ABSTRAK

Latar Belakang: *High-grade glioma* (HGG) merupakan tumor sistem saraf pusat (SSP) dengan tingkat morbiditas dan mortalitas tinggi. Berkembangnya tata kelola saat ini masih belum dapat meningkatkan kesintasan secara signifikan, menunjukkan perlunya pengembangan terapi target yang lebih baik. Ekspresi miRNA-10b dan miRNA-21 dalam plasma telah terbukti meningkat pada penderita HGG namun pengaruh keduanya terhadap toksisitas, rekurensi, dan kesintasan penderita HGG yang menjalani kemoterapi menggunakan temozolomide belum banyak diteliti pada subjek manusia.
Tujuan: Membuktikan nilai prediktif ekspresi miRNA-10b dan miRNA-21 dalam plasma terhadap toksisitas, rekurensi, dan kesintasan penderita HGG yang menjalani kemoterapi menggunakan Temozolomide.
Metode: Penelitian ini merupakan analitik observasional dengan pendekatan *mixed cohort* (prosektif dan retrospektif) di RS Kemenkes Sardjito Yogyakarta dan FK-KMK UGM bulan Januari 2021 hingga Desember 2024. Sampel diperoleh dari penderita HGG yang menjalani pembedahan *maximal safe resection* dan menyelesaikan CCRT. Pengambilan sampel secara prospektif menggunakan *consecutive sampling* hingga besar sampel minimal terpenuhi. Kadar miRNA-10b dan 21 dihitung dari plasma penderita sesaat sebelum induksi anestesi. Luaran yang dinilai adalah toksisitas, rekurensi, dan kesintasan.
Hasil: Didapatkan sebanyak 46 sampel untuk analisis toksisitas, 49 sampel untuk analisis rekurensi, dan 60 sampel untuk analisis kesintasan. Analisis toksisitas, 32 penderita (69,6%) tanpa toksisitas berat dan 16 penderita (30,4%) dengan toksisitas berat. Terbukti hubungan signifikan ekspresi miRNA-21 tinggi dengan kejadian toksisitas berat (p=0,037). Analisis rekurensi, 44,9% penderita mengalami rekurensi. MiRNA-10b (p=0,066) dan miRNA-21 (p=0,488) tidak terbukti berhubungan dengan rekurensi. Analisis kesintasan, 66,7% penderita meninggal dengan median *overall survival* (OS) 338 hari. Penderita dengan kadar miRNA-10b tinggi di atas $3.3x10^{-3}$ terbukti memiliki kesintasan lebih pendek (337 vs. 683 hari; p=0,014) dan risiko meninggal lebih tinggi (HR 2,45 (95% CI 1,21-4,96); p 0,013). Sebagian besar sampel berusia di bawah 60 tahun (78,3%). Usia di atas 60 tahun terbukti berhubungan signifikan dengan kesintasan rendah (p=0,014).
Simpulan: Ekspresi tinggi miRNA-21 terbukti berhubungan dengan tingginya kejadian toksisitas berat. Ekspresi tinggi miRNA-10b dan miRNA-21 tidak terbukti berhubungan dengan kejadian rekurensi, sementara ekspresi tinggi miRNA-10b berhubungan dengan rendahnya angka kesintasan penderita HGG.

Kata kunci: Glioma; Micro-RNA; Prognosis; Radioterapi; Temozolomide

ABSTRACT

Background: *High-grade glioma* (HGG) is a central nervous system (CNS) tumor with high morbidity and mortality rates. Despite advances in current management, overall survival has not improved significantly, indicating the need for better-targeted therapies. Plasma expression levels of miRNA-10b and miRNA-21 have been shown to increase in HGG patients. However, their influence on toxicity, recurrence, and survival in patients receiving temozolomide-based chemotherapy has not been extensively investigated in human subjects.
Objective: To evaluate the predictive value of plasma miRNA-10b and miRNA-21 expression levels on toxicity, recurrence, and survival in HGG patients treated with temozolomide.
Methods: This was an analytical observational study with a mixed cohort design (prospective and retrospective) conducted at Sardjito Ministry of Heath Hospital and the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, from January 2021 to December 2024. Samples were collected from HGG patients who underwent maximal safe resection and completed concurrent chemoradiotherapy (CCRT). Consecutive sampling was applied until the minimum required sample size was achieved. Plasma miRNA-10b and miRNA-21 levels were measured preoperatively, immediately before anesthetic induction. The assessed outcomes included toxicity, recurrence, and survival.
Results: A total of 46 samples were analyzed for toxicity, 49 for recurrence, and 60 for survival. Toxicity analysis, 32 patients (69.6%) did not have severe toxicity while 16 patients (30.4%) had severe toxicity. Significant association was found between high miRNA-21 expression with severe toxicity (p=0.037). Recurrence analysis, 44.9% of patients experienced recurrence. Neither miRNA-10b (p=0.066) nor miRNA-21 (p=0.488) showed a significant association with recurrence. Survival analysis, 66.7% of patients had died, with a median overall survival (OS) of 338 days. Patients with high miRNA-10b levels above 3.3×10^{-3} significantly had shorter survival (337 vs. 683 days; p=0.014) and a higher risk of death (HR 2.45, (95% CI 1.21–4.96); p=0.013). Most of the sample were aged below 60 years old (78.3%). Age over 60 years was significantly correlated with shorter survival (p=0.014).
Conclusion: High expression level of miRNA-21 was significantly associated with the incidence of severe toxicity. High expression of miRNA-10b and miRNA-21 did not associate with recurrence, while high expression of miRNA-10b was significantly associated with reduced overall survival in patients with *high-grade glioma*.

Keywords: Glioma; Micro-RNA; Prognosis; Radiotherapy; Temozolomide