CHAPTER 19

INFLIXIMAB TREATMENT IN DERMATOLOGY

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INTRODUCTION

Infliximab is a chimeric human-mouse IgG1 monoclonal anti-TNF antibody with human constant regions and mouse variable regions.[1,2] It binds soluble and transmembrane forms of anti-TNF-alpha so TNF-alpha can't bind its receptor.[1] It was approved by food and drug administration (FDA) for the treatment of plaque psoriasis in adult patients who are resistant to traditional systemic therapy.[3] It is also FDA approved for use in psoriatic arthritis, rheumatoid arthritis, ankylosing spondylitis, crohn disease and ulcerative colitis.[2]

CHRONIC PLAQUE PSORIASIS

Psoriasis is a chronic immun-mediate skin disease and prevalence of psoriasis is %1-3 in the worl population.[4,5] TNF-alpha is a key mediator in inflammation of psoriasis and anti TNF-alpha inhibitors supresss inflammation in psoriasis.[6] In chronic plaque psoriasis infliximab is given at a dose of 5mg/kg at 0,2,6 weeks and followed by every 8 weeks.[1] It is administered by intravenous infusion.[3] In psoriasis treatment infliximab has more rapid effect than other biologic agents. Patients show clinical improvement one week after the first dose.[7]

In a randomized, placebo-controlled trial after the administration of 5m/kg infliximab, %88 of patients achieved PASI 75 and %57,6 of patients achieved PASI 90.[8] In another study 378 patients with plaque psoriasis were treated with infliximab and they achieved PASI 75.[9] In a prospective, observational, open-label study with 660 patients infliximab were administered 5mg/kg at 0,2,6 weeks and every 8 weeks during 50 weeks. At the end of the study %56,8 of patients achieved PASI 75.[6] In a phase 3 placebo-controlled trial infliximab was given to patients as a dose of 3-5mg/kg and 10 weeks later patients achieved at least PASI 75 score.[10]

In long term treatment with infliximab, it is recommended incresing the dose and/or frequency of infliximab infusions to maintain response. In a retrospective study with 93 patients it was shown that first decreasing the infusion interval followed by increasing the dose better than first increasing the dose followed by decreasing the infusion interval.[3]

Infliximab is not only effective in chronic plaque psoriasis but also in pustular psoriasis. In two case reports two patients with pustular psoriasis who didn't benefit from traditional systemic treatments were treated by infliximab as 3mg/kg. After 48 hours, pustular lesions of patients were cleared.[11]

PSORIATIC ARTHRITIS AND NAIL PSORIASIS

Infliximab treatment is also effective in patients with psoriatic arthritis.[10] In a study 5 mg /kg infliximab treatment were given to patients with psoriatic arthritis at weeks 0, 2, 6, 14 and 22. At the and of the study there was seen a significant improvement.[12] In two case reports; a 62 year-old man and a 23 year-old woman with psoriasis and psoriatic arthritis who had not benefited from variable systemic treatments were given infliximab 5mg/kg and both of patients had complete remission.[10]

Prevalence of nail psoriasis is %50 in psoriatic patients and %90 in patients with psoriatic arthritis.[13] In a phase 3 multicenter, double-blind, placebo-controlled study 5mg/kg infliximab was administered to patients with nail psoriasis at weeks 0,2,6,8. 10 weeks later lesions were improved significantly.[13]

COMBINATION THERAPY

Anti-infliximab antibody cause to reduction of clinical response of infliximab in long-term treatment. Immunosuppressive agents such as methotrexate decrease anti-infliximab antibodies in the serum of psoriatic patients so efficacy of infliximab treatment increase. In a retrospective cohort study it was shown that concurrent use of methotrexate with infliximab extends the usefulness of infliximab.[3]

COMPARATIVE EFFICACY

In psoriasis infliximab is the only biological agent that is administered by intravenous and dose is associated with weight of patient.[7] In a randomized controlled study; efficacy of biological agents that used in psoriasis were compared. At the end of the study infliximab had the highest PASI response.[14] In two meta-analysis it was

REFERENCES

1. Ratel R., Cafardi JM, Patel N et.al. Tumor necrosis factor biologics beyond psoriasis in dermatology. Expert Opin. Biol. Ther.(2011) 11 (10):1341-1359.
2. Schmidt F.B., Shah K.N. Biologic Response Modifiers and Pediatric Psoriasis. Pediatr Dermatol.2015; 26: 1-18.
3. Luber AJ., Tsui CL., Gillian M. et.al. Long-term durability and dose escalation patterns in infliximab therapy for psoriasis. J Am Acad Dermatol. 2014; 70(3):525-32.
4. Sandoval L.F., Pierce A., Feldman S.R. Systemic therapies for psoriasis: An evidence-based update. Am J Clin Dermatol (2014) 15: 165-180.
5. Mansouri Y., Goldenberg G. Biologic safety in psoriasis Review of long-term safety data. J Clin Aesthet Dermatol. 2015; 8(2):30-42.
6. Shear N.H., Hartmann M, Toledo-Bahena M. et.al. Long-term efficacy and safety of infliximab maintenance therapy in patients with plaque-type psoriasis in real-world practice. Br J Dermatol. 2014;171(3):631-41.
7. Eusebio E., Armario-Hita JC., Miquel VA. Treatment of psoriasis: Focus on clinic-based management with infliximab. Am J Clin Dermatol 2014; 15: S5-S16.
8. Gottlieb AB, Evans R., Li S. et.al. Infliximab induction therapy for patients with severe plaque-type psoriasis: a randomized, double-blind, placebo-controlled trial. J Am Acad Dermatol.2004; 51(4):534–42.
9. Reich K., Nestle FO, Papp K., et.al. Infliximab induction and maintenance therapy for moderate-to severe psoriasis: a phase III, multicentre, double-blind trial. Lancet. 2005; 366(9494):1367–74.
10. Papoutsaki M, Osorio F, Morais P. et.al. Infliximab in psoriasis and psoriatic arthritis. Biodrugs 2013; 27: 13-23.
11. Kim HS., You H.S., Cho HH. et.al.Two cases of generalized pustular psoriasis: Successful treatment with infliximab. Ann Dermatol. 2014; 26(6):787-788.
12. Antoni C., Krueger GG., de Vlam K., et al. Infliximab improvessigns and symptoms of psoriatic arthritis: results of the IMPACT 2 trial. Ann Rheum Dis. 2005;64(8):1150–7.
13. Tan ST, Chong WS, Tey HL. et.al. Nail psoriasis: A review Am J Clin Dermatol 2012; 13 (6):375-388.
14. Reich K, Burden AD, Eaton JN, Hawkins NS. Efficacy of biologics in the treatment of moderate to severe psoriasis: a network meta-analysis of randomized controlled trials. Br J Dermatol. 2012;166(1):179–88.
15. Schmitt J, Zhang Z, Wozel G, et.al. Efficacy and tolerability of biologic and nonbiologic systemic treatments for moderate-to severe psoriasis: meta-analysis of randomized controlled trials. Br J Dermatol. 2008;159(3):513–26.
16. Brimhall AK, King LN, Licciardone JC, et.al. Safety and efficacy of alefacept, efalizumab, etanercept and infliximab in treating moderate to severe plaque psoriasis: a meta-analysis of randomized controlled trials. Br J Dermatol. 2008;159(2):274–85.
17. Kim IH., West CE., Kwatra SG, Feldman SR., O'Neill JL. Comparative efficacy of biologics in psoriasis: a review. Am J Clin Dermatol. 2012;13(6):365–74.
18. Lin VW, Ringold S, Devine EB. Comparison of ustekinumab with other biological agents for the treatment of moderate to severe plaque psoriasis: a Bayesian network meta-analysis. Arch Dermatol. 2012;148(12):1403–10.
19. Said TM, Agarwal A., Falcone T. et.al. Infliximab may reverse the toxic effects induced by tumor necrosis factor alpha in human spermatozoa: an in vitro model. Fertil Steril 2005; 83: 1665–73.
20. Paschou S, Voulgari PV, Vrabie IG. et.al. Fertility and reproduction in male patients with ankylosing spondylitis treated with infliximab. J Rheumatol 2009; 36: 351–4.
21. Grunewald S, Jank A. New systemic agents in dermatology with respect to fertility, pregnancy and lactation. J Dtsch Dermatol Ges. 2015 Apr;13(4):277-90.
22. Farnsworth N.N., George S.J., Hsu S. Successful use of infliximab following a failed course of etanercept in a pediatric patient. Dermatol Online J 2005; 11: 11.
23. Pereira TM,Vieira AP, Fernandes JC et.al. Anti-TNFalpha therapy in childhood pustular psoriasis. Dermatology 2006;213:350–352.
24. Diaz-Ley B, Guhl G, Fernandez-Herrera J. Off-Label Use of Biologic Agents in the Treatment of Dermatosis, Part 1:Infliximab and Adalimumab. Actas Dermatosilifiogr. 2007; 98: 657-78.
25. Sanchez-Cano D, Callejas-Rubio JL, Ruiz-Villaverde R. et al. Off-Label Uses of Anti-TNF Therapy in Three Frequent Disorders: Behçet's Disease, Sarcoidosis, and Noninfectious Uveitis. Mediators Inflamm. 2013; 2013: 286857.
26. Özmen I, Koç E. TNF-Alfa Antagonistlerinin Psöriyazis Dışı Dermatolojik Hastalıklarda Kullanım Alanları. Türkiye Klinikleri J Dermatol 2009;19(4).
27. Judson MA, Baughman RP, Costabel U. et al. Efficacy of infliximab in extrapulmonary sarcoidosis: results from a randomized trial. Eur Respir J 2008; 31: 1189-1196.
28. Saleh S, Ghodsian S, Yakimova V. et al. Effectiveness of infliximab in treating selected patients with sarcoidosis. Respiratory Medicine 2006; 100: 2053-2059.
29. Doty JD, Mazur JE, Judson MA. Treatment of Sarcoidosis With Infliximab. Chest. 2005; 127(3):1064-71.
30. Stagaki E, Mountford WK, Lackland DT. et al. The Treatment of Lupus Pernio. Chest. 2009; 135(2):468-76.
31. Hostettler KE, Studler U, Tamm M. et.al. Long-Term Treatment with Infliximab in Patients with Sarcoidosis. Respiration 2012; 83: 218-224.
32. Meyerle JH, Shorr A. The use of infliximab in cutaneous sarcoidosis. J Drugs Dermatol. 2003; 2(4):413-4.
33. Hertl M.S., Haendle I., Schuler G. et al. Rapid improvement of recalcitrant disseminated granuloma annulare uppon treatment with the tumour necrosis factor-a inhibitor, infliximab. British Journal of Dermatology 2005; 152: 552-555.
34. Kolde G, Muche JM, Schulze P. et al. Infliximab: a promising new treatment option for ulcerated necrobiosis lipoidica. Dermatology. 2003; 206(2):180-1.
35. Grant A., Gonzalez T., Montgomery M.O. et al. Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: A randomized, double-blind, placebo-controlled crossover trial. J Am Acad Dermatol. 2010; 62(2):205-17.
36. Mekkes JR, Bos JD. Long-term efficacy of a single course of infliximab in hidradenitis suppurativa. Br J Dermatol. 2008; 158(2):370-4.

37. Sullivan T.P., Welsh E., Kerdel F.A. et al. Infliximab for hidradenitis suppurativa. British Journal of Dermatology 2003; 149: 1046-1049.
38. Fernandez-Vozmediano JM., Armario-Hita JC. Infliximab for the treatment of hidradenitis suppurativa. Dermatology. 2007;215(1):41-4.
39. Fardet L, Dupuy A, Kerob D. et.al. Infliximab for severe hidradenitis suppurativa: Transient clinical efficacy in 7 consecutive patients. J Am Acad Dermatol. 2007; 56(4):624-8.
40. Brezinski E.A., Armstrong A.W. Off-Label Biologic Regimens in Psoriasis: A Systematic Review of Efficacy and Safety of Dose Escalation, Reduction and Interrupted Biologic Therapy. PLoS One. 2012; 7(4):e33486.
41. Adams D.R., Gordon K.B., Devenyi A.G. et al. Severe Hidradenitis Suppurativa Treated With Infliximab Infusion. Arch Dermatol. 2003; 139(12):1540-1542.
42. Roussomoustakaki M, Dimoulios P, Chatzicostas C. et.al. Hidradenitis suppurativa associated with Crohn's disease and spondyloarthropathy: response to anti-TNF therapy. J Gastroenterol 2003; 38: 1000-1004.
43. Lasocki A., Sinclair R., Foley P. et.al. Hidradenitis suppurativa responding to treatment with infliximab. Australasian Journal of Dermatology 2010; 51: 186-190.
44. Elkjaer M, Dinesen L, Benazzato L. et.al. Efficacy of infliximab treatment in patients with severe fistulizing hidradenitis suppurativa. J Crohns Colitis. 2008; 2(3):241-5.
45. Goertz R.S., Konturek P.C., Naegel A. et.al. Experiences with a long-term treatment of a massive gluteal acne inversa wiith infliximab in Crohn's disease. Med Sci Monit, 2008; 14(9): CS14-18.
46. Thielen AM, Barde C, Saurat JH. Long-term infliximab for severe hidradenitis suppurativa. British Journal of Dermatology 2006; 154: 1074-1108.
47. Adler S, Baumgartner I, Villigeer PM. Behçet's Disease: Successful Treatment With Infliximab in 7 Patients With Severe Vascular Manifestations. A Retrospective Analysis. Arthritis Care Res. 2012; 64(4);607-11.
48. Kikuchi H., Aramaki K., Hirohata S. Effect of infliximab in progressive Neuro-Behçet's syndrome. Journal of the neurological sciences 2008; 272: 99-105.
49. Iwata S., Saito K., Yamaoka K. et.al. Effects of anti-TNF alpha antibody infliximab in refractory entero-Behçet's disease. Rheumatology 2009; 48: 1012-1013.
50. Yamada Y., Sugita S., Tanaka H. et.al. Comparison of infliximab versus ciclosporin during the initial 6-month treatment period in Behçet disease. Br J Ophthalmol 2010; 94: 284-288.
51. Estrach C, Mpofu S, Moots RJ. Behçet's syndrome: response to infliximab after failure of etanercept. Rheumatology 2002; 41: 1213-1214.
52. Almoznino G, Ben-Chetrit E. Infliximab for the treatment of resistant oral ulcers in Behçet's disease: a case report and review of the literature. Clin Exp Rheumatol. 2007;25: S99-102.
53. Schreiber BE, Noor N, Juli CF et.al. Resolution of Behçet's syndrome associated pulmonary arterial anaurysms with infliximab. Semin Arthritis Rheum. 2011; 41:482-7.
54. Kasugai C, Watanabe D, Mizutani K. et.al. Infliximab treatment of severe genital ulcers associated with Behçet disease. J Am Acad Dermatol. 2010; 62: 162-4.
55. Goossens PH, Verburg R.J, Breedveld FC. Remission of Behçet's syndrome with tumour necrosis factor alpha blocking therapy. Ann Rheum Dis 2001; 60: 637.
56. Müller H, Gattringer C, Zelger B. et.al. Infliximab monotherapy as first-line treatment for adult-onset pityriasis rubra pilaris: Case report and review of the literature on biologic therapy. J Am Acad Dermatol. 2008; 59: 65-70.
57. Liao WC, Mutasim DF. Infliximab for the treatment of adult-onset pityriasis rubra pilaris. Arch Dermatol. 2005; 141: 423-5.
58. Manoharan S, White S, Gumparthy K. Successful treatment of type 1 adult-onset pityriasis rubra pilaris with infliximab. Australasian Journal of Dermatology 2006; 47: 124-129.
59. Ruzzetti M, Saraceno R, Carboni I. et.al. Type 3 juvenil pityriasis rubra pilaris: a successful treatment with infliximab. J Eur Acad Dermatol Venereol. 2008; 22(1):117-8.
60. Drosou A., Kirsner RS., Welsh E. et.al. Use of infliximab, an anti-tumor necrosis alpha antibody, for inflammatory dermatoses. J Cutan Med Surg. 2003; 7(5): 382-6.
61. Brooklyn TN, Dunnill MG, Bowden JJ. et.al. Infliximab for the treatment of pyoderma gangrenosum: a randomised, double blind, placebo controlled trial. Gut 2006; 55: 505-509.
62. Ljung T, Staun M, Grove O. et.al. Pyoderma gangrenosum associated with crohn disease: effect of TNF-alpha blockade with infliximab. Scand J Gastroenterol. 2002; 37(9):1108-10.
63. Requeiro M, Valentine J, Plevy S. et.al. Infliximab for treatment of pyoderma gangrenosum associated with inflammatory bowel disease. Am J Gastroenterol. 2003; 98(8):1821-6.
64. Foster EN, Nguyen KK, Sheikh RA. et.al. Crohn's disease associated with Sweet's syndrome and Sjogren's syndrome treated with Infliximab. Clinical and Developmental Immunology, June 2005; 12(2): 145-149.
65. Voigtlander C, Luftl M, Schuler G. et.al. A Novel, Highly Effective Treatment of Recalcitrant Subcorneal Pustular Dermatosis. Arch Dermatol. 2001; 137: 1571-4
66. Hunger RE., Hunziker T, Buettiker U. et.al. Rapid resolution of toxic epidermal necrolysis with anti-TNF alpha treatment. J Allergy Clin Immunol. 2005; 116(4): 923-4.
67. Al-Shouli S, Abouchala N, Bogusz MJ. et.al. Toxic Epidermal Necrolysis Associated with High Intake of Sildenafil and its Response to Infliximab. Acta Derm Venereol. 2005;85(6):534-5.
68. Fıscher M, Fiedler E, Marsch WC. et.al. Antitumour necrosis factor-alpha antibodies (infliximab) in the treatment of a patient with toxic epidermal necrolysis. British Journal of Dermatology 2002; 146: 705-718.
69. Scott-Lang W, Tidman M, McKay D. et.al. Toxic Epidermal Necrolysis in a Child Successfully Treated with Infliximab. Pediatric Dermatology 2014; 31: 532-4
70. Iqbal M, Kolodney MS, Acne fulminans with synovitis-acne-pustulosis-hyperostosis-osteitis (SAPHO) syndrome treated with infliximab. J Am Acad Dermatol. 2005; 52: 118-20.
71. Wagner AD, Andresen J, Jendro MJ. et.al. Sustained response to tumor necrosis factor alpha–blocking agents in two patients with SAPHO syndrome. Arthritis Rheum. 2002; 46(7):1965-8.

72. Olivieri I, Padula A, Ciancio G. et.al. Persistent efficacy of tumor necrosis factor alpha blockage therapy in SAPHO syndrome: comment on the article by Wagner et al. Arthritis Rheum. 2003; 48: 1461-1470.

73. Couriel D, Saliba R, Hicks K. et.al. Tumor necrosis factor-alpha blockade for the treatment of acute GVHD. Blood. 2004; 104: 649-54.

74. Patriarca F, Sperotto A, Damiani D. et.al. Infliximab treatment for steroid-refractory acute graft-versus-host disease. Haematologica. 2004; 89(11): 1352-9.

75. Dold S, Justiniano ME, Marquez J. et.al. Treatment of early and refractory dermatomyositis with infliximab: a report of two cases. Clin Rheumatol 2007; 26: 1186-1188.

76. Roddy E, Courtney PA, Morris A. Non-Hodgkin's lymphoma in a patient with refractory dermatomyositis which had been treated with infliximab. Rheumatology 2002; 41: 1194-1214.

77. Korkmaz C, Temiz G, Çetinbaş F. et.al. Case report: successful treatment of alveolar hypoventilation due to dermatomyositis with anti-tumour necrosis factor-alpha. Rheumatology 2004; 43: 937-938.

78. Pardo J, Mercader P, Mahiques L. et.al. Infliximab in the management of severe pemphigus vulgaris. British Journal of Dermatology 2005; 153: 206-239.

79. Jacobi A, Schuler G, Hertl M. Rapid control of therapy-refractory pemphigus vulgaris by treatment with the tumour necrosis factor-alpha inhibitor infliximab. British Journal of Dermatology 2005; 153: 440-466.

80. Mang R, Ruzicka T, Stege H. et.al. Therapy for severe necrotizing vasculitis with infliximab. J Am Acad Dermatol. 2004; 51: 321-2.

81. Uthman IW, Touma Z, Sayyad J. et.al. Response of deep cutaneous vasculitis to infliximab. J Am Acad Dermatol. 2005; 53(2):353-4.

82. Bartolucci P, Ramanoelina J, Cohen P. et.al. Efficacy of the anti-TNF-a antibody infliximab against refractory systemic vasculitides: an open pilot study on 10 patients. Rheumatology 2002; 41: 1126-1132.

83. Diab M, Coloe JR, Magro C. et.al. Treatment of Recalcitrant Generalized Morphea With Infliximab. Arch Dermatol. 2010; 146(6):601-4.

84. Clayton TH, Walker PB, Stables GI. Treatment of chronic erythema nodosum with infliximab. Clin Exp Dermatol. 2006; 31(6):823-4.

85. Simon JA., Burgos-Vargas R. Vitiligo improvement in a patient with ankylosing spondylitis treated with infliximab. Dermatology 2008;216(3):234-5.

86. Meziane L, Caudron A, Dhaille F. et.al. Febrile Ulceronecrotic Mucha-Habermann Disease: Treatment with Infliximab and Intravenous Immunoglobulins and Review of the Literature. Dermatology 2012; 225: 344-348.

87. Haslund P, Lee RA, Jemec GBE. Treatment of Hidradenitis Suppurativa with Tumour Necrosis Factor-alpha Inhibitors. Acta Derm Venereol 2009; 89: 595-600.

88. Sockolov ME, Alikhan A., Zargari O. Non-psoriatic dermatologic uses of monoclonal antibody therapy. Journal of Dermatological Treatment. 2009; 20:319-327.