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温中消疡汤对非甾体抗炎药相关性胃溃疡的疗效研究 *

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摘要 目的：考察温中消疡汤对非甾体类抗炎药(Non-steroidal anti-inflammatory drugs，NSAIDs)相关性胃溃疡的临床疗效。**方法：**以80 例 2017 年 2 月 -2020 年 1 月就诊于我院 NSAIDs 相关性胃溃疡患者为研究对象，采用随机数字表法分为研究组和对照组，每组 40 例。对照组患者进行口服雷贝拉唑治疗，研究组在对照组的基础上服用温中消疡汤。对中医证候疗效指标、中医证候积分和胃镜下疗效对治疗效果进行评价。**结果：**对两组患者中医证候疗效进行比较，研究组的总有效率为 90.00 %，显著高于对照组的 77.50 %(P<0.05)。对治疗前后两组患者的中医证候（胃脘疼痛、腹胀、纳呆食少、反酸、嗳气、倦怠乏力、大便稀溏）积分进行比较，显示治疗前两组各证候积分及总积分无明显差异(P>0.05)；经过治疗，两组患者各项证候积分及总积分均显著降低(P<0.05)；与对照组相比，研究组胃脘疼痛、腹胀、纳呆食少、反酸及总积分均显著减低(P<0.05)。对两组患者胃镜下黏膜改善情况进行比较，研究组的总有效率为 97.50 %，显著高于对照组的 87.50 %(P<0.05)。**结论：**温中消疡汤治疗 NSAIDs 相关性胃溃疡，能显著提高对 NSAIDs 相关性胃溃疡的疗效，能更好的改善胃脘疼痛、腹胀、纳呆食少等症状，能明显促进胃黏膜的恢复。

关键词：温中消疡汤；NSAIDs 相关性胃溃疡；疗效
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Study on Therapeutic Effect of Wenzhong Xiaoyang Decoction on Non-steroidal Anti-inflammatory Drugs Related Gastric Ulcer*

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ABSTACT Objective: To investigate the clinical effect of Wenzhong Xiaoyang Decoction on non-steroidal anti-inflammatory drug-related gastric ulcer. **Methods:** A total of 80 patients with NSAIDs-related gastric ulcer who were admitted to our hospital from February 2017 to January 2020 were selected as the research object. They were divided into a study group and a control group by random number table method, with 40 cases in each group. The patients in the control group were treated with rabeprazole by mouth, and the study group took Wenzhong Xiaoyang Decoction based on the control group. The curative effect index of TCM syndromes, the score of TCM syndromes and the efficacy under gastroscope were evaluated. **Results:** Comparing the efficacy of TCM syndromes of the two groups of patients, the total effective rate of the study group was 90.00 %, which was significantly higher than that of the control group (77.50 %). Compare the points of TCM syndromes (stomach pain, abdominal distension, lack of appetite, less acid, acid reflux, belching, fatigue, fatigue, loose stools) of the two groups of patients before and after treatment, there was no significant difference in the points and total points of the two groups before treatment (P>0.05). After treatment, the syndrome points and total points of the two groups of patients were significantly reduced (P<0.05). Compared with the control group, the stomach pain, abdominal distension, less appetite, acid reflux and total points of the study group were significantly reduced (P<0.05). Comparing the improvement of the mucosa of the two groups of patients under gastroscopy, the total effective rate of the study group was 97.50 %, which was significantly higher than that of the control group (87.50 %, P<0.05). **Conclusion:** Wenneng can significantly improve the curative effect on NSAIDs-related gastric ulcer, can better improve the symptoms such as epigastric pain, abdominal distension, and lack of food, and can obviously promote the recovery of gastric mucosa.

Key words: Wenzhong Xiaoyang Decoction; NSAIDs-related gastric ulcer; Curative effect
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前言

非甾体类抗炎药 (Non-steroidal anti-inflammatory drugs, NSAIDs)相关性胃溃疡指的是因长期服用 NSAIDs 引起的由急慢性胃肠黏膜损伤所导致的胃溃疡及并发出血、穿孔等[1,2]。NSAIDs 具有抗炎、退热、抗血小板凝聚、止痛等作用,用于发热、疼痛、类风湿性关节炎、脑血管疾病预防治疗等[3-5],常见的 NSAIDs 有阿司匹林、对乙酰氨基酚、吲哚美辛、双氯芬酸、布洛芬等,在内外妇儿等领域均广泛使用[6-10],随之引起的不良反应可涉及胃肠道、肝脏、肾脏、皮肤以及血液等,其中对胃肠道黏膜损害的最为常见,可见黏膜充血水肿、糜烂、溃疡、出血、穿孔等,对患者的健康造成极大的影响以及经济负担[11,12]。

根据 NSAIDs 相关性胃溃疡的临床表现,中医可将其归于"胃脘痛"、"痞满",其病位在胃,与肝、脾和肾有关。其病因为脾胃虚寒、胃失和降。治疗当以温中散寒、补益气血为主。温中消疡汤由经方小建中汤合良附丸加减而成,以黄芪、西党参、桂枝、香附、白芍、高良姜、蒲公英等药物组成,小建中汤为经典温里方,用于治疗腹中拘急疼痛、神疲无力、畏寒肢冷、心悸不宁、面色无华等,良附丸由高良姜和香附组成,可疏肝理气、温胃祛寒,用以治疗肝郁气滞、寒凝中焦、脘腹疼痛、胸胁胀痛等症。

本研究以 NSAIDs 相关性胃溃疡患者为研究对象,考察温中消疡汤对非甾体抗炎药相关性胃溃疡的临床疗效,具体如下。

1 资料与方法

1.1 临床资料

以 80 例 2017 年 2 月 -2020 年 1 月就诊于我院的 NSAIDs 相关性胃溃疡患者为研究对象,采用随机数字表法分为研究组和对照组,每组 40 例。一般资料见表 1 所示,两组患者基本信息如性别、年龄、病程等经分析无统计学意义($P>0.05$),具有可比性。患者及家属均充分了解研究内容并签署知情同意书,本研究已获得医院伦理委员会的准许。

表 1 基本资料比较

Table 1 Comparison of basic data

Groups	Age(years)	Gender		Course of disease (years)	Endoscopic staging	
		Male	Female		A1	A2
Control group (n=40)	55.31±7.82	21	19	6.41±2.46	23	17
Research group (n=40)	56.11±6.68	23	17	6.19±3.17	19	21

1.2 诊断标准

1.2.1 **西医诊断标准** ① 有明确的服用 NSAIDs 史;② 长期的反复发作的周期性、节律性慢性上腹部疼痛,上腹部有局限性深压痛,多出现于餐后 0.5~2 h,1~2 h 后可自行缓解;③ 内窥镜检查可见活动期溃疡[13]。

1.2.2 **中医诊断标准** 参照《消化性溃疡中医诊疗共识意见》[14],主症为:胃脘部隐痛,喜暖喜按,得食则痛减;次症为:四肢倦怠乏力,食少纳呆,畏寒肢冷,口淡,便溏,舌淡有齿痕,苔薄白,脉虚弱或迟缓。

1.3 纳入与排除标准

纳入标准:① 符合中西医诊断标准,为胃溃疡活动期;② 年龄为 18~70 岁之间;③ 2 周内未服用相关治疗药物。排除标准:① 不符合中西医诊断标准者;② 患有胃癌或其他恶性肿瘤患者;③ 合并消化道严重疾病或其他系统严重疾病者;④ 孕妇或哺乳期妇女。

1.4 治疗方法

对照组患者进行口服雷贝拉唑治疗(济川药业股份有限公司,10 mg/ 粒),每次 10 mg,一日两次,连续服用 6 w。

研究组在对照组的基础上服用温中消疡汤(炙黄芪 18 g、西党参 18 g、蒲公英 25 g、桂枝 12 g、白芍 12 g、高良姜 10 g、香附 6 g、炙甘草 5 g、生姜 3 片、大枣 3 枚,每剂以 500 mL 水煎煮,早、晚饭前分两次温服。

治疗期间所有患者均不能继续服用 NSAIDs 和其他胃黏膜保护药物,忌生冷辛辣、禁烟酒、不饮浓茶咖啡、保持心情舒畅。

1.5 观察指标

1.5.1 **中医证候疗效判断标准** 基本痊愈:证候基本消失或完全消失,疗效指数≥ 95 %;显效:证候有明显的改善,95 %>疗效指数≥ 70 %;有效:证候有所改善,70 %>疗效指数≥ 30 %[15];无效:证候未出现明显变化,疗效指数<30 %。总有效率 =(痊愈 + 显效 + 有效)/ 总例数×100 %,疗效指数 =(治疗前中医证候积分 - 治疗后中医证候积分)/ 治疗前中医证候积分×100 %。

1.5.2 **中医证候积分** 分别于治疗前后对患者中医证候进行积分,具体为:主要症状积分:对胃脘疼痛、腹胀、嗳气记分,无症状记 0 分,轻症记 2 分、中症记 4 分、重症记 6 分;次要症状积分:对嘈杂泛酸、纳呆少食,无症状记 0 分,轻症记 1 分、中症记 2 分、重症记 3 分。

1.5.3 **胃镜下疗效判断标准** 分别于治疗前后都患者进行胃镜检查,观察其镜下表现,取胃窦和溃疡处组织,用 10 %甲醛固定,石蜡包埋送病理科检验。溃疡疤痕愈合或无痕迹愈合为痊愈;溃疡至愈合期(H2),或溃疡减轻 2 个级别为显效;溃疡至愈合期(H1),或溃疡减轻 1 个级别为有效;镜下无好转者为无效[16]。

1.6 数据处理

以 SPSS 19.0 对数据进行分析,计量资料以 $\bar{x}\pm s$ 表示,使用 t 检验,计数资料采用率(%)表示,计量资料使用 x^2 检验,$P<0.05$ 为具有统计学意义。

2 结果

2.1 中医证候疗效

本研究两组患者中医证候疗效进行比较，研究组的总有效率为 90.00 %，显著高于对照组的 77.50 %($P<0.05$)，即加用温中消疡汤能显著提高对 NSAIDs 相关性胃溃疡的疗效，见表 2。

表 2 中医证候疗效（例，%）

Table 2 Curative effect of TCM syndromes (n,%)

Groups	Healed	Significant effective	Effective	Invalid	Total effective
Research group (n=40)	6(2.50)	11(17.50)	19(47.50)	4(10.00)	36(90.00)
Control group (n=40)	1(0.06)	7(0.44)	23(57.50)	9(22.50)	31(77.50)*

Note: Compared with the control group, * $P<0.05$.

2.2 中医证候积分比较

对治疗前后两组患者的中医证候（胃脘疼痛、腹胀、纳呆食少、反酸、嗳气、倦怠乏力、大便稀溏）积分进行比较，见表 3。治疗前，两组各证候积分及总积分无明显差异（$P>0.05$）；经过治疗，两组患者各项证候积分及总积分均显著的降低($P<0.05$)；与对照组相比，研究组胃脘疼痛、腹胀、纳呆食少、反酸及总积分均显著减低($P<0.05$)。即加用温中消疡汤能更好的改善胃脘疼痛、腹胀、纳呆食少等症状。

表 3 中医证候积分比较

Table 3 Comparison of TCM syndrome points

Groups	Control group (n=40)		Research group (n=40)	
	Before treatment	After treatment	Before treatment	After treatment
Stomachache pain	3.53±0.75	1.23±1.18 *	3.48±0.92	0.70±0.51 *#
Bloating	2.98±0.67	0.41±0.27 *	2.79±0.7	0.19±0.06 *#
Lack of appetite	1.37±0.85	0.74±0.53 *	1.42±0.79	0.37±0.13 *#
Acid reflux	1.33±0.72	0.14±0.06 *	1.31±0.61	0.08±0.04 *#
Belching	0.41±0.32	0.04±0.11 *	0.39±0.16	0.03±0.07 *
Tiredness and fatigue	0.72±0.36	0.33±0.21 *	0.75±0.33	0.23±0.13 *
Loose stools	0.31±0.12	0.00±0.00 *	0.29±0.07	0.05±0.12 *
Total points	10.33±2.67	3.79±1.61 *	10.65±1.95	2.03±0.95 *#

Note: Compared with before treatment, *$P<0.05$; Compared with the control group, #$P<0.05$.

2.3 胃镜下疗效比较

对两组患者胃镜下黏膜改善情况进行比较，见表 4，研究组的总有效率为 97.50 %，显著高于对照组的 87.50 %($P<0.05$)，即加用温中消疡汤能明显促进胃黏膜的恢复。

表 4 胃镜下疗效比较（例，%）

Table 4 Comparison of curative effect under gastroscope[n (%)]

Groups	Healed	Significant effective	Effective	Invalid	Total effective
Research group (n=40)	3(5.00)	15(25.00)	21(52.50)	1(2.50)	39(97.50)*
Control group (n=40)	2(0.13)	10(0.63)	23(57.50)	5(12.50)	35(87.50)

Note: Compared with the control group, *$P<0.05$.

3 讨论

NSAIDs 相关性胃溃疡主要是由长期服用 NSAIDs 后引起的胃黏膜的损伤。随着心脑血管疾病发病率的逐年上升，NSAIDs 的使用也愈加普遍，NSAIDs 相关性胃病发病率也随之增加[17,18]。多表现为消化不良、腹部胀痛、黏膜溃疡出血以及穿孔等。西医主要采用质子泵抑制剂、黏膜保护剂等治疗[19-21]。

关于 NSAIDs 相关性胃溃疡，根据其临床表现，中医可将其归于 " 胃脘痛 "、" 痞满 "，其病因为脾胃虚寒、胃失和降。脾胃虚寒常由中焦气血运行不畅，寒邪凝结于内，阻遏气机运行，不通则痛，脾胃运化不力，则经络、五脏六腑气血不足，患者常有畏寒肢冷、神疲乏力的症状，治疗应以温中散寒、健脾补肾、补益气血为主。

温中消疡汤是在小建中汤合良附丸的基础上加减变化而成，小建中汤药味组成为桂枝、甘草、大枣、芍药、生姜和饴糖组成，治疗腹部拘急疼痛、四肢酸楚寒冷、神疲乏力等，现代研究表明，小建中汤可以提高胃泌素含量，促进胃黏膜细胞的增殖，进一步发挥对已损伤黏膜的修复作用[22,23]。良附丸由高良姜和香附组成，可疏肝理气，温胃散寒，用于治疗肝郁气滞，寒凝中焦，挥发油是高良姜和香附的主要成分，具有很好的抑菌、加快疮疡面的愈合及止痛的作用[24]。

温中消疡汤在小建中汤合良附丸的基础上加用黄芪、党参和蒲公英，方中黄芪补脾益肺、补气升阳，党参补气健脾，蒲公英可清热解毒、消肿散结，桂枝可助阳化气、散寒通脉，高良姜

祛风散寒、温胃止痛，香附疏肝解郁、理气调中，白芍能养阴柔肝、缓急止痛，甘草调和诸药，诸药相合，共奏温中养胃、解毒消痈、理气止痛之功效。黄芪可加快胃溃疡患者疮疡面的愈合，黄芪性温，尤其适用于治疗虚寒性胃溃疡，黄芪可减少胃酸分泌量，降低胃蛋白酶活力，从而减少对胃粘膜刺激，同时促进胃黏膜细胞再生，发挥胃黏膜保护作用[25]。桂枝常治疗脾胃虚寒，其主要成分为桂皮醛，能缓解消化道的疼痛，有一定抗炎功效[26]。党参作用缓和不峻猛，尤其适用于虚寒性的胃溃疡，其主要成分为党参炔苷，可抑制胃酸分泌、保护胃黏膜[27]。香附常用于治疗腹部胀气胀痛等，研究表明，香附能够延缓胃排空运动，从而减少溃疡的发生[28]。高良姜在治疗溃疡、血栓、炎症等方面有较好的药理活性，其抗溃疡的机制可能与清除自由基有关，高良姜总黄酮可以通过抑制胃蛋白酶活性来发挥胃黏膜保护作用[29,30]。

本研究采用温中消疡汤治疗 NSAIDs 相关性胃溃疡，对两组患者中医证候疗效进行比较，结果显示研究组的总有效率为 90.00 %，显著高于对照组的 77.50 %，与赵明铭[31]的研究类似，采用温中消疡汤联合西药治疗胃溃疡脾胃虚寒型的临床疗效，发现温中消疡汤联合西药治疗的总有效率高于单纯西药组，表明加用温中消疡汤能显著提高对 NSAIDs 相关性胃溃疡的疗效。分析其原因为温中消疡汤作用于患者，可以和气缓急、温中补气，在起到杀菌消痛的作用时，也能对胃部有所保护，从而提高患者的疗效。本研究治疗前两组的中医证候（胃脘疼痛、腹胀、纳呆食少、反酸、嗳气、倦怠乏力、大便稀溏）积分及总积分无明显差异；经过治疗，两组各项证候积分及总积分均显著的降低，且研究组胃脘疼痛、腹胀、纳呆食少、反酸及总积分均显著减低。与玉素甫·司马义[32]学者的研究类似，该学者采用温中消疡汤联合雷贝拉唑治疗十二指肠溃疡，发现治疗后联合组的中医证候定积分显著低于对照组，表明加用温中消疡汤能更好的改善胃脘疼痛、腹胀、纳呆食少等症状。分析其原因为温中消疡汤治疗 NSAIDs 相关性胃溃疡患者，可以温中养胃、解毒消痈、理气止痛，从而调理胃功能，减少胃脘疼痛、腹胀、纳呆食少、反酸。本研究也对两组患者胃镜下黏膜改善情况进行比较，研究组的总有效率为 97.50 %，显著高于对照组的 87.50 %，曹生海[33]的研究与本研究结果类似，采用温中消疡汤与三联疗法联合治疗对胃溃疡患者，联合组患者黏膜微血管规则改善情况为 87.80 %，显著高于对照组患者的 58.53 %，表明温中消疡汤能明显促进胃黏膜的恢复。主要是通过温中养胃，减少患者胃痛、腹胀、纳呆食少、反酸等症状，从而减少对胃黏膜的刺激，促进胃黏膜功能的恢复。本研究也有一定的不足之处，样本量少，同时也没有进行远期的随访，观察不良反应，因此后续研究还需要进一步深入探究温中消疡汤治疗 NSAIDs 相关性胃溃疡治疗的远期疗效和作用机制，为该病的治疗提供治疗思路。

综上所述，温中消疡汤治疗 NSAIDs 相关性胃溃疡，能明显的改善胃脘疼痛、腹胀、纳呆食少、反酸、嗳气、倦怠乏力、大便稀溏等证候，具有很好临床疗效。

参考文献(References)

[1] Nishie H, Kataoka H, Kato H, et al. Refractory gastric antral ulcers without Helicobacter pylori infection and non-steroidal anti-inflammatory drugs[J]. Clin J Gastroenterol, 2018, 11(3): 1-6

[2] Francesco DM, Chiara M, Ottavia C, et al. Mo1194 - Natural History of Gastric Ulcer in a 25 Years Follow-Up: Role of Helicobacter Pylori Infection and Nonsteroidal Anti-Inflammatory Drugs [J]. Gastroenterology, 2018, 154(6): S702

[3] Kidon M, Blanca-Lopez N, Gomez E, et al. Diagnosis and management of hypersensitivity reactions to Non-Steroidal Anti-inflammatory drugs in children and adolescents [J]. Pediatr Allergy Immunol Pulmonol, 2018, 29(5): 469-480

[4] Gurbel P, Tantry U, Weisman S. A narrative review of the cardiovascular risks associated with concomitant aspirin and NSAID use[J]. J Thromb Thrombolysis, 2019, 47(1): 16-30

[5] Markovic M, Swanson SA, Stricker BH, et al. Prenatal exposure to non-steroidal anti-inflammatory drugs (NSAIDs) and neuro-developmental outcomes in children[J]. Pharmacoepidemiol Drug Saf, 2019, 28(4): 452-459

[6] 李爽,胡岩芳,刘科.丁苯酞联合阿司匹林及阿托伐他汀对急性脑梗死患者脑血流状态及斑块稳定性的影响[J].川北医学院学报, 2018 (4): 492-495

[7] Webb PM, Na R, Weiderpass E, et al. Use of aspirin, other nonsteroidal anti-inflammatory drugs and acetaminophen and risk of endometrial cancer: the Epidemiology of Endometrial Cancer Consortium[J]. Ann Oncol, 2019, 30(2): 310-316

[8] Ashok K, Asha R, Scheinert RB, et al. Nonsteroidal anti-inflammatory drug, indomethacin improves spatial memory and NMDA receptor function in aged animals[J]. Neurobiol Aging, 2018, 70: 184-193

[9] Benjamine AA, Bede Affoué Lucie, Denis YK, et al. Struc tures, Lipophilicity, Dipole Moments, Acidity and Spectroscopic Properties of Non-Steroidal Anti-Inflammatory Drugs Diclofenac, Bromfenac and Amfenac: A Theoretical Study [J]. J Comput Chem, 2019, 7(4): 95-105

[10] Kaufman DW, Kelly JP, Battista DR, et al. Exceeding the daily dosing limit of nonsteroidal anti-inflammatory drugs among ibuprofen users [J]. Pharmacoepidemiol Drug Saf, 2018, 27 (3): 322-331

[11] Baló-Banga JM, Schweitzer K. The differential diagnosis of adverse reactions to non-steroidal anti-inflammatory drugs. In vitro and in vivo methods[J]. Orv Hetil, 2018, 159(38): 1556-1566

[12] Clare M, Tracy B, Helen MD, et al. Implementing a non-steroidal anti- inflammatory drugs communication bundle in remote and rural pharmacies and dispensing practices [J]. BMJ Open Qual, 2018, 7(3): e000303

[13] 黄玉林. 消化性溃疡患者非甾体类抗炎药服用史和幽门螺杆菌感染的协同致病性[J]. 中国老年学杂志, 2018, 38(2): 389-390

[14] 张声生, 王垂杰. 消化性溃疡中医诊疗专家共识意见 (2017)[J]. 中华中医药杂志, 2017, 32(9): 4089-4093

[15] 张训景, 张颖颖. 自拟安胃促愈汤联合西医四联疗法治疗 Hp 阳性消化性溃疡疗效观察[J]. 中国中医急症, 2018, 242(6): 131-133

[16] 虞旭东, 吴深宝. 自拟活血清热方联合内镜下夹闭术治疗消化性溃疡出血疗效及 6-Keto-PGF1α、TXB2 的影响 [J]. 中国中医急症, 2018, 27(4): 699-701

[17] 孙啸云, 刘茹, 徐建国,等. NSAIDs 相关胃肠损伤防治的研究进展[J]. 临床麻醉学杂志, 2018, 34(11): 87-90

(下转第 4092 页)

Med, 2019, 171(4): JC22

[19] Saag KG, Agnusdei D, Hans D, et al. Trabecular Bone Score in Patients With Chronic Glucocorticoid Therapy-Induced Osteoporosis Treated With Alendronate or Teriparatide [J]. Arthritis Rheumatol, 2016, 68(9): 2122-2128

[20] Gourgari E, Stafford JM, D'Agostino R Jr, et al. Association of metformin and statin medications with surrogate measures of cardiovascular disease in youth with type 1 diabetes: the SEARCH for diabetes in youth study [J]. Ann Pediatr Endocrinol Metab, 2019, 24 (3): 187-194

[21] Wu H, Pang Q. The effect of vitamin D and calcium supplementation on falls in older adults: A systematic review and meta-analysis [J]. Orthopade, 2017, 46(9): 729-736

[22] Van Baarsel ED, Patel V, Kesbeh Y, et al. Atypical femoral fracture in the setting of alendronate treatment for osteoporosis: a case report and literature review [J]. J Community Hosp Intern Med Perspect, 2019, 9(4): 340-343

[23] Okimoto N, Uemura Y, Yoshioka T, et al. Treatment with once-weekly alendronate oral jelly compared with once-weekly alendronate oral tablet for Japanese patients with primary osteoporosis: An open-label, prospective, observational study[J]. Health Sci Rep, 2018, 2(1): e107

[24] Choi JI, Cho HH. Effects of Di (2-ethylhexyl)phthalate on Bone Metabolism in Ovariectomized Mice [J]. J Bone Metab, 2019, 26(3): 169-177

[25] Werner de Castro GR, Buss ZDS, Rosa JS, et al. Evaluation of Bone Metabolism Biomarkers in Paget's Disease of Bone [J]. Cureus, 2019, 11(5): e4791

[26] Fusaro M, Gallieni M, Aghi A, et al. Cigarette Smoking is Associated with Decreased Bone Gla-protein (BGP) Levels in Hemodialysis Patients[J]. Curr Vasc Pharmacol, 2018, 16(6): 603-609

[27] Kim BJ, Yoo HJ, Park SJ, et al. Association of blood n-3 fatty acid with bone mass and bone marrow TRAP-5b in the elderly with and without hip fracture[J]. Osteoporos Int, 2019, 30(5): 1071-1078

[28] Zhang H, Ding W, Ji F, et al. MicroRNA-410 participates in the pathological process of postmenopausal osteoporosis by downregulating bone morphogenetic protein-2 [J]. Exp Ther Med, 2019, 18(5): 3659-3666

[29] Kunisaki C, Tanaka Y, Kosaka T, et al. A Comparative Study of Intravenous Injection Form and Oral Jelly Form of Alendronate SodiumHydrate for Bone Mineral Disorder after Gastrectomy [J]. Digestion, 2017, 95(2): 162-171

[30] Ding N, Liu C, Yao L, et al. Alendronate induces osteoclast precursor apoptosis via peroxisomal dysfunction mediated ER stress [J]. J Cell Physiol, 2018, 233(9): 7415-7423

(上接第 4079 页)

[18] 刘伟. 消化性溃疡反复出血与幽门螺杆菌感染及长期服用非甾体类抗炎药物的关系研究[J]. 实用医院临床杂志, 2018, 15(5): 48-51

[19] Guillermo, Garcí a-Rayado, Mercedes, et al. NSAID induced gastrointestinal damage and designing GI-sparing NSAIDs[J]. Expert Rev Clin Pharmacol, 2018, 159(38): 1556-1566

[20] Lind KE, Raban MZ, Georgiou A, et al. NSAID use among residents in 68 residential aged care facilities 2014 to 2017: An analysis of duration, concomitant medication use, and high risk conditions [J]. Pharmacoepidemiol Drug Saf, 2019, 28(11): 1480-1488

[21] Cea Soriano, Lucía, Fowkes FG, Allum A, et al. Predictors of Bleeding in Patients with Symptomatic Peripheral Artery Disease: A Cohort Study Using The Health Improvement Network in the United Kingdom[J]. Thromb Haemost, 2018, 118(06): 1101-1112

[22] 崔番瑜. 小建中汤加减治疗对慢性萎缩性胃炎患者胃泌素及细胞因子的影响[J].湖南中医药大学学报, 2018, A01: 903-904

[23] Yuma M, Hidenori Y, Toru K, et al. Gastrin-Releasing Peptide Is Involved in the Establishment of Allergic Rhinitis in Mice [J]. Laryngoscope, 2018, 128(11): E377-E384

[24] 马平平, 毕珺辉, 徐丹,等. 良附丸对 4 种实验性胃溃疡模型大鼠的防治效果[J].中医药信息, 2018, 35(5): 9-12

[25] LIU Qing, JIA Wei, HAO Jian, et al. Clinical Experience of Wang Hongjing in Treating Spleen and Stomach Disease through Herb Couples for Strengthening Spleen and Invigorating Qi and Warming Spleen and Stomach Drugs [J]. Chin Med Mod Edu, 2018, 16(4): 65-66

[26] Jia G, Zhang Y, Li W, et al. Neuroprotective role of icariin in experimental spinal cord injury via its antioxidant, anti-neuroinflammatory and anti apoptotic properties[J]. Mol Med Report, 2019, 20(4): 3433-3439

[27] JIN Ziming, SONG Zhirong, DOU Xia. Protective Effects of Codonopsis Radix on Gastric Mucosa in Rats with Gastric Ulcer [J] Chin J Mod Appl Pharm, 2017, 22(12): e2258

[28] 刘玉岩, 段富津. 国医大师段富津治疗胃脘痛的用药规律研究[J]. 长春中医药大学学报, 2019, 35(2): 48-52

[29] Zou WW, Xu SP. Galangin inhibits the cell progression and induces cell apoptosis through activating PTEN and Caspase-3 pathways in retinoblastoma[J]. Biomed Pharmacother, 2018, 97: 851-863

[30] Elgazar AA, Selim NM, Abdel-Hamid NM, et al. Isolates from Alpinia officinarum Hance attenuate LPS induced inflammation in HepG2: Evidence from In Silico and In Vitro Studies [J]. Phytother Res, 2018, 32(7): 1273-1288

[31] 赵明铭. 温中消痈汤联合西药治疗胃溃疡脾胃虚寒型的临床疗效探讨[J].中国医药指南, 2017, 15(1): 162-162, 163

[32] 玉素甫·司马义. 温中消疡汤联合雷贝拉唑治疗十二指肠溃疡疗效及对 NF-κB 及 TNF-α 的影响 [J]. 现代中西医结合杂志, 2016, 25(4): 38-40+44

[33] 曹生海. 温中消痈汤与三联疗法联合治疗对胃溃疡患者黏膜微血管形态、组织成熟度和功能成熟度的影响[J]. 四川中医, 2017, 35 (11): 93-95