Short Report

Antitumor Effect of 1α -Hydroxyvitamin D_3

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SATO, T., TAKUSAGAWA, K., ASOO, N. and KONNO, K. *Antitumor Effect of 1α -Hydroxyvitamin D_3* . Tohoku J. exp. Med., 1982, 138 (4), 445-446 — Sarcoma 180 and the Lewis lung carcinoma were implanted s.c. into male ddY mice and C57B1/6 mice, respectively. 1α -Hydroxyvitamin D_3 was administered orally by a stomach tube at a dose of 0.1 μ g/kg and 0.2 μ g/kg daily. The results demonstrated that 1α -hydroxyvitamin D_3 suppressed s.c. tumor growth of sarcoma 180 and inhibited pulmonary metastases of the Lewis lung carcinoma. ——— 1α -hydroxyvitamin D_3 ; antitumor effect; Sarcoma 180, Lewis lung carcinoma

1α -Hydroxyvitamin D_3 ($1\alpha(OH)D_3$) is converted to $1\alpha,25$ -dihydroxyvitamin D_3 ($1\alpha,25(OH)_2D_3$) in the liver. The latter has been known to function at target tissues in a similar manner to steroid hormones. It has more recently been reported that some tumor cells possessed $1\alpha,25(OH)_2D_3$ receptor proteins and were inhibited in vitro by $1\alpha,25(OH)_2D_3$ (Colston et al. 1981).

The purpose of this study is to examine wheter $1\alpha,(OH)D_3$ affect tumor cells in vivo which are extensively employed as experimental material for cancer chemotherapy.

MATERIALS AND METHODS

Twenty-five-week-old male ddY mice weighing about 40 g and 7-week-old male C57B1/6 mice weighing about 22 g were used. The former were inoculated s.c. with 10^6 ascitic cells of Sarcoma 180, and the latter were implanted s.c. with approximately 2 mm³ fragments of the Lewis lung carcinoma into the back. These animals were divided into 4 groups, and the following solutions were administered into the stomach by a stomach tube daily from a day after inoculation to a day before sacrifice. $1\alpha(OH)D_3$ (Chugai pharmaceutical Co., Ltd., Tokyo) was dissolved in medium chain triglyceride (ODO*) (Nisshin Oil Mills Ltd., Tokyo). Groups I and II were given distilled water alone and medium chain triglyceride alone, respectively. Groups III and IV were given $1\alpha(OH)D_3$ at a dose of 0.1 μ g/kg and 0.2 μ g/kg, respectively. The animals were fed standard mouse chow and water ad libitum, and were sacrificed on Day 14 in Sarcoma 180 and Day 21 in the Lewis lung carcinoma. Primary tumors were removed and weighed. The number of pulmonary metastases was determined at sacrifice by examining the surface of the lungs.

Blood from each group of animals with Sarcoma 180 was obtained from the inferior vena cava at sacrifice, and serum calcium levels were measured with a calcium analyzer.

RESULTS AND DISCUSSION

The results are summarized in Tables 1 and 2. In Sarcoma 180, primary tumor weight of mice treated with $1\alpha(OH)D_3$ was smaller than that of Group I or Group II. In the Lewis lung carcinoma, primary tumor weight was not significantly different. However, the number of pulmonary metastases evidently decreased in mice treated with $1\alpha(OH)D_3$ in contrast to Group I or Group II.

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TABLE 1. *Effect of treatment with $1\alpha(\text{OH})\text{D}_3$ on Sarcoma 180*

Group	Effective number of mice*	Primary tumor weight (g)	Serum Ca (mEq/liter)
I	4	0.71 ± 0.11	4.96 ± 0.36 (3) †
II	6	0.56 ± 0.11	4.76 ± 0.07 (5)
III	6	0.35 ± 0.08	4.77 ± 0.30 (4)
IV	4	0.20 ± 0.03 ‡	5.20 ± 0.14 (4)

Values are the mean $\pm$ S.E.

* Although the initial number of mice was six in each group, some animals died with handling error.

† Number of mice examined.

‡ Significantly different from Group I, $p < 0.05$.

TABLE 2. *Effect of treatment with $1\alpha(\text{OH})\text{D}_3$ on the Lewis lung carcinoma*

Group	Effective number of mice*	Primary tumor weight (g)	Number of pulmonary metastases		
			Large †	Small	Total
I	5	2.39 ± 0.52	4.2 ± 1.0	10.8 ± 1.8	15.0 ± 2.6
II	6	1.77 ± 0.34	7.3 ± 4.3	8.7 ± 2.8	16.0 ± 4.9
III	3	2.04 ± 0.44	0.3 ± 0.3 ‡	3.0 ± 1.0 ‡	3.3 ± 2.1 ‡
IV	5	1.81 ± 0.53	1.4 ± 1.0	1.8 ± 0.7 ‡	3.2 ± 2.1 ‡

Values are the mean $\pm$ S.E.

* Although the initial number of mice was six in each group, some animals died with handling error. In Group III, three mice were excluded from the table because of tumor regression until about 10 days.

† Diameter larger than 1 mm.

‡ Significantly different from Group I, $p < 0.05$.

The serum calcium levels were not significantly different among 4 groups.

Colston et al. (1981) described that treatment with $1\alpha,25(\text{OH})_2\text{D}_3$ increased cell doubling time, and suppressed cell growth in melanoma cells in vitro. Myeloid leukemia cells in culture were induced to differentiate and were inhibited the growth by $1\alpha,25(\text{OH})_2\text{D}_3$ and its analogs (Miyaura et al. 1981). Although $1\alpha,25(\text{OH})_2\text{D}_3$ influences the growth of some tumor cells in vitro, there is no report concerning antitumor effect in vivo. The results presented here demonstrated that $1\alpha(\text{OH})\text{D}_3$ suppressed tumor growth or inhibited pulmonary metastases at the dose which did not cause a serious condition (Nishii et al. 1979).

References

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