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INTRODUCTION

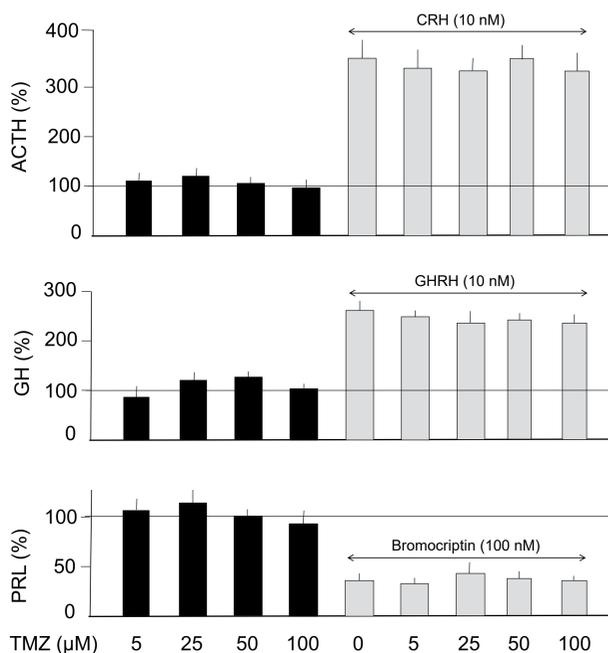
The alkylating drug Temozolomide (TMZ) is used in the treatment of aggressive pituitary adenomas with considerable success. TMZ can induce tumor shrinkage and reduce excessive hormone production. As this occurs in parallel, whether TMZ has a direct suppressive role on hormone secretion or whether this is a consequence of reduced tumor cell numbers. TMZ has recently been suggested for the treatment of invasively growing somatotroph or lactotroph macroadenomas resistant to octreotide or bromocriptine therapy. Here we have studied in vitro, whether TMZ can directly suppress normal and tumoral hormone secretion and whether it can suppress the proliferation of somatotropinomas and prolactinomas resistant to octreotide or bromocriptine, respectively.

METHODS

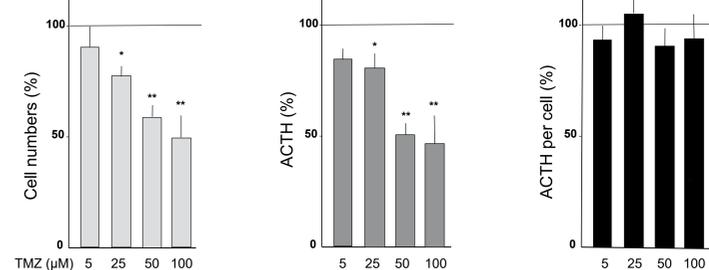
For primary cell culture, rat pituitaries and human adenoma tissues were dispersed with collagenase. For hormone measurements, cells were treated with TMZ for 4 and 24 h; for growth experiments, cells were treated for 24 and 48 h. Hormones were measured in the cell culture supernatants by RIA. Growth was determined by directly counting the cells with the Scepter Cell Counter (AtT20 and GH3 cells) or by measuring 3H-thymidine incorporation (human adenoma cells).

RESULTS

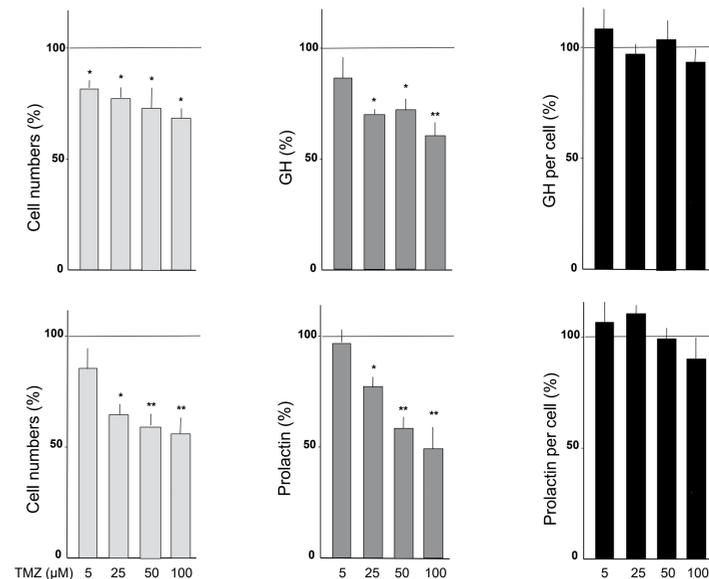
Effects of TMZ on ACTH, GH and PRL secretion in primary rat pituitary cell culture



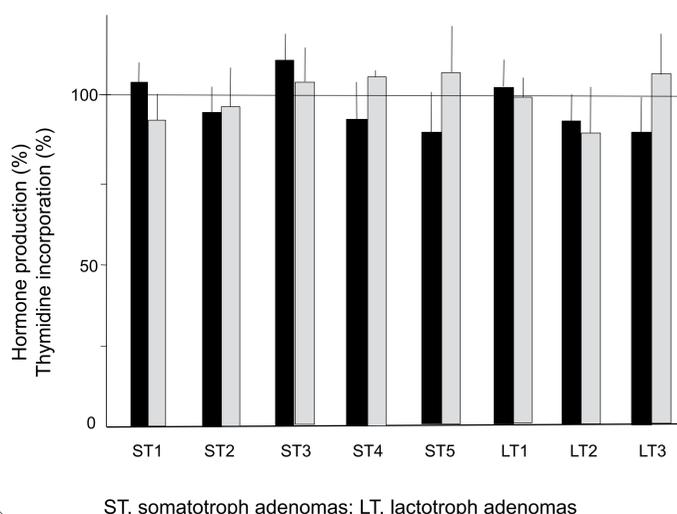
Effects of TMZ in corticotroph AtT20 cells



Effects of TMZ in lactosomatotroph GH3 cells



Effects of TMZ (100 µM) on the growth and hormone secretion of cultured human pituitary adenoma cells



Temozolomide has no effect on hormone secretion in normal rat pituitary cells.

The suppressive effect of TMZ on hormone secretion in AtT20 and GH3 cells is a consequence of the concomitant inhibition of cell proliferation, as the hormone production per cell is not altered.

In a small series of somatotroph adenomas resistant to octreotide and prolactinomas resistant to bromocriptine TMZ had no effect on proliferation or hormone secretion in primary adenoma cell culture.

CONCLUSION

Our data clearly show, that Temozolomide has no direct effect on hormone secretion in normal and tumoral pituitary cell suggesting that the reported suppressive effects of TMZ on excessive hormone secretion are a consequence of concomitant tumor shrinkage. Our data provide no evidence, that TMZ could serve as an alternate drug in the treatment of non-aggressive somatotropinomas or prolactinomas resistant to somatostatin analogs or dopaminergic drugs, respectively.

