Ekspresi gen Manganese Superoxide Dismurase WnSOD) pada sel Glioma manusia: tinjauan khusus pada hipoksia sel tumor

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Abstrak

Latar Belakang: Glioma merupakan tumor otak primer yang sering ditemukan di Indonesia. Sampai saat ini, terapi glioma belum memuaskan karena sering timbul resistens] dan rekurensi sehingga diperlukan terapi tambahan misalnya terapi gen. MnSOD diduga berperan sebagai supresor tumor, namun peran tersebut masih kontroversial. Tumor padat termasuk glioma mempunyai status oksigen yang kurang baik dibandingkan dengan jaringan normal. MnSOD sebagai antioksidan dapat mempengaruhi kadar ROS (Reactive Oxygen Species) yang meningkat pada kondisi hipoksia. Oleh karena itu perlu dianalisis bagaimana ekspresi gen MnSOD pada sel glioma manusia yang hipoksia. Hipoksia pada sel glioma diduga mempengaruhi respon sel tumor terhadap terapi radiasi. Hipoksia tersebut dapat dideteksi dengan suatu petanda Jaringan hipoksia yaitu HIF-1.
Tujuan: Untuk menganalisis ekspresi gen MnSOD, kondisi hipoksia pada sel glioma melalui analisis ekspresi gen HIF-1a serta menganalisis ekspresi gen MnSOD pada sel glioma yang hipoksia.
Desain: Cross Sectional
Metode: Ekspresi gen MnSOD dianalisis dengan membandingkan leve] mRNA dan aktivitas spesifik enzim MnSOD pada sel glioma dengan sel lekosit (kontrol). Ekspresi gen HIF-1a@ dianalisis dengan mebandingkan level MRNA HIF-1la pada sel glioma dengan sel jekosit. Ekspresi MnSOD dan HIF-1 dideteksi pada 20 pasien glioma menggunakan quantitative Real Time RT-PCR untuk kadar relatif mRNA MnSOD dan HIF-1, serta pemeriksaan biokimia untuk mengukur aktivitas enzim MnSOD. Analisis statistik dengan menggunakan SPSS 16.0.
Hasil: Ekspresi gen MnSOD baik mRNA maupun aktivitas spesifik enzim MnSOD pada sebagian besar sampel sel glioma manusia ditemukan lebih rendah secara signifikan (p< 0.01) dibandingkan dengan sel lekosit. Sedangkan mRNA HIF-la pada sebagian besar sel glioma manusia ditemukan lebih tinggi secara signifikan (p< 0.05) dibandingkan dengan sel lekosit. Sebanyak 80 % (16 sampel) menunjukkan mRNA HIF-1 yang tinggi, yang berarti terdapat hipoksia pada sel glioma. Dari 16 sampel tersebut, 11 sampel menunjukkan ekspresi mRNA MnSOD yang rendah dan 4 sampel menunjukkan ekspresi mRNA MnSOD yang tinggi.
Kesimpulan: Ekspresi gen MnSOD pada sebagian besar sampel ditemukan rendah. Ekspresi HIF-1a@ yang tinggi menunjukkan terdapat hipoksia pada sebagian besar sampel scl glioma. Terdapat perbedaan ekspresi MnSOD pada kondisi hipoksia sel glioma.
<hr><i>Background: Glioma is one of the most frequently found primary brains tumors in Indonesia. Until now, treatment of the glioma is far from succesfull due to resistancy and recurrance. Therefore, additional therapy is required, such as gene therapy. MnSOD is antioxidant enzymes which is suggested as tumor suppressor, despite its controversies. Solid tumor such as glioma have low oxygen level in the tissue compare to normal tissues. MnSOD as antioxidant enzyme have potential effects on increased ROS (reactive oxygen species) concentration in hypoxia condition. Therefore, further analysis is needed to explain

MnSOD gene expression in hypoxic human gliomal cells. Hypoxia in gliomal cells are suggested to influence tumor cells responses toward radiotherapy. Hypoxia state can be detected using tissues hypoxic marker, hypoxia inducible factor-la (HIF1).
Desaign: Cross sectional
Aim: To analyzed MnSOD gene expression, hypoxia condition in human glioma cells by analyzing the gene expression of HIF-a and to analyzed MnSOD gene expression in hypoxic human gliomal cells.
Methode: MnSOD gene expression was analyzed by comparing MnSOD mRNA level and enzyme specific activity in glioma cells with leucocytes (control). HIF-1 gene expression was analyzed by comparing HIF-la mRNA level in glioma cells with leucocytes. Twenty glioma patients were included in this study. Quantitative Real Time RT-PCR was used to analyzed MnSOD and HIF-1 mRNA level. Biochemistry test was used to analyzed MnSOD enzyme spesific activity. Statistical analysis was performed using SPSS 16.0.
Results: MnSOD gene expression at mRNA level and enzyme spesific activty in most human glioma samples were significantly lower ($p < .01$) than leucocytes. While HIF-lao mRNA level in most human glioma samples were significantly higher ($p < .05$) than leucocytes, Eighty percents (16) of the samples showed high HIF-1 mRNA level, this mean that glioma samples were in hypoxic state. Among the 16 samples, 11 samples showed low MnSOD mRNA level and 4 samples showed high mRNA MnSOD level. This mean that there were differences in MnSOD gene expression in hypoxic human glioma cells.
Conclusion: MnSOD gene expression in most human glioma samples were low. High HIF-1 mRNA level were found in mosi of plioma samples, meaning that glioma sample were in hypoxic state. There were differences in MnSOD expression in hypoxic human glioma cells.</i>