SKRIPSI

PENGARUH FAKTOR PERTUMBUHAN PLATELET TERHADAP KADAR *INTERLEUKIN-1β* (IL-1β) PADA TIKUS PUTIH MODEL OSTEOARTHRITIS

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FAKULTAS KEDOKTERAN

UNIVERSITAS SRIWIJAYA

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Diajukan untuk memenuhi salah satu syarat memperoleh gelar
Sarjana Kedokteran (S.Ked)

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HALAMAN PENGESAHAN

PENGARUH *ACTIVATED GROWTH FACTOR* (AGF) DARI PLATELET TERHADAP KADAR *INTERLEUKIN-1β* (IL-1β) PADA TIKUS PUTIH MODEL OSTEOARTHRITIS

LAPORAN AKHIR SKRIPSI

Diajukan untuk memenuhi salah satu syarat memperoleh gelar Sarjana Kedokteran (S.Ked)

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Karya tulis ilmiah berupa laporan akhir skripsi dengan judul "Pengaruh *Activated Growth Factor* (AGF) dari Platelet terhadap Kadar *Interleukin-1β* (IL-1β) pada Tikus Putih Model Osteoarthritis" telah dipertahankan di hadapan Tim Penguji Karya Tulis Ilmiah Program Studi Pendidikan Dokter Fakultas Kedokteran Universitas Sriwijaya pada tanggal 11 Desember 2023.

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Menyatakan bahwa Skripsi saya merupakan hasil karya sendiri didampingi tim pembimbing dan bukan hasil penjiplakan/plagiat. Apabila ditemukan unsur penjiplakan/plagiat dalam Skripsi ini, maka saya bersedia menerima sanksi akademik dari Universitas Sriwijaya sesuai aturan yang berlaku.

Demikian, pernyataan ini saya buat dalam keadaan sadar dan tanpa ada paksaan dari siapapun.

Palembang, 11 Desember 2023

Muhammad Rizky Hidayatullah

ABSTRAK

PENGARUH FAKTOR PERTUMBUHAN PLATELET TERHADAP KADAR *INTERLEUKIN-1B* (IL-1B) PADA TIKUS PUTIH MODEL OSTEOARTHRITIS

(Muhammad Rizky Hidayatullah, 11 Desember 2023)

Fakultas Kedokteran, Universitas Sriwijaya

Latar Belakang: Osteoarthritis (OA) adalah penyakit degeneratif tulang rawan sendi yang diikuti oleh peradangan rongga synovial. *Interleukin-1β* (IL-1β) bertanggung jawab pada proses terjadi OA. Faktor pertumbuhan platelet diprediksi mampu memodulasi penyembuhan OA. Tujuan penelitian ini untuk mengetahui pengaruh pemberian FPP terhadap kadar IL-1β.
Metode: Eksperimental *in vivo* menggunakan pendekatan *post-test only with control group*, dilaksanakan pada bulan September – November 2023 di Eureka Research Laboratory. Setelah melewati proses aklimatisasi, 30 ekor tikus putih jantan (*Rattus norvegicus*) galur Wistar dibagi ke dalam lima kelompok perlakuan yaitu kontrol normal (tanpa perlakuan), kontrol negatif (induksi OA), dan tiga lainnya yaitu induksi OA+ injeksi FPP (TGF-β 100 pg/mL, 1000 pg/mL, dan 10.000 pg/mL). Induksi OA menggunakan *monoiodoasetat* (MIA) dosis 4,8 mg/60μL secara intra-artikular dan dievaluasi setelah 28 hari melalui pengukuran diameter sendi. Selanjutnya, sendi lutut tikus diberikan injeksi FPP selama 21 hari. Setelah perlakuan selesai, sendi lutut tikus diambil dan dilakukan pemeriksaan kadar IL-1β dengan ELISA metode *sandwich.* Data kemudian diolah dengan software IBM SPSS Statistic 25 menggunakan uji *one-way* ANOVA dan *post-hoc* Bonferroni.
Hasil: Rerata kadar IL-1β dalam pg/mL secara berurutan: 6.50 ± 0.67; 95.02 ± 2.45; 79.14 ± 1.68; 51.97 ± 1.34; 29.34 ± 2.03. Pemberian FPP berpengaruh dalam menurunkan kadar IL-1β secara signifikan (*p value* < 0.05). Penurunan kadar IL-1β berbanding lurus dengan dosis FPP yang diberikan, semakin tinggi dosis maka semakin besar penurunan kadar IL-1β.
Kesimpulan: FPP dari platelet berpengaruh dalam menurunkan kadar IL-1β.

Kata Kunci: *Growth factor, IL-1β, Osteoarthritis, Platelet, TGF-β.*

ABSTRACT

THE EFFECT OF ACTIVATED GROWTH FACTOR (AGF) FROM PLATELETS ON INTERLEUKIN-1β (IL-1β) LEVELS IN OSTEOARTHRITIS-INDUCED ALBINO RAT

(Muhammad Rizky Hidayatullah, December 11th, 2023)

Faculty of Medicine, Universitas Sriwijaya

Background: Osteoarthritis (OA) is a degenerative joint cartilage disease followed by synovial cavity inflammation. Interleukin-1β (IL-1β) is responsible for the process of OA. Activated growth factor (AGF) from platelets is predicted to modulate OA healing. This study aims to determine the effect of AGF administration on IL-1β levels.

Methods: In vivo experiment by using a post-test only with a control group approach, conducted in September - November 2023 at Eureka Research Laboratory. After the acclimatization process, 30 white rats (Rattus norvegicus) Wistar strain were divided into five treatment groups, namely standard control (no treatment), negative control (OA induction), and three others, namely OA induction + AGF injection (TGF-β 100 pg/mL, 1000 pg/mL, and 10,000 pg/mL). OA was induced by using monoiodoacetate (MIA) in a dose of 4.8 mg/60µL intra-articularly and evaluated after 28 days through measurement of joint diameter. Subsequently, rat knee joints were injected with AGF for 21 days. After the treatment, rat knee joints were taken, and IL-1β levels were examined using the sandwich method ELISA. Data were then processed with IBM SPSS Statistic 25 software using one-way ANOVA and Bonferroni post-hoc tests.

Results: Mean IL-1β levels in pg/mL were: 6.50 ± 0.67; 95.02 ± 2.45; 79.14 ± 1.68; 51.97 ± 1.34; 29.34 ± 2.03. AGF administration had an effect in reducing IL-1β levels significantly (p-value < 0.05). The decrease in IL-1β levels were directly proportional to the dose of AGF given; the higher the dose, the greater the decrease in IL-1β levels.

Conclusion: AGF from platelets has an effect in reducing IL-1β levels.

Keywords: Activated growth factor, IL-1β, Osteoarthritis, Platelet, and TGF-β.

RINGKASAN

PENGARUH FAKTOR PERTUMBUHAN PLATELET TERHADAP KADAR *INTERLEUKIN-1B* (IL-1B) PADA TIKUS PUTIH MODEL OSTEOARTHRITIS

Karya tulis ilmiah berupa skripsi, 11 Desember 2023

Muhammad Rizky Hidayatullah; Dibimbing oleh dr. Rachmat Hidayat, M.Sc dan Ibu Rara Inggarsih, S.ST., M.Kes

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xx + 148 halaman, 13 tabel, 47 gambar, 8 lampiran

Osteoarthritis (OA) adalah penyakit degeneratif tulang rawan sendi yang diikuti oleh peradangan di rongga synovial. OA menjadi alasan utama untuk nyeri sendi dan gangguan fungsional di dunia. Mediator pro-inflamasi yaitu *interleukin-1β* (IL-1β) bertanggung jawab untuk proses katabolisme sehingga terjadi OA. Faktor pertumbuhan platelet diprediksi memiliki kapasitas untuk memodulasi penyembuhan OA. Tujuan dari penelitian ini untuk mengetahui pengaruh pemberian FPP terhadap kadar IL-1β.

Penelitian ini merupakan eksperimental *in vivo* menggunakan pendekatan *post-test only with control group.* Penelitian dilaksanakan pada bulan September – November 2023 di Eureka Research Laboratory, Palembang. Penelitian ini menggunakan 30 ekor tikus putih (*Rattus norvegicus*) galur Wistar. Sebelum diberi perlakuan, tikus melewati proses aklimatisasi. Setelah melewati proses aklimatisasi, tikus dibagi ke dalam lima kelompok perlakuan yaitu kontrol normal (tanpa perlakuan), kontrol negatif (induksi OA), tiga lainnya yaitu induksi OA+ injeksi FPP (TGF-β 100 pg/mL, 1000 pg/mL, dan 10.000 pg/mL). Induksi OA menggunakan *monoiodoasetat* (MIA) dosis 4,8 mg/60µL diberikan secara intra-artikular dan dievaluasi setelah 28 hari melalui pengukuran diameter sendi dengan jangka sorong. Selanjutnya, sendi tikus diberikan perlakuan injeksi faktor pertumbuhan platelet selama 21 hari. FPP diproduksi dari darah intravena tikus dan dilakukan penilaian kadar TGF-β menggunakan ELISA. Setelah semua perlakuan selesai, tikus dilakukan euthanasia dan diambil sendi lututnya untuk pemeriksaan kadar *interleukin-1β* (IL-1β) dengan ELISA metode *sandwich.* Data kemudian diolah dengan software IBM SPSS Statistic 25 menggunakan uji *one-way* ANOVA dan *post-hoc* Bonferroni.

Didapatkan rerata kadar IL-1β dalam pg/mL secara berurutan adalah sebagai berikut: 6.50 ± 0.67; 95.02 ± 2.45; 79.14 ± 1.68; 51.97 ± 1.34; 29.34 ± 2.03. Pemberian FPP yaitu TGF-β sebesar 100 pg/mL, 1.000 pg/mL, dan 10.000 pg/mL berpengaruh dalam menurunkan kadar IL-1β secara signifikan (p *value* < 0.05). Penurunan kadar IL-1β berbanding lurus dengan dosis FPP yang diberikan, semakin tinggi dosis maka semakin besar penurunan kadar IL-1β.

Faktor pertumbuhan platelet berpengaruh dalam menurunkan kadar IL-1β.

Kata Kunci: *Growth factor, IL-1β, Osteoarthritis, Platelet, TGF-β.*

SUMMARY

THE EFFECT OF ACTIVATED GROWTH FACTOR (AGF) FROM PLATELETS ON INTERLEUKIN-1β (IL-1β) LEVELS IN OSTEOARTHRITIS-INDUCED ALBINO RAT

Scientific Paper in the form of Skripsi, December 11th, 2023

Muhammad Rizky Hidayatullah; supervised by dr. Rachmat Hidayat, M.Sc and Rara Inggarsih, S.ST., M.Kes

Medical Science Department, Faculty of Medicine, Universitas Sriwijaya

xx + 148 pages, 13 tables, 47 pictures, 8 attachments

Osteoarthritis (OA) is a degenerative joint cartilage disease followed by synovial cavity inflammation. OA is the main reason for joint pain and functional impairment in the world. The pro-inflammatory mediator interleukin-1β (IL-1β) is responsible for the catabolic process that cause OA. Activated growth factor (AGF) from platelets is predicted to have the capacity to modulate OA healing. This study aims to determine the effect of AGF administration on IL-1β levels.

This research is an in vivo experiment by using a post-test only with a control group approach. The research was conducted from September to November 2023 at Eureka Research Laboratory, Palembang. This study used 30 white rats (Rattus norvegicus) Wistar strain. Before being treated, the rats went through an acclimatization process. After the acclimatization process, the rats were divided into five treatment groups: normal control (no treatment), negative control (OA induction), the other three were OA induction + AGF injection (TGF-β 100 pg/mL, 1000 pg/mL, and 10,000 pg/mL). OA was induced by using monoiodoacetate (MIA) in a dose of 4.8 mg/60μL was given intra-articularly and evaluated after 28 days by measuring joint diameter with a caliper. Furthermore, rat joints were treated with activated growth factor (AGF) injection for 21 days. AGF was produced from the intravenous blood of rats, and TGF-β levels were assessed using ELISA. After all treatments, rats were euthanized, and knee joints were taken to examine interleukin-1β (IL-1β) levels by ELISA sandwich method. Data were then processed with IBM SPSS Statistic 25 software using one-way ANOVA and Bonferroni post-hoc tests.

The results revealed that mean IL-1β levels in pg/mL were sequentially as follows: 6.50 ± 0.67; 95.02 ± 2.45; 79.14 ± 1.68; 51.97 ± 1.34; 29.34 ± 2.03. The administration of AGF, namely TGF-β at 100 pg/mL, 1,000 pg/mL, and 10,000 pg/mL had an effect in reducing IL-1β levels significantly (p-value <0.05). The decrease in IL-1β levels were directly proportional to the dose of AGF given; the higher the dose, the greater the decrease in IL-1β levels.

Activated growth factor (AGF) from platelets has an effect in reducing IL-1β levels.

Keywords: Activated growth factor, IL-1β, Osteoarthritis, Platelet, and TGF-β.

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Alhamdulillahirabbilalamin, puji dan syukur saya panjatkan kepada Allah Swt. yang telah melimpahkan rahmat dan hidayah-Nya sehingga karya tulis dengan judul "Pengaruh Faktor Pertumbuhan Platelet terhadap Kadar *Interleukin-1β* (IL-1β) pada Tikus Putih Model Osteoarthritis" yang menjadi salah satu syarat untuk memperoleh gelar S.Ked dapat diselesaikan dengan baik. Keberhasilan penyelesaian skripsi ini tidak terlepas dari berbagai pihak yang telah memberikan doa, arahan, dan bantuan selama proses penyusunannya. Oleh karena itu, pada kesempatan ini penulis ingin menyampaikan rasa terima kasih yang tulus kepada:

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Palembang, 11 Desember 2023

Muhammad Rizky Hidayatullah

DAFTAR ISI

DAFTAR GAMBAR

DAFTAR TABEL

DAFTAR LAMPIRAN

DAFTAR SINGKATAN

ADAMTS	: *a disintegrin and metalloproteinase with thrombospondin motifs*
ALK	: *anaplastic lymphoma kinase*
Alpha SMA	: *alpha smoth muscle actin*
AP-1	: *activating protein-1*
BMP	: *bone morphogenetic protein*
CCL5	: *C-C motif chemokine ligand 5*
CDK	: *cyclin dependent kinase*
Col2a1	: *colagen type II alpha 1*
COX	: *cyclooxygenase*
ECM	: *extracellular matrix*
EGF	: *epidermal growth factor*
ELISA	: *enzyme linked immunosorbent assay*
ERK	: *extracellular signal-regulated kinase*
FADD	: *Fas-associated death domain*
FGF	: *fibroblast growth factor*
Grb2	: *growth factor receptor-bound protein 2*
HGF	: *hepatosit growth factor*
IGF-1	: *insulin like growth factor-1*
IKK	: *inhibitor of kappa B kinase*
IL-1B	: *interleukin 1-beta*
IL1R	: *interleukin 1 receptor*
IL-6	: *interleukin 6*
iNOS	: *inducible nitric oxide synthase*
JNK	: *c-Jun N-Kinase*
MAPK	: *mitogen activated protein kinase*
MCH	: *mean cospuscular hemoglobin*
MCHC	: *mean corpuscular hemoglobin concentration*
MCV	: *mean corpuscular volume*

MIA : *monoiodoacetate*
MMP : *matrix metalloproteinase*
MPV : *mean platelet volume*
NF-kB : *nuclear factor of kappa beta*
NO : *nitric oxide*
NOS : *nitric oxide synthase*
OA : *osteoarthritis*
OD : *optical density*
PDGF : *platelet derived growth factor*
PGE2 : *prostaglandin E2*
PI3K : *phosphatidylinositol 3-kinase*
PKCδ : *protein kinase c omega*
PLCγ : *phospholipase c gamma*
pRB : *protein retinoblastoma*
RANKL : *receptor activator of nuclear factor kappa beta ligand*
RANTES : *regulated upon activation normal T-cell expressed and secreted*
RIP1 : *receptor interacting serine/threonine kinase 1*
SMAD : *supressor of mothers of against decapentaplegic*
STAT : *signal transducers and activator of transcription*
TAB : *TAK1-binding protein*
TAD : *trans activation domain*
TAK1 : *transforming growth factor beta activated kinase-1*
TBR : *transforming growth factor beta receptor*
TGF-B : *transforming growth factor beta*
TNF-a : *tumor necrosis factor alpha*
TNFR : *tumor necrosis factor receptor*
TRADD : *tumor necrosis factor receptor type-1 associated death domain*
TRAF : *TNF receptor associated factor*
VEGF : *vascular endothelial growth factor*

BAB 1
PENDAHULUAN

1.1 Latar Belakang

Osteoarthritis (OA) adalah penyakit degeneratif tulang rawan sendi yang diikuti oleh peradangan di rongga sinovial yang menjadi alasan utama untuk nyeri sendi dan gangguan fungsional di dunia.[1] Perubahan patologis yang terlihat pada sendi OA termasuk kehilangan progresif dan penghancuran tulang rawan artikular, penebalan tulang subkondral, pembentukan osteofit, peradangan sinovium, degenerasi ligamen dan menisci lutut, serta hipertrofi kapsul sendi.[2] Menurut World Health Organization (WHO), sekitar 528 juta orang di seluruh dunia hidup dengan OA pada tahun 2019 yang meningkat 113% sejak 1990. Lutut adalah sendi yang paling sering terkena dengan prevalensi 365 juta, diikuti oleh pinggul dan tangan. Selain itu, 344 juta orang yang hidup dengan OA mengalami tingkat keparahan sedang atau berat.[3] Prevalensi OA di Indonesia cukup tinggi, sebesar 15,5% pada pria dan 12,7% pada wanita, serta 70% pasien osteoartritis berusia di atas 65 tahun.[4]

Gejala utama OA termasuk rasa sakit, kekakuan, hilangnya fungsi, kelemahan otot, keseimbangan yang buruk, deformitas sendi, dan ketidakstabilan.[5] Gejala klinis yang umum terjadi pada OA adalah timbulnya nyeri yang timbul secara bertahap dan memburuk dengan aktivitas.[6] Faktor-faktor yang mempengaruhi risiko dan tingkat keparahan OA secara signifikan terkait dengan usia yang lebih tua, jenis kelamin perempuan, cedera sendi, faktor anatomi, aktivitas kerja berat, beberapa kegiatan olahraga profesional, obesitas, dan genetika.[5] Perkembangan OA yang sangat signifikan, gejala yang sangat menggangu, dan faktor risiko yang banyak membuat OA perlu menjadi perhatian.

Osteoarthritis dihasilkan dari kegagalan kondrosit untuk mempertahankan homeostasis atau keseimbangan antara sintesis dan degradasi komponen matriks ekstraseluler. Berbagai faktor menyebabkan hilangnya homeostasis tulang rawan, yang mengakibatkan degradasi matriks ekstraseluler.[7] Produk degradasi termasuk fragmen tulang rawan dan molekul endogen yang berasal dari kondrosit nekrotik

yang dilepaskan ke dalam cairan sinovial akan dikenali oleh makrofag sinovial sehingga memulai respons inflamasi. Aktivasi makrofag pada sendi mengarah pada produksi sitokin proinflamasi dan *matrix metalloproteinases* (MMP), termasuk IL-1β, IL-6, IL-8, TNF-α, dan MMP-13 yang dianggap sebagai pendorong utama kerusakan sendi dan patogenesis OA. *Matrix metalloproteinases* (MMP) menyebabkan degradasi kolagen, sedangkan *a disintegrin and mtalloproteinase with thrombospondin motifs* (ADAMTS) akan mendegradasi proteoglikan. Hilangnya tulang rawan tersebut melemahkan fungsi normal sendi yang pada akhirnya menghasilkan perkembangan rasa sakit dan cacat OA.[8]

Mediator pro-inflamasi, seperti sitokin juga bertanggung jawab untuk proses katabolisme dan pelepasan enzim proteolitik, menurunkan matriks ekstraseluler, dan memediasi kehilangan tulang rawan. Salah satu contoh sitokin utama pro-inflamasi adalah *interleukin-1β* (IL-1β).[9] IL-1β meningkat pada penyakit peradangan sendi salah satunya osteoarthtiris (OA). Pada OA, IL-1β adalah penyebab utama degradasi tulang rawan, mampu mengurangi sintesis kolagen tipe II dan proteoglikan, serta dapat merangsang pelepasan enzim pendegradasi matriks (MMP, ADAMTS 4 dan 5) dari kondrosit. IL-1β memberikan tindakan pleiotropik pada banyak sel tulang rawan, termasuk kondrosit, osteoblas, osteoklas, makrofag sinovial, dan fibroblast. Tingkat membran reseptor IL-1 (IL-1RI) serta protein sitoplasma yang terlibat dalam transduksi pensinyalan IL-1β diregulasi dalam kondrosit osteoarthritis.[10]

Sebuah studi *Canakinumab Anti-Inflammatory Thrombosis Outcomes Study* (CANTOS) dengan menggunakan lebih dari 10.000 pasien, termasuk uji coba kontrol acak, menyelidiki peran canakinumab (antibodi monoklonal yang diarahkan pada IL-1β) dalam pencegahan kardiovaskular sekunder. Hasil sekunder pasien yang menerima canakinumab menunjukkan kurang rentan untuk menjalani operasi penggantian sendi untuk OA lutut dibandingkan dengan kontrol. Penelitian ini menunjukkan peran penghambatan IL-1β pada OA diperlukan. Oleh karena itu, IL-1β menjadi pusat perhatian dan target dalam terapi osteoarthritis.[11]

Strategi pengobatan untuk OA dapat dibagi menjadi tiga kategori yaitu intervensi non-farmakologis, intervensi farmakologis, dan intervensi bedah. Intervensi non-farmakologis seperti modifikasi gaya hidup tidak cukup efektif bagi banyak pasien yang mengalami gejala OA. Intervensi bedah harus dipertimbangkan sebagai tahap akhir untuk mengganti sendi agar mendapatkan kembali fungsinya. Intervensi farmakologis OA, seperti *nonsteroidal anti-inflammatory drugs* (NSAID), asetaminofen, *duloxetine*, dan injeksi glukokortikoid intra-artikular dapat efektif, tetapi juga memiliki keterbatasan substansial.[12]

Di antara intervensi farmakologis yang direkomendasikan, *nonsteroidal anti-inflammatory drugs* (NSAID) yang sangat efektif dalam mengurangi rasa sakit. Namun, konsekuensi yang terkait dengan penggunaan NSAID jangka panjang, terutama pada orang tua.[13] Pada orang tua, NSAID meningkatkan risiko tukak lambung fatal hampir lima kali, risiko komplikasi ulkus peptikum meningkat tiga sampai lima kali lipat. Hal tersebut dapat menyebabkan morbiditas dan mortalitas yang signifikan. Selain itu, NSAID dapat menyebabkan disfungsi ginjal termasuk penurunan perfusi glomerulus, penurunan laju filtrasi glomerulus, dan gagal ginjal akut. NSAID juga telah terbukti menyebabkan atau memperburuk gagal jantung, dan NSAID dosis tinggi (dosis anti-inflamasi) dapat meningkatkan risiko gangguan kognitif.[14] Sebagian besar pasien OA adalah lansia dan kebanyakan dari mereka akan memiliki beberapa komorbiditas. Oleh karena itu, perhatian khusus harus diberikan pada kemungkinan interaksi dan efek samping yang dapat ditimbulkan oleh obat sistemik pada populasi ini.[15] Dengan demikian, ada kebutuhan klinis yang belum terpenuhi untuk studi etiologi dan pengobatan alternatif untuk OA.

Saat ini agen biologis sangat berpotensi menjadi solusi untuk terapi osteoarthritis seperti platelet. Platelet adalah fragmen sitoplasma kecil yang berasal dari megakariosit sumsum tulang yang mengandung lebih dari 800 protein dan molekul, contohnya yaitu *growth factor*.[16] *Growth factor* telah terbukti memiliki efek yang menguntungkan pada beberapa penyakit. Sebagai contoh, *platelet derived growth factor* (PDGF) adalah *growth factor* rekombinan pertama dan satu-satunya yang disetujui oleh Food and Drug Administration (FDA) di AS untuk pemberian topikal dan digunakan untuk pengobatan ulkus kaki diabetik. Dalam uji

coba terkontrol secara acak, pasien yang diobati dengan PDGF, 48% sembuh dibandingkan dengan 25% pasien yang diobati dengan plasebo.[17] Selain itu, Roberto Seijas et al. merawat pasien dengan robekan ligamentum cruciatum anterior parsial dengan plasma intraligamen kaya *growth factor*, mereka menemukan bahwa kemampuan pasien dapat dikembalikan ke tingkat sebelum cedera.[18] Pada tulang, *growth factor* diyakini memiliki peran penting dalam memengaruhi kemotaksis, diferensiasi, proliferasi dan aktivitas sintetis tulang rawan dan sel-sel tulang, sehingga mengatur *remodelling* fisiologis dan penyembuhan tulang rawan.[19]

Growth factor yang diaktifkan yang dilepaskan oleh platelet memiliki kapasitas untuk memodulasi penyembuhan dan potensial untuk terapi osteoarthritis. Di antara banyak *growth factor*, TGF-β dianggap sebagai kelompok yang memainkan salah satu dari banyak peran kunci dalam pemeliharaan homeostasis metabolik dalam jaringan tulang. TGF-β merupakan salah satu FPP utama yang dilepaskan oleh platelet terutama penting untuk pertumbuhan matriks tulang rawan. TGF-β memiliki efek anabolik pada tulang rawan, menginduksi proliferasi sel, produksi matriks, dan diferensiasi osteokondrogenik. TGF-β juga meningkatkan ekspresi gen kolagen tipe II dan aggrecan.[20] Selain itu, FPP platelet lainnya seperti PDGF, IGF, EGF, HGF, dan FGF diyakini mempunyai peran pada perbaikan osteoarthritis.[21] Oleh karena itu, penelitian ini bertujuan untuk melihat pengaruh faktor pertumbuhan platelet terhadap kadar *interleukin-1β* (IL-1β) dengan menggunakan tikus putih sebagai model osteoarthritis.

1.2 Rumusan Masalah

Bagaimana pengaruh faktor pertumbuhan platelet terhadap kadar *interleukin-1β* (IL-1β) pada tikus putih model osteoarthritis?

1.3 Tujuan Penelitian

1.3.1 Tujuan Umum

Mengetahui pengaruh faktor pertumbuhan platelet terhadap kadar *interleukin-1β* (IL-1β) pada tikus putih model osteoarthritis.

1.3.2 Tujuan Khusus

1. Mengetahui rerata kadar *interleukin-1β* (IL-1β) pada setiap kelompok perlakuan yang diukur dengan *enzyme-linked immunosorbent assay* (ELISA).
2. Mengetahui signifikasi pemberian faktor pertumbuhan platelet terhadap kadar *interleukin-1β* (IL-1β) pada tikus putih model osteoarthritis.
3. Mengetahui mekanisme pengaruh faktor pertumbuhan platelet pada penyakit osteoarthritis.

1.4 Hipotesis

Terdapat pengaruh pemberian faktor pertumbuhan platelet terhadap kadar *interleukin-1β* (IL-1β) pada tikus putih model osteoarthritis.

1.5 Manfaat Penelitian

1.5.1 Manfaat Teoritis

1. Sebagai landasan teoritis mengenai pemanfaatan faktor pertumbuhan platelet terhadap kadar *interleukin-1β* (IL-1β) untuk terapi osteoarthritis.
2. Sebagai bahan bacaan dan sumber referensi bagi peneliti lain untuk mengeksplorasi potensi dalam bidang kesehatan.

1.5.2 Manfaat Tatalaksana

1. Faktor pertumbuhan platelet diharapkan dapat menjadi terapi alternatif pada osteoarthritis apabila memiliki efektivitas yang signifikan berdasarkan uji klinisnya.
2. Menjadi referensi rujukan untuk uji klinis terkait pengaruh faktor pertumbuhan platelet terhadap penyakit osteoarthritis.

1.5.3 Manfaat Masyarakat

1. Memberi informasi kepada masyarakat mengenai pengobatan alternatif osteoarthritis dengan pemanfaatan agen biologis tubuh yaitu faktor pertumbuhan platelet.
2. Masyarakat diharapkan mendapatkan strategi pengobatan osteoarthritis terbaru yang efektif dan aman.

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