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The Anti-neoplastic Effects of Alpha-Lipoic Acid: Clinical Benefits in System Tumors besides Lung Carcinomas

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I read with great interest the recent article by Kim et al. [1]. Interestingly, alpha-lipoic acid has recently been shown to exert anti-neoplastic effects in a number of systemic tumors other than lung carcinomas. For instance, alpha-lipoic acid exerts anti-neoplastic effects in colon carcinomas. DHL-HisZnNa is a newer alpha-lipoic acid derivative that has shown similar anti-neoplastic effects in colon cancer cell lines [2]. Levels of retinoblastoma protein are attenuated by DHL-HisZnNa while a simultaneous accentuation of p21 levels is seen. Similarly, anti-proliferative effects have been seen in hepatocellular carcinomas following the administration of alpha-lipoic acid in conjunction with caffeic acid and a new synthesized lipoyl-caffeic conjugate. This combination results in enhanced interleukin 10 levels and attenuated tumor necrosis factor-α levels.

Similarly, alpha-lipoic acid derivatives such as CPI-613 demonstrate anti-neoplastic effects in pancreatic malignancies by disrupting the mitochondrial metabolism in tumor cells resulting in accentuated apoptosis in these cells. For instance, Schwartz et al. [3] have recently reported the case of an 80-year-old female with pancreatic adenocarcinoma and hepatic metastases who responded favorably to a treatment regimen in which the efficacy of gemcitabine was enhanced by using a combination of hydroxycitrate in conjunction with alpha-lipoic acid.

Hydroxycitrate and alpha-lipoic acid combinations also exert anti-proliferative effects in mouse bladder carcinoma-2 cell line bladder transitional cell carcinoma lines, which is equivalent to the anti-neoplastic effects exerted by conventional chemotherapeutic agents such as 5-fluorouracil [4].

Similarly, alpha-lipoic acid exerts anti-proliferative effects in breast carcinomas. These anti-neoplastic effects are mediated by its attenuating effect on matrix metalloproteinase (MMP)-2 and MMP-9 levels. It not only down-regulates the expression of these molecules but also decreases their activity. In particular, it decreases cellular migration and cellular motility, resulting in decreased metastases. Besides this, it also alters the Bax/Bcl-2 ratio [5]. A simultaneous increase in p27 (kip1) expression is seen, resulting in accentuated apoptosis in breast malignancies.

Alpha-lipoic acid also demonstrates benefits in the management of dermatological malignancies. It exerts these effects by inhibiting proliferation and by accentuating apoptosis in these tumors. It also enhances the apoptosis of cells with aberrant nuclei, thus further attenuating tumor growth in these malignancies. These effects have been seen particularly in B16-F10 melanoma cell lines [5].

The above examples clearly illustrate the anti-neoplastic effects of alpha-lipoic acid and the need for further studies to assess its potential efficacy in the management of other systemic tumors.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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