缘水肿评分、复发率、肛周出血评分、疗效、肛周瘙痒评分,其中肛周瘙痒评分、肛周出血评分、肛缘水肿评分均采用 0~3 分的 4 级评分法评估,得分越高,则症状越严重<sup>[9]</sup>。(2)分别于术前、术后 7 d 抽取两组患者的空腹外周静脉血 5 mL,经常规离心处理分离血清待测。血清 C 反应蛋白(CRP)、肿瘤坏死因子- $\alpha$ (TNF- $\alpha$ )以及白介素-6(IL-6)的水平参考上海晶抗生物工程有限公司生产的试剂盒说明书步骤,采用双抗体夹心酶联免疫吸附法检测完成。(3)分别于术前、术后 3 个月检测两组患者的肛肠动力学指标:直肠感觉阈、直肠-肛管压力差、直肠耐受量。检测时患者身体放松,采用涂抹润滑油的安全套内嵌直肠测压气囊插入肛管,在距离肛缘 50 mm 以上测量肛肠动力学指标。

### 1.5 统计学方法

应用 SPSS 25.0 软件处理数据,计量资料以( $\bar{x} \pm s$ )表示,行 t 检验,计数资料以例及率表示,行  $\chi^2$  检验, $P<0.05$  为差异有统计学意义。

## 2 结果

### 2.1 两组临床总有效率比较

观察组的临床总有效率较对照组高( $P<0.05$ ),见表 1。

表 1 两组临床总有效率比较 [例(%)]

Table 1 Comparison of total clinical effective rates between the two groups [n(%)]

Groups	Recovery	Reverse	Invalid	Total effective rate
Control group(n=57)	16(28.07)	27(47.37)	14(24.56)	43(75.44)
Observation group(n=58)	21(36.21)	31(53.45)	6(10.34)	52(89.66)
$\chi^2$				4.044
$P$				0.044

### 2.2 两组肛肠动力学指标比较

手术前,两组患者的直肠耐受量、直肠-肛管压力差、直肠感觉阈比较,组间未见统计学差异( $P>0.05$ ),两组患者术后 3 个月的直肠感觉阈、直肠耐受量升高,直肠-肛管压力差下降( $P<0.05$ ),且观察组术后 3 个月的直肠感觉阈、直肠耐受量高于对照组,直肠-肛管压力差低于对照组( $P<0.05$ ),见表 2。

### 2.3 两组血清炎症因子水平比较

手术前,两组患者的血清 CRP、TNF- $\alpha$ 、IL-6 水平比较,组间未见差异( $P>0.05$ ),两组患者术后 7 d 的血清 IL-6、CRP、TNF- $\alpha$  水平均下降( $P<0.05$ ),且观察组低于对照组( $P<0.05$ ),见表 3。

表 2 两组肛肠动力学指标比较( $\bar{x} \pm s$ )

Table 2 Comparison of anorectal dynamic indexes between the two groups( $\bar{x} \pm s$ )

Groups	Rectal sensory threshold(mL)		Rectal anal pressure difference(mmHg)		Rectal tolerance(mL)	
	Before operation	3 months after operation	Before operation	3 months after operation	Before operation	3 months after operation
Control group (n=57)	5.26± 1.21	8.37± 1.38 <sup>a</sup>	17.62± 2.16	13.21± 3.59 <sup>a</sup>	2.15± 0.32	3.86± 0.43 <sup>a</sup>
Observation group (n=58)	5.29± 1.31	13.18± 2.19 <sup>a</sup>	17.14± 2.35	8.07± 2.61 <sup>a</sup>	2.09± 0.34	5.19± 0.39 <sup>a</sup>
t	0.128	14.063	1.140	8.793	0.974	17.380
P	0.899	0.000	0.257	0.000	0.332	0.000

Note: Compared with the same group before operation, <sup>a</sup>P<0.05.

表 3 两组血清炎症因子水平比较( $\bar{x} \pm s$ )

Table 3 Comparison of serum inflammatory factors between the two groups( $\bar{x} \pm s$ )

Groups	IL-6(pg/mL)		CRP(mg/L)		TNF-α(pg/mL)	
	Before operation	7 days after operation	Before operation	7 days after operation	Before operation	7 days after operation
Control group (n=57)	26.09± 3.94	18.03± 4.16 <sup>a</sup>	32.47± 3.62	24.26± 4.71 <sup>a</sup>	34.16± 4.27	23.58± 4.83 <sup>a</sup>
Observation group (n=58)	25.98± 3.87	12.69± 3.67 <sup>a</sup>	32.18± 4.51	17.95± 3.08 <sup>a</sup>	33.86± 5.76	16.25± 2.36 <sup>a</sup>
t	0.151	7.303	0.380	8.517	0.321	10.367
P	0.880	0.000	0.705	0.000	0.749	0.000

Note: Compared with the same group before operation, <sup>a</sup>P<0.05.

### 2.4 两组症状评分比较

评分均低于对照组患者(P<0.05),见表4。

观察组患者的肛周出血评分、肛周瘙痒评分以及肛缘水肿

表 4 两组症状评分比较( $\bar{x} \pm s$ ,分)

Table 4 Comparison of symptom scores between the two groups( $\bar{x} \pm s$ , score)

Groups	Perianal edema score	Perianal pruritus score	Perianal bleeding score
Control group(n=57)	1.76± 0.23	1.87± 0.25	1.71± 0.23
Observation group(n=58)	1.15± 0.25	1.23± 0.24	1.19± 0.17
t	13.611	14.006	13.804
P	0.000	0.000	0.000

### 2.5 两组复发率比较

截止至术后3个月,对照组复发9例,其复发率为15.79%,而观察组只复发了2例,其复发率为3.45%,观察组的复发率明显低于对照组( $\chi^2=5.062, P=0.024$ )。

## 3 讨论

痔疮约占所有肛肠科疾病的80%,是肛管或直肠末端黏膜下屈曲或扩张而形成的静脉丛充血或瘀血并肿大<sup>[10]</sup>。有研究表明<sup>[11,12]</sup>,混合痔的发病与肛垫下移密切相关,肛垫的主要功能在于肛管闭合及排便节制,肛垫下移则会引发肛门肿块脱出、排便困难、潮湿瘙痒或异物感等症状。混合痔的常规保守治疗效果一般,常促使病情进展进而引起局部感染、脓毒血症、贫血等严重并发症,故多数患者均倾向于手术治疗<sup>[13,14]</sup>。PPH手术是在

"肛垫学说"理论上设计的一种新型治疗术式,其原理是通过环形切除直肠下端2~3cm的黏膜和黏膜下层,然后进行黏膜及黏膜下组织的吻合,使脱出的肛垫向上悬吊,让原本上移的肛垫恢复到正常位置,从而恢复直肠下端正常的解剖结构<sup>[15]</sup>。通常情况下,PPH术后4~5周内即可痊愈,但由于混合痔手术部位特殊,术后切口容易受到污染,术后易发生肛周创面水肿、瘙痒、出血、疼痛等症状而影响康复进程<sup>[16]</sup>。这主要是由于PPH术中会对肛周局部解剖结构产生破坏,导致机体局部炎症反应、并且应激反射性引起肛门括约肌痉挛,血管通透性增加,加重组织水肿、瘙痒、出血<sup>[17,18]</sup>。此外PPH术后造成的广泛裸露区易形成组织纤维化和瘢痕,引起肛门狭窄,造成肛肠动力学异常,影响患者生活质量。因此,PPH术后给予适当的药物治疗有助于改善患者手术治疗效果。

地奥司明为增强静脉张力性药物和血管保护剂,主要活性成分为黄酮类物质,而黄酮类物质具有抗自由基和抗氧化、抑菌、改善血管通透性、调节体内激素水平和提高机体免疫机能等生物学效应<sup>[19,20]</sup>。此外,既往也有报道证实地奥司明可改善直肠微循环<sup>[21,22]</sup>。本次研究结果显示,观察组的临床总有效率较对照组高,肛肠动力学、症状改善效果优于对照组,提示混合痔患者在 PPH 术后给予地奥司明治疗,疗效值得肯定,对患者的康复有益。PPH 术式的优点在于,处理病变混合痔的同时,还可尽可能地保留了黏膜桥、皮桥,这有利于维持患者肛门的精细感觉,改善其肛肠动力学。既往有药理学研究<sup>[23,24]</sup>证实,地奥司明可通过提高体内去甲肾上腺素水平,实现对静脉壁和淋巴管壁的收缩效应,从而促进静脉血液和淋巴液回流,并加快组织液排出,改善局部组织微循环,减轻水肿症状。

局部炎症反应是引起 PPH 术后瘙痒、水肿、出血的主要原因之一,其中 IL-6 可刺激免疫细胞增殖、分化,引起免疫炎症反应;CRP 可激活补体,增强吞噬细胞的吞噬功能;TNF- $\alpha$  可刺激机体释放 IL-6 等促炎介质,引起或加重炎症反应,损伤血管内皮细胞<sup>[25,26]</sup>。本研究中混合痔患者在 PPH 术后给予地奥司明治疗,其炎症反应得到明显控制。这主要与地奥司明具有抑制白细胞和内皮细胞的迁移以及黏附、促进炎性渗出物吸收,从而减轻炎性损伤程度,改善微循环的作用有关<sup>[27,28]</sup>。此外,本研究经过随访发现,观察组的复发率较对照组更低,可能是因为地奥司明可促进患者微循环改善,利于患者术后恢复,降低患者致病风险<sup>[29,30]</sup>。本研究的局限性在于缺乏对肛肠动力指标的动态观察,患者病例数过少,且随访时间较短,后续研究中将通过改进研究设备、扩大样本量、延长随访时间等措施减少数据的误差。

综上所述,PPH 术后联合地奥司明治疗混合痔患者疗效确切,可促进机体肛肠动力学改善,明显改善术后症状,降低炎症因子水平,同时还可减少复发率。

#### 参考文献(References)

[1] Idrees JJ, Clapp M, Brady JT, et al. Evaluating the Accuracy of Hemorrhoids: Comparison Among Specialties and Symptoms[J]. *Dis Colon Rectum*, 2019, 62(7): 867-871

[2] Gallo G, J Martellucci, Sturiale A, et al. Consensus statement of the Italian society of colorectal surgery (SICCR): management and treatment of hemorrhoidal disease [J]. *Techniques in Coloproctology*, 2020, 24(2): 365-372

[3] Wang T H, Kiu K T, Yen M H, et al. Comparison of the short-term outcomes of using DST and PPH staplers in the treatment of grade III and IV hemorrhoids[J]. *Scientific Reports*, 2020, 10(1): 384-389

[4] Li, Xu, Honglei. Stapled Hemorrhoidectomy Versus Transanal Hemorrhoidal Dearterialization in the Treatment of Hemorrhoids: An Updated Meta-Analysis [J]. *Surgical laparoscopy, endoscopy & percutaneous techniques*, 2019, 37(12): 132-137

[5] Trenti L, Biondo S, Kreisler Moreno E, et al. Short-term Outcomes of Transanal Hemorrhoidal Dearterialization With Mucopexy Versus Vessel-Sealing Device Hemorrhoidectomy for Grade III to IV Hemorrhoids: A Prospective Randomized Multicenter Trial [J]. *Dis Colon Rectum*, 2019, 62(8): 988-996

[6] 张超杰, 张卫平. 地奥司明联合高渗硫酸镁溶液坐浴治疗痔疮急性

发作的疗效分析[J]. *实用临床医药杂志*, 2016, 20(11): 170-171

[7] 范勇. 地奥司明联合麝香痔疮膏治疗肛肠病 112 例[J]. *中国中西医结合外科杂志*, 2016, 22(2): 138-140

[8] 中华医学会外科学分会结直肠肛门外科学组, 中华中医药学会肛肠病专业委员会, 中国中西医结合学会结直肠肛门病专业委员会. 痔临床诊治指南 (2006 版)[J]. *中华胃肠外科杂志*, 2006, 9(5): 461-463

[9] 宋小平, 陈显韬, 闫晓春. 改良外剥内扎术治疗环状混合痔的临床疗效观察[J]. *中国现代医学杂志*, 2020, 30(8): 105-109

[10] Aibuedefe B, Kling S M, Philp M M, et al. An update on surgical treatment of hemorrhoidal disease: a systematic review and meta-analysis [J]. *International Journal of Colorectal Disease*, 2021, 29(12): 1-9

[11] Zhang AM, Chen M, Tang TC, et al. Somatosensory stimulation treatments for postoperative analgesia of mixed hemorrhoids: Protocol for a systematic review and network meta-analysis [J]. *Medicine (Baltimore)*, 2019, 98(6): e14441

[12] Wu J, Yu K, Lv C, et al. Segmental resection combined with anoplasty for the treatment of circumferential mixed hemorrhoids[J]. *Braz J Med Biol Res*, 2019, 52(5): e8102

[13] 常贵建, 卓信斌, 夏悦明, 等. 改良 PPH 术治疗 IV 度混合痔的临床研究[J]. *福建医科大学学报*, 2018, 52(1): 60-62

[14] Yu JH, Huang XW, Wu ZJ, et al. Clinical study of use of large C suture in procedure for prolapse and hemorrhoids for treatment of mixed hemorrhoids [J]. *J Int Med Res*, 2021, 49 (3): 300060521997325

[15] 詹敏, 李适, 严建, 等. 两种微创术式治疗老年混合痔的临床疗效比较[J]. *现代生物医学进展*, 2017, 17(12): 2256-2259

[16] Shen K, Wang C, Gao ZD, et al. Procedure for prolapse and hemorrhoids versus stapled transanal rectal resection in the treatment of grade IV hemorrhoids [J]. *Zhonghua Wei Chang Wai Ke Za Zhi*, 2019, 22(12): 1165-1169

[17] 李帅军, 李梅, 许崇斯, 等. 老年混合痔患者自动痔疮套扎术、吻合器痔上黏膜环切术和改良外剥内扎术的疗效对比[J]. *中国老年学杂志*, 2018, 38(2): 403-405

[18] Chen YY, Cheng YF, Wang QP, et al. Modified procedure for prolapse and hemorrhoids: Lower recurrence, higher satisfaction [J]. *World J Clin Cases*, 2021, 9(1): 36-46

[19] Sheikh P, Lohsiriwat V, Shelygin Y. Micronized Purified Flavonoid Fraction in Hemorrhoid Disease: A Systematic Review and Meta-Analysis[J]. *Advances in Therapy*, 2020, 37(7): 309-316

[20] Chiaretti M, Fegatelli D A, Pappalardo G, et al. Comparison of Centella with Flavonoids for Treatment of Symptoms in Hemorrhoidal Disease and After Surgical Intervention: A Randomized Clinical Trial [J]. *Scientific Reports*, 2020, 10 (1): 8009-8012

[21] Feldo M, Wójciak-Kosior M, Sowa I, et al. Effect of Diosmin Administration in Patients with Chronic Venous Disorders on Selected Factors Affecting Angiogenesis[J]. *Molecules*, 2019, 24(18): 3316

[22] Zheng Y, Zhang R, Shi W, et al. Metabolism and pharmacological activities of the natural health-benefiting compound diosmin[J]. *Food Funct*, 2020, 11(10): 8472-8492

- [16] Hu D. Chitosan-Based Biomimetically Mineralized Composite Materials in Human Hard Tissue Repair [J]. *Biomedicines*, 2020, 25(20): 223-229
- [17] Innocentini L, Santos T T, Reis M B L, et al. Juvenile Spongiotic Gingival Hyperplasia: Clinicopathological Features of Eight Cases and a Literature Review[J]. *J Int Med Res*, 2020, 18(1): 953-958
- [18] Needleman I, Worthington H V, Giedrys-Leeper E, et al. WITHDRAWN: Guided tissue regeneration for periodontal infra-bony defects [J]. *Cochrane Database Syst Rev*, 2019, 5(5): 1724-1729
- [19] Murata T, Maseki T, Nara Y. Effect of immediate dentin sealing applications on bonding of CAD/CAM ceramic onlay restoration[J]. *Dent Mater J*, 2018, 37(6): 928-939
- [20] Andrade GS, Pinto ABA, Tribst JPM, et al. Does overlay preparation design affect polymerization shrinkage stress distribution? A 3D FEA study[J]. *Comput Methods Biomech Biomed Engin*, 2021, 7(1): 1-10
- [21] Kumar S. Evidence-Based Update on Diagnosis and Management of Gingivitis and Periodontitis [J]. *Dent Clin North Am*, 2019, 63(1): 69-81
- [22] Abduo J, Sambrook RJ. Longevity of ceramic onlays: A systematic review[J]. *J Esthet Restor Dent*, 2018, 30(3): 193-215
- [23] Pulyodan M K, Paramel Mohan S, Valsan D, et al. Regenerative Endodontics: A Paradigm Shift in Clinical Endodontics [J]. *J Pharm Bioallied Sci*, 2020, 12(Suppl 1): 20-26
- [24] Spencer P, Ye Q, Song L, et al. Threats to adhesive/dentin interfacial integrity and next generation bio-enabled multifunctional adhesives [J]. *Immunol Rev*, 2019, 107(8): 2673-2683
- [25] Tadakamadla S K, Connelly S T, Sforza C, et al. Middle distal canal of mandibular first molar: A case report and literature review[J]. *Ther Adv Drug Saf*, 2019, 22(2): 285-288
- [26] Cantner F, Cacaci C, Mücke T, et al. Clinical performance of tooth- or implant-supported veneered zirconia single crowns: 42-month results [J]. *Clin Oral Investig*, 2019, 23(12): 4301-4309
- [27] De Angelis F, D'Arcangelo C, Malásková N, et al. Wear Properties of Different Additive Restorative Materials Used for Onlay/Overlay Posterior Restorations[J]. *Oper Dent*, 2020, 45(3): E156-E166
- [28] Yu N. Personalized scaffolding technologies for alveolar bone regenerative medicine[J]. *J Funct Biomater*, 2019, 22(Suppl 1): 69-75
- [29] Ren Q, Li Z, Zhang L, et al. Strategies for Managing the Risk of Mucogingival Changes During Impacted Maxillary Canine Treatment [J]. *Molecules*, 2020, 33(2): 123-132
- [30] Um I W, Ku J K, Kim Y K, et al. Histological Review of Demineralized Dentin Matrix as a Carrier of rhBMP-2 [J]. *Turk J Orthod*, 2020, 26(3): 284-293
- [31] Serra-Pastor B, Loi I, Fons-Font A, et al. Periodontal and prosthetic outcomes on teeth prepared with biologically oriented preparation technique: a 4-year follow-up prospective clinical study [J]. *J Prosthodont Res*, 2019, 63(4): 415-420
- [32] Sharka R, Abed H, Hector M. Oral health-related quality of life and satisfaction of edentulous patients using conventional complete dentures and implant-retained overdentures: An umbrella systematic review[J]. *Gerodontology*, 2019, 36(3): 195-204
- [33] Aloy-Prósper A, Peñarrocha-Oltra D, Peñarrocha-Diago M, et al. Peri-implant Tissues and Patient Satisfaction After Treatment of Vertically Augmented Atrophic Posterior Mandibles with Intraoral Onlay Block Bone Grafts: A Retrospective 3-Year Case Series Follow-up Study [J]. *Int J Oral Maxillofac Implants*, 2018, 33(1): 137-144
- [34] Yadav N, Kumar A. Palatoradicular groove: The hidden predator and etiological factor - Advanced proposed classification and literature review[J]. *Indian J Dent Res*, 2020, 31(4): 656-661
- [35] Silva L M, Brenchley L, Moutsopoulos N M. Primary immunodeficiencies reveal the essential role of tissue neutrophils in periodontitis[J]. *Orthod Craniofac Res*, 2019, 287(1): 226-235

(上接第 1699 页)

- [23] 邓开智, 冷明敏, 唐建. 马应龙麝香痔疮膏联合地奥司明片对混合痔术后创面水肿的防治效果[J]. *世界中医药*, 2019, 14(4): 946-949
- [24] Hnátek L. Therapeutic potential of micronized purified flavonoid fraction (MPFF) of diosmin and hesperidin in treatment chronic venous disorder[J]. *Vnitr Lek*, 2015, 61(9): 807-814
- [25] 张红涛. 痔疮自动套扎术联合地奥司明对混合性痔疮的治疗效果及对炎症因子水平的影响 [J]. *中华保健医学杂志*, 2018, 20(6): 510-512
- [26] 刘史佳, 申龙树, 戴国梁, 等. IL-17、IL-6、TNF- $\alpha$  细胞因子在痔疮患者中的表达[J]. *药学与临床研究*, 2016, 24(3): 201-204
- [27] 张涛. 微创痔疮手术联合地奥司明片治疗痔疮的效果观察 [J]. *山西医药杂志*, 2019, 48(9): 1085-1088
- [28] Bashankaev BN, Wexner SD, Arkharov AV. Common sense of diosmin administration in combined treatment of hemorrhoids [J]. *Khirurgiia (Mosk)*, 2018, (8. Vyp. 2): 83-89
- [29] 蓝菲, 赵刚. 地奥司明联合麝香痔疮膏治疗痔疮疗效及对患者生活质量影响[J]. *辽宁中医药大学学报*, 2016, 18(4): 225-227
- [30] 应江伟, 朱锦德. 地奥司明联合麝香痔疮膏治疗痔疮疗效及对患者疼痛和生活质量影响 [J]. *药物流行病学杂志*, 2014, 23(6): 360-362