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Antitumor activity of new combination chemotherapy with irinotecan hydrochloride and nedaplatin against human cervical cancer celllines

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Introduction: Antitumor activity of combination chemotherapy with irinotecan hydrochloride (CPT-11) and nedaplatin was compared to that with CPT-11 and cisplatin.

Methods: *In vitro* cytotoxicity of SN-38 (an active metabolite of CPT-11) in combination with nedaplatin or cisplatin was evaluated using three human cervical cancer cell lines (ME-180, CaSki and SiHa). Interactions between two drugs in combination were investigated using a simultaneous-exposure schedule and analyzed by the IC₅₀-based isobologram method. *In vivo* antitumor effects of CPT-11 in combination with each platinum were studied using SiHa xenografts.

Results: IC₅₀ values of nedaplatin against these three human cervical cancer cell lines were about 2-fold as high as those of cisplatin, indicating somewhat weak cytotoxic effects of nedaplatin. Simultaneous exposure to SN-38 with each platinum preparation showed synergistic and additive effects against ME-180 and SiHa. While CPT-11, nedaplatin and cisplatin alone hardly showed any antitumor effects even at the maximum tolerated dose (MTD) levels, the combination chemotherapy with CPT-11 and nedaplatin or cisplatin resulted in significant anti tumor effects even at three-quarter MTD of CPT-11 combined with two-third MTD of platinum. All treatments were tolerable for mice, indicating that the combinations did not cause significant enhancement in toxicity.

Discussion: In clinical application, nedaplatin causes a lower incidence of nephropathy and does not require the replacement of a large volume of fluid, which is needed for cisplatin administration, facilitating treatment at the outpatient clinic. In addition, the incidences of digestive disorder, peripheral neuropathy and auditory disorder are lower.

Conclusion: These findings suggest that the combination chemotherapy with CPT-11 and nedaplatin for squamous cell cancer of uterine cervix is very useful in clinical practice.

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