Efek Pemberian Kinin Topikal Terhadap Pertumbuhan Rambut Mencit Model Alopesia Androgenetik yang DiinduksiTestosteron: Kajian docking in silico, enzim 5α reduktase, prostaglandin E2, malondialdehid, kaspase-3, dan histologi = The Effect of Topical Administration Qunine on Hair Growth in Testosterone-induced Alopecia Mice. in silico docking, 5α reductase, prostaglandyn E2, malondyaldehide, caspase-3, histologi study

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Abstrak

Latar Belakang: Alopesia androgenetik (AAG), merupakan kelainan rambut yang mengganggu secara psikososial bagi sebagian besar lelaki. Pengobatan yang ada saat ini masih terbatas. Kinin secara empirik telah digunakan sebagai zat penumbuh rambut. Namun belum ada penelitian untuk menilai mekanisme kerja dan efektivitas kinin topikal terhadap pertumbuhan rambut.
Metode: Kajian in silico molecular docking dan molecular dynamic simulation dilakukan untuk menilai afinitas kinin terhadap enzim 5α-reduktase dengan kontrol finasterid. Uji hambatan kinin terhadap 5α-reduktase secara in vitro dinyatakan sebagai nilai IC50 kinin, dengan finasterid sebagai pembanding. Pada percobaan in vivo, 28 ekor mencit C57BL/6 dibagi secara acak menjadi 7 kelompok terdiri dari 4 ekor. Kelompok (A) testosteron (alopesia),yang di suntik 1 mg testosteron secara subkutan,(B) testosteron+finasterid 2%(C) kelompok normal, dan kelompok (D-G) testosteron+kinin 0,5%,1%,1,5% dan 2 %. Dioles bahan uji sesuai kelompok setiap hari selama 28 hari. Luas dan panjang rambut dinilai secara visual setiap minggu. Pemeriksaan histologi (morfologi dan kepadatan folikel rambut), pemeriksaan imunohistokimia kaspase-3, pemeriksaan ELISA PGE2 dan pemeriksaan MDA dilakukan setelah 28 hari.
Hasil : Hasil in silico menunjukkan kinin mempunyai afinitas yang cukup baik terhadap 5β-reduktase, meskipun lebih rendah dibanding finasterid (ΔG kinin -31,67 kj/mol dan ΔG finasterid -42,89 kj/mol dari hasil penambatan molekuler; serta ΔG kinin -6,32±12,84 kj/mol dan ΔG finasterid -11,17±18,92 kj/mol dari hasil simulasi dinamika molekuler. Hasil pengukuran hambatan enzim 5α-reduktase didapatkan IC50 kinin 10,6 ±1,40 uM dan IC50 finasterid 0,623 ± 0,14 nM. Luas area pertumbuhan rambut semua kelompok perlakuan kinin lebih luas dibandingkan kelompok alopesia dan berbeda bermakna pada pada minggu ke-3 dan ke-4. Gambaran histopatologi morfologi rambut semua kelompok didominasi fase anagen . Rasio anagen: telogen kelompok perlakuan kinin lebih tinggi dibandingkan kelompok alopesia. Kepadatan folikel rambut kelompok perlakuan kinin lebih tinggi secara bermakna daripada kelompok alopesia. Kinin 0,5%, 1%, dan finasterid menurunkan ekspresi kaspase-3. PGE2 meningkat pada semua kelompok perlakuan kinin, tertinggi pada kinin 2%. dan berbeda bermakna terhadap kelompok alopesia. Pemberian kinin tidak mampu menurunkan kadar MDA.
Kesimpulan: Pemberian kinin pada mencit jantan yang diinduksi testosteron mempunyai efek menumbuhkan rambut, meningkatkan kepadatan folikel rambut. Kinin menghambat enzim 5α-reduktase, meningkatkan kadar PGE2, menurunkan ekspresi Kaspase-3, tetapi tidak menurunkan MDA. Kinin potensial dikembangkan sebagai penumbuh rambut.

Background: Androgenetic alopecia (AGA), is a hair disease which lead to negative psychological effects in most of its sufferers. Currently, treatments of AGA are limited to topical minoxidil and oral finasterid, which possess many side effects. Quinine had empirically used as herbal hair grower, but its mechanism of action and effectiveness are not studied yet.
Methods: Molecular docking was done to analyse the inhibition affinity of the 5β-reductase enzyme of both quinine and finasteride as control. Further, an in vitro test for inhibition of 5α-reductase was carried out by measuring the IC50 on both compounds. The experimental study used male C57BL/6 mice aged 7 weeks. Mice were randomly divided into 7 groups of 4 animals, namely (A) testosterone (alopecia group) which was performed subcutaneous injection of 1 mg testosterone on the back of mice (B) testosterone+2% finasterid, (C) normal group, (D-G) testosterone+0.5%, 1% , 1.5% and 2% quinine. Application of the test material on the back of the mice was carried out daily for 28 days. Hair growth assessment was done visually by assessing hair growth area every week. Histologic examination (hair morphology and density of hair follicles), immunohistochemical examination of caspase-3, ELISA examination for PGE2, and lipid peroxidase by MDA examination were carried out after 28 days.
Results: The results of molecular docking showed that quinine had a good affinity for 5β-reductase, but it was lower than finasterid (ΔG quinine = -31.67 kJ/mol vs ΔG finasterid = 42.89 kJ/mol and from dynamic simulation ΔG quinine -6,32±12,84 kj/mol and ΔG finasteride -11,17±18,92 kj/mol). The IC50 of quinine was 10.6 ± 1.40 uM, while finasterid was 0.623 ± 0.14 nM.The area of hair growth in the quinine treatment group was wider than the alopecia group and showed significance on the 3rd and 4th week. Histopathological features all of the groups was dominated by the anagen phase. The anagen:telogen ratio of the alopecia group was lower than that of the quinine group. The density of hair follicles in the treatment group and the alopecia group was statistically significant.The administration of 0.5% and 1% quinine, as well as finasterid, decreased the expression of caspase-3. PGE2 was increased in the quinine treatment group and significant compared to the alopecia group. MDA levels were higher in quinine compared to alopecia group.
Conclusion: Quinine was efficacious in promoting hair growth in AGA mouse models. It is inhibited 5α-reductase enzyme, increasing PGE2, decreasing caspase-3. However it was unable to suppress MDA levels. Hence, topical quinine has the potential to be further developed into a herbal medicine for hair growth.