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Short review of SEC, a potential dexamethasone-sparing regimen for glioblastoma: spironolactone, ecallantide, clotrimazole

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Abstract

This paper presents a short review of data supporting a dexamethasone sparing regimen, SEC, to reduce glioblastoma related brain edema. The conclusion of the reviewed data is that the rationale and risk/benefit ratio favors a pilot study to determine if the three drug regimen of SEC can reduce need for corticosteroid use during the course of glioblastoma. Details of selected pathophysiological aspects of brain edema occurring during the course of glioblastoma and its treatment intersect with the established action of the three old drugs of SEC indicate that they can be repurposed to reduce that edema. Current first-line treatment of this edema is dexamethasone or related corticosteroids. There are multiple negative prognostic implications of both the edema itself and of dexamethasone, prime among them shortened survival, making a dexamethasone sparing regimen highly desirable. SEC uses spironolactone, an antihypertensive potassium-sparing diuretic acting by mineralocorticoid receptor inhibition, ecallantide acting to inhibit kallikrein activation marketed to treat hereditary angioedema, and clotrimazole, an old antifungal drug that inhibits intermediate conductance Ca++ activated K+ channel (KCa3.1). These three old drugs are well known to most clinicians, have a well-tolerated safety history, and have a robust preclinical database showing their potential to reduce the specific edema of glioblastoma. Additionally, these three drugs were chosen by virtue of each having preclinical evidence of glioblastoma growth and/or migration inhibition independent of their edema reduction action. A clinical study of SEC is being planned.

Keywords: clotrimazole; ecallantide; edema; glioblastoma; glioblastome; repurposed; réutilisation; spironolactone; œdème.