Evaluation of Efficacy and Safety of Oral Glyburide for Prevention of Severe or Malignant Cerebral Edema

Eresi Ojebe, PharmD

PGY-1 Pharmacy Resident

Northeast Georgia Medical Center

Gainesville, Georgia

Northeast Georgia Medical Center

- Large community health system
- Serves over 18 counties in Northeast Georgia
- Leading cardiac, comprehensive stroke and level 1 trauma center

Disclosure Statement

- These individuals have the following to disclose concerning possible financial or personal relationships with commercial entities (or their competitors) that may be referenced in this presentation

  - Eresi Ojebe, PharmD: Nothing to disclose
  - Leslie Roebuck, PharmD: Nothing to disclose
  - Phillip Mohorn, PharmD, BCCCP: Nothing to disclose

Background

Cerebral edema (CE) life-threatening complication of CNS injury

An accumulation of intracerebral fluid

Increases morbidity and mortality

Risk factors:

- Younger age
- Severe clinical symptoms
- Large infarct volume
- Higher admission temperature, blood pressure and leukocytes

Background

- Pathophysiology is heterogenous and complex
- Classification:
  - Cytotoxic edema
  - Ionic edema
  - Vasogenic edema
- Current approved therapy focuses on symptomatic management
  - Hyperosmolar therapy
  - Decompressive craniectomy
- Research advancement to identify novel agents for preventative therapy

Background

SUR1-TRPM4:

- Central contributor to CE in different brain pathology
- SUR1-TRPM4 are upregulated in cerebral injury or ischemia
- In animal stroke model, Sur1 protein is increased 2.5-fold within 8h

Glyburide

- SUR1 receptor antagonist
- Preclinical studies project potential role of preventing cerebral edema and/or hemorrhage progression
- GAMES-RP (IV glyburide):
  - Reduction in midline shift in large hemispheric stroke

Sulfonylurea receptor 1 (SUR-1)
Transient Receptor Potential Melastatin 4 (TRPM4)

Purpose

Evaluating the efficacy and safety of oral glyburide therapy in patients with high-risk of developing cerebral edema

Study Design

- IRB-approval pending
- Observational, cohort study using chart review from June, 2022 to June, 2023 of all patients who received oral glyburide compared to patients who did not receive glyburide therapy
- Patients were identified using reports generated from the electronic health record

Study Design

- Inclusion criteria
  - Age ≥ 18 years
  - Admission to NGMC Gainesville critical care service with high risk of developing cerebral edema
- Exclusion criteria
  - Oral glyburide therapy for any other indication
  - Protected population (< 18 years, pregnant, incarcerated)
- Statistical analysis
  - Descriptive statistics
  - Inferential statistics
  - Logistic regression

Treatment Arms

Endpoints

Primary Endpoint

- Progression of cerebral edema defined as development or worsening of edema

Secondary Endpoint

- Timing of initiation
- Incidence of hypoglycemic events
- Incidence of hypoglycemia interventions
- Portion of patients requiring surgical intervention
- Portion of patients with new onset edema or progression of existing edema

Baseline Characteristics

Patient Characteristics	
Age	**Clinical symptoms** • Headache • Disorders of consciousness • Pupillary dilatation • Vomiting
Gender • Male • Female	**Type of injury** • Ischemic stroke • Hemorrhagic stroke • TBI • Tumor
Race • White • Black/African American • Asian • Other	**Charlson Comorbidity index**
Ethnicity • Hispanic • Non-Hispanic	**Weight**

Baseline Characteristics

Patient Characteristics	
Clinical parameters • Blood pressure • POC blood glucose • A1c • Temperature • Leukocytes • ICP • DWI infarct volume • GCS	**Antidiabetic drug prior to admission** • Sulfonylurea • Insulin
Scoring System at Admission • NIHSS • ICH score • Hunt/Hess • mRS score > 4	**Sulfa Allergy**
Treatments • Hyperosmolar therapy • Corticosteroids • Craniectomy	**Interacting drugs** • Warfarin • Carbamazepine • Phenobarbital • Dexamethasone

Conclusions

Limitations

Future Directions

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- Phillip Mohorn, PharmD, BCCCP
  - Cardiovascular Critical Care Clinical Pharmacist Specialist