# Efek Madu Manuka 100% dan Trigona Terhadap Proses Re-epitelisasi Membran Timpani Pascaoperasi pada Otitis Media Supuratif Kronik Tipe Aman Tenang:Peran Keratinocyte Growth Factor, Basic Fibroblast Growth Factor, Serta Pertumbuhan Keratinosit dan Fibroblas = Effects of 100% Manuka and Trigona Honey on Re-epithelialization Post-tympanoplasty in Chronic Suppurative Otitis Media: the Role of Keratinocyte Growth Factor, Basic Fibroblast Growth Factor, and Proliferation of Keratinocytes and Fibroblasts

Harim Priyono, author



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Abstrak

Manfaat madu untuk penyembuhan luka sudah banyak diteliti, namun informasi manfaatnya untuk penyembuhan luka timpanoplasti masih terbatas. Penelitian ini bertujuan mengevaluasi efek madu manuka (Mn) dan madu trigona (Tr) asli Indonesia pada re-epitelisasi membran timpani (MT) melalui potensi proliferasi fibroblas, keratinosit, sekresi KGF dan basic-FGF.
Penelitian in vivo berupa uji klinis acak, tersamar ganda, pada 64 pasien dewasa otitis media supuratif kronik (OMSK) tipe aman tenang yang menjalani timpanoplasti di RSUPN dr. Cipto Mangunkusumo pada bulan Juni 2021–Agustus 2022. Pasien diacak dan disamarkan ke dalam dua kelompok, yaitu diberikan gelfoam plus gel  Mn 100% medical grade (intervensi) atau hanya diberikan gelfoam (kontrol) di liang telinga saat timpanoplasti. Tampon telinga diangkat setelah dua minggu dan pasien diminta kontrol setiap minggu selama enam minggu. Penelitian in vitro dilakukan di Laboratorium Universitas YARSI. Kultur fibroblas dan keratinosit yang diisolasi dari pasien OMSK diberikan pajanan Mn dan Tr dengan tiga konsentrasi yaitu 0,04%, 0,1%, dan 0,25%, kemudian dilakukan uji proliferasi, KGF dan bFGF juga diukur dan dibandingkan dengan kelompok kontrol.
Proporsi pengeringan luka pascatimpanoplasti kelompok intervensi lebih banyak secara bermakna dibandingkan kontrol pada minggu ke-3, ke-4, dan ke-6. Madu manuka dan Tr tidak meningkatkan jumlah sel kultur fibroblas, tetapi mempersingkat durasi doubling time. Jumlah sel kultur keratinosit lebih tinggi secara bermakna dibandingkan kontrol pada semua kelompok Mn dan Tr 0,04%. Sekresi KGF meningkat seiring pertambahan sel. Pada hari ke-6 dan hari ke-8, sekresi KGF lebih tinggi pada beberapa kelompok intervensi dibandingkan kontrol. Sebaliknya, kadar bFGF menurun seiring pertambahan sel. Terdapat korelasi positif antara lama pajanan kedua jenis madu dengan proliferasi fibroblas. Lama pajanan Mn 0,04%, 0,1%, dan Tr 0,04% berkorelasi positif dengan jumlah sel kultur keratinosit.
Disimpulkan pemberian Mn saat timpanoplasti meningkatkan pencapaian re-epitelisasi MT sempurna melalui efeknya pada fibroblas dan keratinosit, serta berpotensi meningkatkan keberhasilan timpanoplasti. Penelitian ini juga menunjukkan efek positif Tr pada fibroblas dan keratinosit, sehingga potensi terapeutik madu ini dapat diteliti lebih lanjut
.....Benefits of honey on wound healing have been widely reported, but information about its effect on the re-epithelialization of the tympanic membrane (TM) is limited. This study aims to evaluate the effect of manuka honey (MH) and trigona honey (TH) from Indonesia, on TM re-epithelization through their potential action on the proliferation of fibroblasts, keratinocytes, secretion of KFG and basic-FGF.

The in vivo study was a randomized, controlled, double-blind clinical trial on 64 adult patients with mucosal type chronic suppurative otitis media (CSOM) undergoing tympanoplasty at Cipto Mangunkusumo General Hospital from June 2021–August 2022. Patients were randomized and blinded into two groups, receiving either gel foam soaked in 100% medical grade MH (intervention group) gel or only gel foam (control group) placed in the external auditory canal during tympanoplasty. The ear tampon was removed after two weeks, and patients were followed up weekly for six weeks. The in vitro study was conducted at the YARSI University Laboratory. Fibroblast and keratinocyte cultures isolated from CSOM patients were exposed to MH and TH with three dilutions: 0.04%, 0.1%, and 0.25%. The cells were then subjected to proliferation assays, KGF and bFGF were also assessed and compared with the control group.

The intervention group had a significantly higher proportion of dry tympanoplasty wounds than control at the 3rd, 4th, and 6th visit. Manuka honey and TH did not increase the number of fibroblasts but shortened the doubling time duration. A significantly higher number of keratinocytes than control was observed in all MH groups and the 0.04% TH group. KGF secretion increased as the number of cells increased. On day 6 and day 8, KGF secretion was higher in some of the intervention groups compared with the control group. In contrast, fibroblast bFGF secretion decreased as the number of cells increased. There was a positive correlation between the exposure time of all intervention groups and the number of cells in the fibroblast culture. Prolonged exposure time to 0.04% MH, 0.1% MH, and 0.04% TH were positively correlated with the number of keratinocytes.

The application of MH during tympanoplasty increased complete TM re-epithelialization through its effect on fibroblasts and keratinocytes proliferation. MH has the potential to improve tympanoplasty outcomes. This present study also illustrated the positive effects of TH on fibroblasts and keratinocytes; thus, its potential therapeutic properties could be further explored.