Studi biodistribusi radiofarmaka lutesium hidroksiapatit (177Lu-HA) untuk terapi kanker hati = Biodistribution study of radiopharmaceutical lutetium hydroxyapatite (177Lu-HA) for liver cancer therapy.

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Abstrak

Studi biodistribusi pada hewan uji memainkan peran utama dalam menentukan efektivitas dan keamanan radiofarmaka sebelum uji klinis pada manusia. Namun, sejauh pengetahuan peneliti berdasarkan literatur, belum ada studi biodistribusi lutesium hidroksiapatit (177Lu-HA) yang dilakukan. Oleh karena itu, pada penelitian ini dilakukan studi biodistribusi kemanan 177Lu-HA untuk terapi kanker hati dengan cara menentukan organ at risk (OAR) radiofarmaka tersebut. Data farmakokinetik 177Lu-HA pada tikus Wistar dari organ yang berbeda, seperti hati, ginjal dan limpa, diperoleh dari literatur. Administrasi radiofarmaka dilakukan secara langsung pada intra arteri hati tikus Wistar dengan cara operasi. Secara total, 13 fungsi sum of exponentials (SOE) dan 1 fungsi logistik digunakan untuk fitting data farmakokinetik. Goodness of fit ditentukan berdasarkan visualisasi grafik, Coefficient of Variation (CV <50%) dan elemen-elemen off-diagonal dari Correlation Matrix (-0,8 CM 0,8). Fungsi terbaik dipilih berdasarkan Corrected Akaike Information Criterion (AICc) dan digunakan untuk perhitungan Time-Integrated Activity Coefficients (TIACs). TIACs manusia diprediksi dengan mentranslasikan TIACs tikus menggunakan metode time-scalling. Dalam penelitian ini OAR ditentukan dengan metode perbandingan TIACs/massa organ pada seluruh organ. Dengan metode perbandingan TIACs/massa organ ini, nilai terbesar mengindikasikan OAR. Secara umum, fitting data farmakokinetik 177Lu-HA dengan fungsi SOE berhasil dilakukan pada semua organ dengan terpenuhinya kriteria goodness of fit. Prediksi massa TIACs/organ manusia menunjukkan bahwa hati yang merupakan organ target akan menerima dosis internal yang paling tinggi (TIACs/masahati=2,78E+0 jam/gram). Tulang dan limpa akan menerima dosis lebih sedikit daripada hati tetapi relatif lebih tinggi daripada organ lainnya (TIACs/masatulang=7,40E-2 jam/gram, TIACs/massalimpa=5,55E-2 jam/gram). Berdasarkan perhitungan TIACs/massa organ tersebut, dapat disimpulkan bahwa OAR radiofarmaka 177Lu-HA yang diadmisitrasikan langsung ke intra arteri hati tikus Wistar adalah hati, tulang, dan limpa.
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Biodistribution study in animal plays a major role in determining the effectiveness and safety of radiopharmaceutical before clinical test in human. However, to the best of author knowledge, there is no biodistribution study of Lutetium Hydroxyapatite (177Lu-HA) available in the literature. Therefore, this study conducted 177Lu-HA biodistribution study of safety for liver cancer therapy by determining organ at risk (OAR) of the radiopharmaceutical. Pharmacokinetics data of 177Lu-HA in Wistar rats from different organs, such as liver, kidneys, and spleen, was obtained from the literature. Radiopharmaceutical administration was carried out directly on the intra artery of Wistar rat liver by surgery. In total, 13 sum of exponentials (SOE) functions and 1 logistic function were used and were fitted to the pharmacokinetics data. The goodness of the fittings was tested based on the visualization of the fitted graphs, coefficient of variations of the fitted parameters (CV<50%) and the elements of correlation matrix (-0,8 CM 0,8). The best function was selected based on the corrected Akaike information criterion (AICc) and was used for the

subsequent calculation of time-integrated activity coefficients (TIACs). Human's TIACs was predicted by extrapolating rat's TIACs using time-scalling method. In this study, OAR was determined by comparison method of TIACs/organ mass in all organs. With this comparison method, the biggest value indicates the OAR. In general, the SOE functions were successfully fitted to the pharmacokinetic data of 177Lu-HA in all organs with a good fit based on the goodness of fit criteria. Human's TIACs/organ mass prediction shows that liver as the organ target will receive high internal doses (TIACs/massliver=2,78E+0 hour/gram). Skeleton and spleen will receive less doses then liver but relatively higher than other organs. (TIACs/massskeletpm=7,40E-2 hour/gram, TIACs/masspleen=5,15E-2 hour/gram). Based on that calculation of TIACs/organ mass, it can be concluded that the OAR of 177Lu-HA pharmaceutical that was administrated directly into the intra-arterial liver of the Wistar rat are liver, skeleton, and spleen.