Scientific and medical evidence demonstrating the effectiveness of subcutaneous immunoglobulins

Bibliographic reference	Study type	Study aim	Number of patients	Patient characteristics	Intervention	Outcome measures	Organisation/ Contacts
Chapel H. et al, The comparison of the efficacy and safety of intravenous versus subcutaneous Ig replacement therapy. Clin.Immunol.2000; 20:94-100	International, multicenter, open label, crossover study was designed	Compare the efficacy of immunoglobulin replacement therapy given intravenously versus subcutaneously to prevent infections in patients with primary antibody deficiency syndromes	40		Patients were randomized to receive either subcutaneous or intravenous immunoglobulin replacement therapy for 1 year. In the second year, patients were switched to the alternative treatment, enabling patients to act as their own controls.	There are no significant differences in efficacy or adverse reaction rates between immunoglobulin replacement therapy given subcutaneously or intravenously.	Department of Immunology, John Radcliffe Hospital, Oxford, England.

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Gardulf A, Nicolay U, Asensio O, Bernatowska E, Bock A, Carvalho BC, Granert C, Haag S, Hernandez D, Kiessling P, Kus J, Pons J, Niehues T, Schmidt S, Schulze I, Borte M. Rapid Subcutaneous IgG Replacement Therapy is Effective and Safe in Children and Adults with Primary Immunodeficiencies-A Prospective, Multi-National Study. J Clin Immunol. 2006 Apr 26; [Epub ahead of print]	Prospective multi-national study.	Evaluate the (i) IgG levels when switching patients from intravenous IgG (IVIG) infusions in hospital to subcutaneous (SCIG) self-infusions at home using the same cumulative monthly dose, (ii) protections against infections, and (iii) safety of a new, ready-to-use 16% IgG preparation	60	16 children, 44 adults	All children and 33 adults had received IVIG therapy for >6 months at enrolment. Ten adults who had been on SCIG therapy for many years served as controls	The SCIG administration route was safe. High IgG levels were easily maintained resulting in a very good protection against infections	Department of Laboratory Medicine, Section of Clinical Immunology, The Swedish Centre for Immunodeficiencies, Karolinska Institutet at Karolinska University Hospital Huddinge, Stockholm, Sweden. ann.gardulf@ki.se
Lim D.L., Thong B.Y., Ho S.Y., Shek L.P., Lou J., Leong K.P., Chng H.H., Lee B.W. Primary immunodeficiency diseases in Singapore--the last 11 years. Singapore Med J. 2003 Nov;44(11):579-86	Questionnaire	To describe the clinical features, disease complications, treatment modalities and overall outcome of 39 local patients with Primary Immunodeficiency Diseases (PID) in Singapore over the last 11 years	39	Age: three weeks to 69 years between January 1990 and December 2000	Patient data were collated from case files and compiled using a standard questionnaire.	Antibody deficiencies are the most common form of PID in Singapore. Treatment with antibiotics, IVIG and HSCT are the main therapeutic modalities currently available. Early referral to an immunologist is needed to achieve good outcomes	Department of Paediatrics, The Children's Medical Institute, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074. paelimd@nus.edu.sg

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Remvig L, Andersen V, Hansen NE, Karle H. Prophylactic effect of self-administered pump-driven subcutaneous IgG infusion in patients with antibody deficiency: a triple-blind cross-over study comparing P-IgG levels of 3 g l-1 versus 6 g l-1. Journal of internal medicine 1991; 229:73-77.	A triple-blind cross-over.	Comparitson P-IgG levels of 3 g l-1 versus 6 g l-1.	8	Adult patients with hypoimmunoglobulinaemia.	Patients were randomly allocated to initiation of low- or high-level IgG-substitution. IgG was administered subcutaneously, at 50 or 150 mg ml-1, 20 ml per infusion, by means of a pocket-portable electric infusion pump. Infusions were given 2 to 4 times weekly for 24 months, with a change of dose regimen after 12 months.	A plasma IgG concentration of 6 g l-1 can readily be achieved by subcutaneous IgG substitution, and the prophylactic effect is superior to that obtained with a plasma IgG concentration of 3 g l-1.	Department of Medicine TTA, Rigshospitalet, Copenhagen, Denmark.
Ochs HD et al. Safety and efficacy of self-administered subcutaneous immunoglobulin in patients with primary immunodeficiency diseases.J Clin Immunol. 2006 May;26(3):265-73	open-label study	Investigate the efficacy and safety of a subcutaneously administered immunoglobulin preparation (16% IgG) in patients with PIDD	65		After their final IVIg infusion, 65 patients entered a 3-month, wash-in/wash-out phase, designed to bring patients to steady-state with subcutaneously administered immunoglobulin. This was followed by 12 months of weekly SCIg infusions, at a dose determined in a pharmacokinetic substudy to provide noninferior intravascular exposure. This resulted in a mean weekly dose of 158 mg/kg, calculated to equal 137% of the previous intravenous dose. No treatment-related serious adverse events were reported.	We conclude that subcutaneous administration of 16% SCIg is a safe and effective alternative to IVIg for replacement therapy of PIDD.	Department of Pediatrics, University of Washington School of Medicine, Seattle, Washington, USA.

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Nicolay U et al. Measuring treatment satisfaction in patients with primary immunodeficiency diseases receiving lifelong immunoglobulin replacement therapy. Qual Life Res. 2005 Sep;14(7):1683-91	Investigation on treatment satisfaction of patients with primary immunodeficiency diseases receiving hospital-based intravenous (IVIG) or home-based subcutaneous (SCIG) immunoglobulin infusions	Evaluation of the properties and suitability of the Life Quality Index (LQI), as an instrument to assess treatment satisfaction			Patients received weekly SCIG and completed the LQI, two global treatment satisfaction questions and the CHQ-PF50 (children) or the SF-36 (adults) at baseline and 10 months. The LQI was psychometrically evaluated.	The LQI comprised four scales: treatment interference (I), therapy related problems (II), therapy setting (III), treatment costs (IV). Convergent/discriminant validity for scales I, II, III was acceptable, for scale IV moderate. CHQ-PF50 scales behavior, bodily pain, global behavior, global health, mental health, parental impact-emotion significantly correlated with LQI scale II, the family activity scale with LQI scales I, III. SF-36 scale bodily pain significantly correlated with scale III. Internal consistency was good for scales I, II, III, but poor for scale IV. Score values significantly increased for scales I, III, IV in patients switching from IVIG to SCIG. CONCLUSIONS: Three valid LQI scales were determined. Cost-related questions should be removed due to low reliability. Patients-perceived therapy effectiveness and patient-physician/nurse interaction should be included in the instrument.	The Swedish Center for Immunodeficiencies, Department of Laboratory Medicine, Section of Clinical Immunology, Karolinska Institutet at Karolinska University Hospital, Stockholm, Sweden. uwe.nicolay@labmed.ki.se

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Gardulf A. et al. Immunoglobulin treatment for primary antibody deficiencies : advantages of the subcutaneous route. BioDrugs. 2007;21(2):105-16	Review of international studies	Review treatment of PIDs with SCIG as Subcutaneous IgG (SCIG) therapy, using small portable pumps for once-per-week self infusions, has shown many advantages compared with the two other routes of administration				This review highlights findings from international studies and demonstrates that: (i) SCIG therapy is safe, with very few adverse effects; (ii) the therapy can be used for patients with previous adverse effects to intravenous administration of IgG; (iii) the therapy leads to high serum IgG levels and good protection against infections; (iv) the therapy facilitates home therapy, as the infusion technique is easy for children, adults and elderly people to learn and there is no need for venous access; (v) SCIG home therapy leads to significantly improved life situations for the patients; (vi) the SCIG home therapy regimen in particular reduces the costs of treatment.	Department of Laboratory Medicine, Section of Clinical Immunology, Karolinska Institute, Karolinska University Hospital, Huddinge, Stockholm, Sweden

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Gardulf A, et al. Children and adults with primary antibody deficiencies gain quality of life by subcutaneous IgG self-infusions at home. J Allergy Clin Immunol. 2004 Oct;114(4):936-42.		Investigate whether a switch from hospital-based intravenous IgG (IVIG) to home-based subcutaneous IgG (SCIG) therapy would improve the HRQOL and TS	47	Fifteen children (<14 years; hospital-based IVIG therapy at enrollment) and 32 adults (> or =14 years; 22 on hospital-based IVIG and 10 on home-based SCIG therapy at enrollment) were included	Questionnaires were completed at baseline and at 6 and 10 months: the Child Health Questionnaire-Parental Form 50 (children) or Short Form 36 (adults), the Life Quality Index, and questions regarding therapy preferences	The SCIG home therapy improved TS because it led to greater independence and better therapy convenience. The patients preferred the SCIG administration route and having the treatment at home. Home-based SCIG therapy improves several important aspects of HRQOL and provides the patients with primary antibody deficiencies and their families with greater independence and better control of the therapy situation and daily life. SCIG home therapy is an appreciated therapeutic alternative for adults and children in need of lifelong IgG replacement therapy	Swedish Centre for Immunodeficiencies, Division of Clinical Immunology at the Department of Laboratory Medicine, Karolinska Institutet at Karolinska University Hospital, Stockholm, Sweden. ann.gardulf@labmed.ki.se

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Gaspar J, et al. Immunoglobulin replacement treatment by rapid subcutaneous infusion. Arch Dis Child. 1998 Jul;79(1):48-51.		Long term intravenous immunoglobulin (IVIG) infusion is an effective treatment for children with immunodeficiencies, but can be complicated by poor venous access, systemic adverse reactions, and the need for frequent hospital admission. Rapid subcutaneous immunoglobulin (SCIG) infusion has been found to be effective in adults with primary immunodeficiency.		Twenty six children were treated with SCIG for a median period of two years (range six months to 3.5 years). Fifteen children had previously been treated with IVIG	Retrospective analysis showed that trough IgG concentrations while receiving SCIG were comparable with those while receiving IVIG during maintenance treatment. In severe hypogammaglobulinaemia, however, initial loading with SCIG or IVIG is probably indicated. During the treatment period there was no systemic adverse reaction nor severe reaction requiring admission to hospital. The subjective impression of all families was a significant improvement in the quality of life.	This preliminary experience with SCIG in children suggests that it is an effective, convenient, and well tolerated alternative to intravenous treatment. Larger prospective studies are required to determine the place of SCIG in the management of immunodeficiencies	Department of Immunology, Great Ormond Street Hospital for Children, NHS Trust, London, UK.

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Hansen S. et al. Women with primary antibody deficiencies requiring IgG replacement therapy: their perception of prenatal care during pregnancy. J Obstet Gynecol Neonatal Nurs. 2004 Sep-Oct;33(5):604-9.	Exploratory study using a written questionnaire	Investigate how a group of women with primary antibody deficiencies (PAD) and receiving replacement therapy with IgG experienced the care they received in their prenatal clinics in relation to PAD and IgG therapy.	9	Nine women (25-43 years) attending an immunodeficiency unit and who fulfilled inclusion criteria for simultaneously having PAD, replacement IgG therapy, and full-term pregnancy (the latter within the past 5 years	The study originates from an immunodeficiency unit but evaluates care experienced at prenatal clinics	This study is the first attempt to investigate the prenatal experience of women with PAD (Search of PubMed, 1980 to present, including search terms primary immunodeficiency, pregnancy, and prenatal care). This study demonstrates that increased knowledge about PAD and IgG replacement therapy among midwives and physicians working in prenatal care clinics is needed. This can prevent misleading advice that puts the health of the mother and her fetus at risk. Sensitizing staff about this special group of women can create conditions in which women feel respected, heard, and satisfied with their prenatal care	Department of Nursing, Karolinska Institutet, Stockholm, Sweden
Nicolay U, et al. Health-related quality of life and treatment satisfaction in North American patients with primary immunedeficiency diseases receiving subcutaneous IgG self-infusions at home. J Clin Immunol. 2006 Jan;26(1):65-72.		Investigate the impact of weekly SCIG self-infusions at home on the health-related quality of life, treatment satisfaction, and preferences in patients treated with IVIG at the hospital/doctor's office (Group A) or at home (Group B)	44	Forty-four adult North American PIDD patients were included in the study, 28 patients in Group A and 16 in Group B		Patients in Group A reported significantly less limitations with their work/daily activities, a significantly improved vitality, and better general health. Treatment satisfaction was significantly improved in Group A. The preference for the subcutaneous route and for home therapy was respectively 81% and 90% in Group A. In Group B, 69% preferred the subcutaneous route and 92% home therapy	Section of Clinical Immunology, Department of Laboratory Medicine, Karolinska Institutet at Karolinska University Hospital, Stockholm, Sweden. uwe.nicolay@labmed.ki.se

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Hansen S. et al. Express subcutaneous IgG infusions: decreased time of delivery with maintained safety. Clin Immunol. 2002 Sep;104(3):237-41.		Evaluate the safety and feasibility of weekly express subcutaneous replacement IgG self-infusions (E-SCIG, 35 mL/h/syringe driver) in 50 patients and to evaluate their perceptions of the therapy	50		A total of 4900 E-SCIG infusions at separate infusion sites were given on 1228 treatment occasions	The E-SCIG method seems to be safe, with few pronounced local reactions, and is appreciated by the patients. Express delivery could also potentially facilitate IgG delivery in a wide variety of diseases, such as autoimmune and autoimmune-like conditions of a neurological or rheumatological character	Immunodeficiency Unit, Department of Immunology, Microbiology and Pathology, Section of Clinical Immunology, Karolinska Institutet, Huddinge University Hospital, Stockholm, Sweden