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奈达铂联合多西他赛治疗晚期食道癌的临床观察

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[摘　要]　**目的：**观察奈达铂联合多西他赛治疗晚期食道癌的近期疗效及不良反应。**方法：**将80例晚期食道癌患者随机分为治疗组和对照组，每组40例，治疗组：采用奈达铂联合多西他赛治疗，其中奈达铂25 mg/(m^2·d)第1~3天给予；对照组：采用顺铂联合多西他赛治疗，其中顺铂 25 mg/(m^2·d)第1~3天给予，两组均在第1天给予多西他赛75 mg/m^2，21天为1个周期。化疗2个周期后按WHO标准评价疗效及毒副作用。**结果：**治疗组完全缓解2例，部分缓解14例，稳定18例，进展6例，有效率为40.0% (16/40)；对照组完全缓解2例，部分缓解16例，稳定16例，进展6例，有效率45.0% (18/40)，两组有效率比较差异无统计学意义(P>0.05)。治疗组和对照组消化道不良反应分别为10.0%和30.0%；肾毒性分别为0和15.0%，血小板下降分别为30.0%和5.0%，差异有统计学意义(P<0.05)；白细胞减少分别为70.0%和65.0%，差异无统计学意义(P>0.05)。**结论：**奈达铂联合多西他赛方案与顺铂联合多西他赛方案治疗晚期食道癌的疗效相近，在毒副作用方面多西他赛联合奈达铂方案耐受性良好，具有优势。

[关键词]　晚期食道癌；奈达铂；顺铂；多西他赛；有效率；不良反应

Clinical study on the combined chemotherapy with nedaplain and docetaxel for advanced esophageal cancer

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Abstract　**Objective:** To observe the efficacy and adverse reaction of the combined chemotherapy with nedaplatin and docetaxel for patients with advanced esophageal cancer. **Methods:** A total of 80 patients with advanced esophageal cancer were divided into a treatment group (n=40) and a control group (n=40). Nedaplatin was given intravenously at dose of 25 mg/(m^2·d) for three days in the treatment group. Cisplatin was administrated

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intravenously at dose of 25 mg/(m^2·d) for three days in the control group. Docetaxel was infused intravenously at dose of 75 mg/m^2 at the first day in both groups. The duration of treatment was 21 days in both groups. The efficacy and toxicity were evaluated according to the standard of WHO at the end of experiments. **Results:** In the treatment group, there was complete response (CR) in 2 cases, partial response (PR) in 14, stability of disease (SD) in 18 and progress of disease (PD) in 6. The rate of response rate (RR) was 40.0% (16/40). In the control group, there was CR in 2 cases, PR in 16, SD in 16 and PD in 6. The rate of RR was 45.0% (18/40). The rate of RR was similar in the 2 groups (P>0.05). The rate of vomiting in the control group was higher than that in the treatment group (30.0% vs 10.0%, P<0.05). The rate of renal toxicity was 0 in the treatment group and 15.0% in the control group (P<0.05). The rate of hepatic toxicity was all 12.5% in the both groups (P>0.05). The rate of decrease of WBC was 70.0% in the treatment group and 65.0% in the control group (P>0.05). The rate of decrease of platelet was 30.0% in the treatment group and 5.0% in the control group (P<0.05). **Conclusion:** The nedaplatin combined with docetaxel has the similar therapeutic effect on advanced esophagus cancer to cisplatin combined with docetaxel, and has advantage on the toxicity due to well tolerance by the patients

Key words advanced esophageal cancer; nedaplatin; cisplatin; docetaxel; effective rate; adverse effect

食管癌是我国高发的消化道恶性肿瘤之一，病死率占恶性肿瘤的第4位。大多数食管癌患者在确诊时已属晚期，失去了根治性手术的机会，预后较差[1]。化疗是晚期食管癌的主要治疗手段之一。顺铂联合多西他赛是目前临床治疗食管癌疗效较好的药物[2-3]，但因顺铂的肾毒性及消化道反应限制了其临床应用。奈达铂是近年来在临床常用的第2代铂类抗癌药，与顺铂作用机制类似，肾毒性和消化道反应比顺铂轻，容易被患者接受[4]。湖南省脑科医院采用奈达铂联合多西他赛与顺铂联合多西他赛治疗晚期食管癌80例，观察近期疗效与毒副作用，现将结果报告如下。

1 资料与方法

1.1 一般临床资料

收集2010年2月至2014年2月在湖南省脑科医院经病理学和/或细胞学证实的晚期食道癌患者80例。入选标准：1)为局部晚期或转移性食管癌患者，全部患者1个月内均未接受放疗或化疗。2)均有可测量病灶。3)卡氏评分(KPS)≥70分。4)预计生存期3个月以上。5)血液学指标、心、肝、肾功能基本正常。6)无严重内科疾患。所有患者均符合入组条件，其中男性53例，女性27例，年龄为40~69(中位数54)岁；鳞癌73例，腺癌7例。按照国际抗癌联盟(Union for International Cancer Control，UICC)食道癌TNM分期，III期24例，IV期56例。随机分为治疗组(奈达铂+多西他赛方案即DN方案)40例与对照组(顺铂+多西他赛方案即DC方案)40例，两组年龄、性别构成比、病理分期方面差异均无统计学意义(P>0.05)。

1.2 治疗方法

治疗组：采用奈达铂联合多西他赛治疗，其中奈达铂25 mg/(m^2·d)第1~3天给予。对照组：采用顺铂联合多西他赛治疗，其中顺铂 25 mg/(m^2·d)第1~3天给予，两组均在第1天给予多西他赛75 mg/m^2，静脉滴注1 h，21天为1个周期。化疗2个周期后复查各项指标，包括患者自觉症状，食管钡餐检查、胸部CT、腹部B超、颈部彩超等，按WHO标准评价疗效及不良反应。使用多西他赛前1 d开始预防性给予地塞米松、雷尼替丁，当天化疗前肌注苯海拉明，以预防过敏和体液潴留，化疗前后均给予昂单司琼预防性止吐等治疗。顺铂治疗中充分水化。并且在治疗过程中根据出现病情进展、不良反应或不能耐受等情况进行对症治疗。化疗药物滴注完毕后48 h，根据患者骨髓抑制情况，酌情予以升白细胞或血小板治疗。

1.3 疗效评定标准

2个化疗周期结束后4周，参照WHO实体瘤疗效评价标准进行疗效评价，分为完全缓解(complete response，CR)、部分缓解(partial response，PR)、稳定(stability of disease，SD)和进展(progress of disease，PD)，以 CR+PR 计算有效率(response rate，RR)。化疗毒性反应评价参照WHO抗肿瘤药物急性及亚急性毒性反应分度评价标准，分为0~IV度共5个级别。

1.4 统计学处理

采用SPSS14.0统计软件分析，率的比较采用χ^2检验，P<0.05为差异有统计学意义。

2 结 果

2.1 疗效

治疗组的有效率为40.0%(16/40)；对照组为41.2%(18/40)，两组有效率比较差异无统计学意义(P>0.05；表1)。

2.2 毒副作用

消化道反应：治疗组和对照组分别为10.0%和30.0%，差异有统计学意义(P<0.05)。肾毒性分别为0和15.0%，差异有统计学意义(P<0.05)。骨髓抑制：治疗组白细胞减少占70.0%，对照组为65.0%，差异无统计学意义(P>0.05)；治疗组血小板下降占30.0%，对照组为5.0%，差异有统计学意义(P<0.05)。肝功能损害：治疗组为12.5%，对照组为12.5%，差异无统计学意义(P>0.05；表2)。

表 1 两组患者近期疗效比较 /[No.(%)]

Table 1 Comparison of the efficacy of the 2 groups/[No.(%)]

组别	n	CR	PR	SD	PD	RR
治疗组	40	2(5.0)	14(35.0)	18(45.5)	6(15.0)	16(40.0)
对照组	40	2(5.0)	16(40.0)	16(40.0)	6(15.0)	18(45.0)

表 2 两组患者毒副作用情况的比较 (n=40)

Table 2 Comparison of the adverse reaction of the 2 groups (n=40)

毒副作用	治疗组			对照组			P
	I+II	III+IV	发生率 /%	I+II	III+IV	发生率 /%	
消化道反应	3	1	10.0	9	3	30.0	<0.05
肾功能损害	0	0	0	6	0	15.0	<0.05
白细胞减少	24	4	70.0	23	3	65.0	>0.05
血小板减少	10	2	30.0	2	0	5.0	<0.05
肝功能损害	5	0	12.5	5	0	12.5	>0.05

3 讨 论

食管癌总的疗效很差，为缓解晚期食管癌患者诸如疼痛、吞咽困难等症状，减轻患者的痛苦，许多晚期食管癌患者需要接受姑息治疗。化疗是晚期食管癌姑息治疗的主要手段，目前食管癌的一线化疗以顺铂/氟尿嘧啶为主，其有效率为30%~40%；中位生存时间分别为6~10个月[5-6]。近年来，研究[2-3]表明以紫杉醇、多西紫杉醇或奈达铂组成的治疗方案用于治疗食管癌，疗效肯定。

多西他赛属于紫杉类化合物抗肿瘤药，其作用机制与紫杉醇相同，但稳定微管作用比紫杉醇大2倍，并能诱导微管束的装配，而不改变原丝数量。它是细胞周期特异性药物，能将细胞阻断于M期，对增殖细胞作用大于非增殖细胞[7]。研究[8]表明单药多西他赛在晚期食管癌的疗效，其缓解率约20%，而毒副作用可耐受。奈达铂的抗癌作用机制与顺铂相似，在进入细胞后，甘醇酸酯配基上的醇性氧与铂之间的键断裂，水与铂结合，导致离子型物质(活性物质或水合物)形成。然后，断裂的甘醇酸酯配基变得不稳定并被释放，产生多种离子型物质与DNA结合，并抑制DNA复制，从而产生抗肿瘤活性[4]。Hirata等[9]研究证实，单药奈达铂治疗食管癌的有效率为30%，且耐受性好，无严重不良反应。Osaka等[10-12]进行了多西紫杉醇联合奈达铂联合化疗治疗晚期食管癌，其有效率在30%~50%，中位生存时间分别为5.9~11.4个月，均未出现3~4级非血液学毒性，未观察到因不良反应致死病例。

本组均为晚期食道癌患者，奈达铂联合多西

他赛化疗有效率达40.0%，顺铂联合多西他赛化疗有效率达45.0%，两组有效率比较差异无统计学意义；与国内外研究[10-13]报道相近。两药联用有效率高于单用多西他赛有效率，说明多西他赛与铂类联合应用有协同和相加作用。

奈达铂的毒性谱与顺铂不同，其剂量限制性毒性主要为骨髓抑制所致的血小板减少，肾毒性和胃肠道不良反应发生率均较低，主要是I~II度骨髓抑制，以白细胞和血小板减少为主。本研究结果显示：奈达铂联合多西他赛治疗晚期食道癌的消化道不良反应、肾毒性低于顺铂联合多西他赛，血小板下降高于后者，但骨髓抑制能耐受，且不需要水化利尿，使用方便，安全有效，增加了患者的耐受性和依从性。

综上所述，奈达铂联合多西他赛治疗晚期食道癌的有效率不低于顺铂联合多西他赛，胃肠道毒性显著减轻，且从临床的实用性上考虑，奈达铂更容易为临床医生和患者所接受。因本研究观察的患者数有限，下一步需增加样本量进行追踪观察。

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