INTISARI

Latar Belakang: Kanker prostat merupakan kanker dengan prevalensi tinggi setelah kanker paru-paru pada laki-laki. Pada stadium lanjut, penanganan kanker prostat menjadi semakin sulit karena terjadi perkembangan ke arah CRPC(*Castration Resistant Prostate Cancer*). Deteksi perkembangan kanker prostat ke arah CRPC sangat penting dilakukan karena berhubungan dengan prognosis penderita CRPC. Biomarker perkembangan kanker prostat ke arah CRPC perlu bersifat *non-invasive* karena dapat dilakukan berulang-ulang sehingga dapat digunakan untuk mengobservasi hasil terapi maupun menilai progresivitas kanker. Eksosom merupakan salah satu vesikel ekstraseluler yang dikeluarkan oleh sel yang dapat ditemukan di plasma darah dan urin.. Eksosom mengandung konten molekuler yang menjadi fingerprint dari jenis dan status sel yang melepasnya. Dengan mendeteksi ekspresi komponen molekuler *hsa-miR-21-5p,* mRNA reseptor androgen (AR) dan PTEN pada eksosom urin, dapat berpotensi menjadi biomarker alternatif dalam penegakan diagnosis CRPC.
Tujuan: Penelitian ini bertujuan untuk mengkaji ekspresi *hsa-miR-21-5p,* mRNA AR, dan PTEN pada eksosom urin subjek kanker prostat non CRPC (nCRPC) dan CRPC
Metode: Sampel urin dikumpulkan dari 30 pasien (18 nCRPC dan 12 CRPC). Eksosom diekstraksi dari sampel urin menggunakan kit isolasi eksosom miRCURY (Exiqon, Denmark). Isolasi total RNA dilakukan menggunakan miRCURY RNA Isolation Kit-kit Biofluid (Exiqon, Denmark) diikuti oleh sintesis cDNA menggunakan kit Sintesis cDNA Universal (Exiqon, Denmark) Kuantifikasi ekspresi relatif *hsa-miR-21-5p* diperoleh menggunakan qPCR dibandingkan dengan gen referensi, *miR-16-5p*. Sementara kuantifikasi ekspresi mRNA AR dan PTEN dinilai melalui metode RT-PCR semi-kuantitatif dengan gen referensi GAPDH.
Hasil: Hasil pengukuran ekspresi *hsa-miR-21-5p* dan mRNA AR subjek CRPC secara bermakna lebih tinggi dibandingkan subjek nCRPC ($p<0,05$ dan $p<0,01$ masing-masing). Peningkatan ekspresi *hsa-miR-21-5p* juga memiliki korelasi yang kuat dengan mRNA AR pada uji *Pearson*. Sedangkan ekspresi mRNA PTEN kedua kelompok tidak menunjukkan perbedaan yang signifikan ($p>0,05$). Tidak terdapat korelasi yang kuat antara ekspresi mRNA PTEN dengan *hsa-miR-21-5p* dan mRNA AR.
Kesimpulan: Ekspresi *hsa-miR-21-5p* dan mRNA AR pada CRPC lebih tinggi dibandingkan nCRPC. Indentifikasi ekspresi *hsa-miR-21-5p* dan mRNA AR di eksosom urin memiliki potensi untuk mengidentifikasi pasien CRPC.

Kata Kunci: kanker prostat, CRPC, *hsa-miR-21-5p*, AR, PTEN, eksosom urin

ABSTRACT

Background: Prostate cancer is known with high prevalence after lung cancer in men. The treatment of prostate cancer becomes difficult at advanced stage because of the development of CRPC (Castration Resistant Prostate Cancer). It is important to search biomarkers which have ability to detect the progression of CRPC because of it's relation with prognosis. The biomarkers should be can repeatedly used in order to be performed to observe the results of therapy and assess the progression of the cancer. Exosomes, an extracellular vesicle is released by cells and can be found in urin and blood plasma. Exosome contain molecular content which is represent the type and status of cell. Detecting the expression of the molecular component *hsa-miR-21-5p*, androgen receptor mRNA (AR) and PTEN in urine exosomes, it can potentially become an alternative biomarker in establishing the diagnosis of CRPC.
Objective: The aims of this study is to examine the expression of *hsa-miR-21-5p*, mRNA AR, and PTEN in urine exosomes of subjects with non-CRPC (nCRPC) and CRPC prostate cancer
Methods: The urine samples were collected from 30 patients (18 nCRPC and 12 CRPC). Exosomes were extracted from urine samples using the miRCURY exosome isolation kit (Exiqon, Denmark). Isolation of total RNA was performed using the miRCURY RNA Isolation Kit-Biofluid kit (Exiqon, Denmark) followed by cDNA synthesis using the Universal cDNA Synthesis kit (Exiqon, Denmark) Quantification of the relative expression of *hsa-miR-21-5p* was obtained using qPCR compared to the reference gene, *miR-16-5p*. While quantification of mRNA AR and PTEN expressions were assessed through the semi-quantitative RT-PCR method with reference gene GAPDH.
Results: The expression of *hsa-miR-21-5p* and mRNA AR of CRPC subjects were significantly higher than nCRPC subjects ($p<0,05$ and $p<0,01$ respectively). Increased expression of *hsa-miR-21-5p* also had a strong correlation with mRNA AR in the Pearson test. While the expression of mRNA PTEN did not show significant differences between two groups ($p>0,05$). There is also no strong correlation between mRNA PTEN expression with *hsa-miR-21-5p* and AR mRNA.
Conclusion: The expression of *hsa-miR-21-5p* and mRNA AR of CRPC is higher than nCRPC. Detection of *hsa-miR-21-5p* and mRNA AR expression in urine exosomes is potential to be used for diagnostic tools of CRPC patients.

Keywords: prostate cancer, CRPC, *hsa-miR-21-5p*, AR, PTEN, urine exosomes