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PROGESTERONE, A NEUROSTEROID, AS A POTENTIAL NOVEL GLIOMA THERAPEUTIC AGENT

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BACKGROUND: Glioblastoma multiforme (GBM) is the most common and aggressive malignant primary brain tumor with a median survival of only 4. months without treatment and 50% of mortality rate within a year. For unknown reasons, GBM occurs more commonly in males. Therefore, we hypothesized that the female hormone progesterone, also known as a neurosteroids in the central nervous system (CNS), may play an important role. In this study, we aimed to explore the effects of progesterone (P4) on both human and rat glioma cell lines, as well as its combined effect with temozolomide (TMZ).

METHODS AND RESULTS: Human glioma cell lines U87, D54, U251 and rat glioma cell line C6 were used to study the cytotoxic effect of progesterone (P4) and its combined effect with TMZ using MTT cell proliferation assay. 5000 cells per well of each cell line were seeded into 96-well culture plate for 24 hours before exposure to P4. The testing concentrations of P4 were 100μM to 1μM in a . dilution ratio. The survival of each cell line showed a dose-dependent cytotoxic effect after 72 hours exposure to P4. The half maximal inhibitory concentration (IC50) of all the cell lines varied from 30μM to 100μM. The combined effect of P4 with TMZ was also studied using ascending concentrations of TMZ. The final concentrations of TMZ in the wells reached 250μM, 500μM, 750μM and 1000μM respectively. Relative cell survival rate of glioma indicated that combining P4 with TMZ increased glioma cell death by about 25% when the concentration of TMZ was close to or above its original IC50 (600μM to 800μM).

CONCLUSIONS: Progesterone has been known as a neuro-protective agent. Our findings, however, show that it also has ability to the inhibit glioma cell proliferation or induce cell death. Moreover, when combined with TMZ, P4 can enhance cytotoxicity of TMZ. Therefore, P4 should be further explored as a potential novel therapeutic adjunct in the treatment of GBM.