

排胚汤协同米非司酮抗早孕流产物超微结构改变的研究

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摘要 为探讨中药排胚汤协同米非司酮抗早孕作用的机理,将 68 例药流患者与人工流产 22 例分组对照,分为西药组、中药组、中西医结合组、人流组,各组取 5 例相应的蜕膜和绒毛组织进行超微结构观察。结果与其他各组相比,中西医结合组蜕膜和绒毛的坏死程度最重。说明中药排胚汤取效的可能途径除加重蜕膜组织的变性坏死外,还可能直接作用于绒毛组织本身。

主题词 蜕膜/超微结构 绒毛膜/超微结构 @ 排胚汤

中药排胚汤协同米非司酮抗早孕,在临床显示了提高流产率、减少出血量及缩短出血时间的优势,为了探讨其机理,我们通过透射电镜和扫描电镜,观察了流产物蜕膜及绒毛等超微结构的变化,并与人工流产、单用米非司酮、单用排胚汤者进行对照,现将结果报告如下。

1 临床资料

1997 年 9 月~1998 年 1 月,选择北京中医药大学东直门医院妇科门诊早孕妇女 90 例。对象入选标准^[1]: (1) 年龄 18~35 岁,身体健康; (2) 经妇科检查、尿 HCG 测定、B 超检查确认为正常宫内早孕,停经 49 天以内; (3) 了解本实验的性质、目的,能按规定用药,接受随访、体检和处置; (4) 无急、慢性器质性疾病,无心血管、血液和内分泌系统疾病,无肝肾功能异常; (5) 近 3 月未哺乳,未用任何甾体避孕药及宫内节育器; (6) 无长期服药史及药物过敏史,无烟酒嗜好者。

将 90 例对象随机分为 4 组。I 组: 13 例,行负压吸引人工流产。II 组: 34 例,米非司酮(上海华联制药厂生产,每片 25mg)150mg,第 1 天清晨空腹顿服,第 3 天早晨来院空腹顿服米索前列醇(英国 Searele 公司生产,每片 200μg)600μg 后留院观察至完全流产。III 组: 34 例,服西药方法同 II 组,在第 1 天服用米非司酮的同时开始服用排胚汤(由寒水石、莪术、水蛭、急性子等药组成,北京中医药大学药厂制,每瓶 100ml),每次 50ml,每日 2 次,连服 3 天,第 3 天服用米索前列醇后留院观察至完全流产。IV 组: 9 例,连服 3 天排胚汤,每日 2 次,每次 50ml,第 4 天上午来院行负压吸引人工流产。将上述 4 组流产物分别收集起来,各组取 5 例,将绒毛和蜕膜组织分离,固定于 2.5% 的戊二醛

(4℃)中待用。

2 观察方法

由中日友好医院电镜室将固定于戊二醛中的蜕膜、绒毛组织 1% 锇酸后固定、脱水、浸透、包埋、超薄切片、醋酸铀—枸橼酸铅染色, H-500 型电子显微镜观察。另一部分以 1% 锇酸固定 1 小时,丙酮逐级脱水,醋酸异戊酯置换,日立 HCP-2 临界点干燥器干燥,镀金后日立 S-520 扫描电镜观察。

透射电镜分度国内外目前尚无统一标准。我们参考文源等的标准制定透射电镜的分度标准如下^[2]: 轻度: 细胞尚完整,胞质内各种细胞器有不同程度形态学改变;胞核形态尚正常,可有染色质增多的改变。重度: 细胞膜受损,形态不规则;细胞胞质内各种细胞器改变极明显,内质网扩大如囊,线粒体甚至呈空泡变;胞核及核膜超微结构不清或核固缩或染色质增多且边聚。

因国内外无统一标准,故扫描电镜采用描述性诊断进行观察。

3 结果

3.1 透射电镜下的改变: I 组蜕膜细胞为形态结构基本正常,常染色质分布均匀,见 1~2 个核仁,核膜清晰。胞浆中见丰富细长粗面内质网及椭圆形线粒体。绒毛合体滋养层细胞表面有许多微绒毛,胞浆含丰富内质网;细胞间连接结构较好。II 组蜕膜组织细胞有的线粒体嵴消失,粗面内质网轻度扩张、脱颗粒,细胞核异染色质增多。绒毛合体滋养层细胞粗面内质网明显扩大,微绒毛减少,细胞核异染色质增多且边聚。呈轻度到重度改变。III 组蜕膜组织细胞缩小,细胞核异染色质增多、边聚,或结构不清,核固缩;胞浆空泡变性。绒毛合体滋养层细胞粗面内质网池明显扩大,溶酶体明显增多,微绒毛减少甚至消失,细胞核异染色质增多且边聚;朗罕氏细胞线粒体肿胀、空泡变,细胞核异染色质边聚。呈重度改变。IV 组蜕膜组织细胞线粒体嵴消失,粗面内质网扩张,绒毛合体滋养层细胞粗面内质网轻度扩大,溶酶体增多,微绒毛减少;线粒体肿胀、空泡变,细胞核异染色质边聚。细胞间连接结构较好。呈轻度改变。

3.2 扫描电镜下的改变: I 组为正常早孕绒毛,微绒毛结构清晰; II 组部分出现微绒毛缺失,减少,形态变

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异:Ⅲ组绒毛严重退变,甚至已经看不出绒毛结构;Ⅳ组绒毛部分缺失,微绒毛轻度改变。

4 讨论

随着米非司酮药物流产在国内的广泛开展,针对其完全流产率尚不够理想,流产时出血量多,流产后出血时间长,甚至因流产不全而潜在引起大出血的危险等缺点,近 5 年来,中医药科研人员在这方面做了大量的工作。大量临床研究显示,米非司酮配伍中药后,能提高流产率,尤其是能减少出血量,缩短流产后出血时间^[3]。我科经严格科研设计,精选方药组成的排胚汤协助米非司酮序贯抗早孕应用于临床后,经过大量的临床和病理(光镜)观察,得到相似的结果^[4,5]。但中医药的这种协同作用研究仍仅限于临床观察,尚无进一步的实验研究,亦无更深入的机理探讨。另一方面,中药无论是复方,还是单味药,其药理已经显示较好的抗生育的前景,故此我们在排胚汤协同米非司酮抗早孕临床观察和光镜观察的基础上,再从超微结构改变的角度试图来探讨排胚汤在其中的作用机理。

本研究表明,米非司酮配伍米索前列醇流产物的病理变化、电镜下组织的改变再次证实了蜕膜呈不同程度的变性、坏死,绒毛组织也因缺乏蜕膜的营养保护作用而继发性地在一定程度上发生退变,与文献报道相符^[6]。也与我们对相同病例光镜下观察结果相同。但

在单用排胚汤后与不用排胚汤的对象行人工流产后,蜕膜和绒毛组织两组之间的改变却有一定的差异,应用排胚汤后蜕膜和绒毛组织的改变多数程度较轻,并且蜕膜和绒毛的退变是同步的。在米非司酮及米索前列醇序贯应用的基础上加用排胚汤,流产物的蜕膜和绒毛组织也呈变性、坏死,但以绒毛组织的这种改变显得更重一些。因此,可能排胚汤的作用不仅在蜕膜,对胎盘绒毛本身也有一定的作用。因此,排胚汤协同米非司酮作用后,一方面可能使蜕膜的变性、坏死加重,另一方面可能直接作用于胎盘绒毛组织,导致孕产物较完整的脱落,而使流产率得到提高,流产物排出时间缩短,从而也相应地使药物流产后的出血时间得到缩短。

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KAHWA

ABSTRACTS FROM ORIGINAL ARTICLES

A Clinical Observation on Treating 17 Cases with Osteoporosis by Yi Shen Zhuang Gu He Ji

Gong Ling, Wang Mingyue, Cao Junqing, et al.

51 cases of osteoporosis were put on clinical trial in our OPD and randomly assigned to TCM treatment group (N=17), TCM control group and blank group. The total effective rate in the TCM treatment group obtained was 94.1% and the significantly effective rate achieved 88.2%. After the treatment, the density of the osseous tissue increased by 3.4%, main symptoms improved markedly, the serum calcium increased and the urine pyridine phenol decreased. All the findings were superior than that in the rest two groups. This composite is effective and safe (no side reactions) and worth put into large sale production.

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Key words: osteoporosis/TCM therapy @Yi Shen Zhuang Gu He Ji

(Original article on page 606)

Ultrastructural Study on Apoplema in Termination of Early Pregnancy by Pai Pei Tang and Mifepristone

Wang Qing, Zhao Hong, Wang Shilin, et al.

To elucidate the mechanism of Pai Pei Tang in combination with mifepristone in termination of early pregnancy, samples of apoplema (5 each) were collected from the Pai Pei Tang group, mifepristone group, Pai Pei Tang and mifepristone group (N=68) and routine artificial abortion group (N=22). We found that atrophy of the decidua and chorion was the utmost in the Pai Pei Tang and mifepristone group under the electron microscope. The result suggested that Pai Pei Tang could induce degenerative and atrophic changes in the decidua and affect the chorion directly.

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Key words: decidua/ultrastructure chorion/ultrastructure @Pai Pei Tang

(Original article on page 612)

A Study on Fu Zheng Hua Yu Fang and its Ingredients on Production of Collagen in the Liver

Liu Chenghai, Wang Xiaoling, Wang Zhennan, et al.

To explore the effect of Fu Zheng Hua Yu Fang and its ingredient (s) on collagen production we cultured the astrocytes isolated from the dimethyl nitrosamine-induced rat fibrosis model in serum with the extract of the complete

prescription and its ingredient (s) and observed their effect in treating the model rats. The ingredients included those for strengthening the body resistance, those for removing stasis, that of Cordyceps, that of Radix Salviae Miltiorrhizae and that of Radix Salviae Miltiorrhizae plus Cordyceps. The results showed that though inhibition of proliferation and activation of the astrocytes was found in all the groups, the effect of the extract of drugs for removing stasis was the strongest. Similarly, inhibition of production of collagen type I and expression of its mRNA was found in all the groups while the effect of drugs for strengthening the body resistance was the strongest. In treating the model rats, the complete prescription was the strongest in reducing the collagen deposition and hydroxyproline content. Combination of drugs for removing stasis with those for strengthening body resistance could further reduce the formation of collagen. The prescription proved to be a comprehensive one in inhibiting collagen production.

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Key words: compatibility of TCM drugs liver/pharmacological action @ Fu Zheng Hua Yu Fang

(Original article on page 620)

A Quantitative Analysis of 5-hydroxytryptamine and Norepinephrine Content in the Brain, Hypophysis and Adrenals in Cold-deficiency Rats Administered with Drugs Warm and Hot in Properties

Li Liang, Liu Guozhen, Liang Yuehua

Content of the neurotransmitters 5-Hydroxytryptamine (5-HT) and Norepinephrine (NE) in the neurons of the brain and adrenals and in the nerve fibers of the hypophysis after administration of drugs warm and hot in properties in the cold-deficiency rats were studied immunohistochemically and fluorimetrically. The results showed that both drugs for warming yang and replenishing qi could similarly increase the content of norepinephrine and decrease the content of 5-hydroxytryptamine in the neurons in the brain and in the nerve fibers of the hypophysis. Their content in the adrenal medulla did not show significant change.

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Key words: cold deficiency syndrome/TCM treatment warming yang and supplementing qi, cold deficiency/metabolism

(Original article on page 623)