Dr. Henrik Ekberg

Dr. Henrik Ekberg is Senior Transplant Surgeon at the University Hospital in Malmö, Sweden, and Professor of Transplant Surgery at Lund University. His main research interests concern immunosuppressive treatment, clinically as well as experimentally. He received his MD degree in 1977 and his board certification in General Surgery in 1985. He presented his PhD thesis in 1986 and after two years of research in the field of transplantation at the University of Sydney in Australia, focusing on pancreas transplantation, he was appointed to his present clinical position and Associate Professor. In 2001, Dr. Ekberg was appointed Professor of Transplant Surgery at Lund University. In the last 15 years, he has had an active role in a large number of pivotal multicenter trials on immunosuppression in renal transplantation. At present time, Dr. Ekberg is sponsor and chairman of the steering committee of the ongoing multicenter international Symphony study. Dr. Ekberg is Associate Editor of the American Journal of Transplantation and member of the editorial board of Transplantation and that of Transplant International. He is also Councillor for The Transplantation Society (TTS) and vice-president of the European Society of Organ Transplantation (ESOT). Dr. Ekberg is a frequently invited lecturer and has published more than 150 original articles and reviews in the field of transplantation.
**Symphony – Balancing efficacy and toxicities in renal transplant patients**

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**Abstract**

The CAESAR study showed that the use of low-dose cyclosporine A (CsA) in combination with daclizumab, mycophenolate mofetil (MMF, CellCept®) and corticosteroids is safe and effective. However, complete CsA withdrawal at 4-6 months after transplantation was associated with an increased risk of acute rejection. Thus, a balance needs to be found between reducing toxicity and maintaining efficacy.

The main objective of the Symphony trial was to determine whether low doses of CNIs or sirolimus (SRL) in conjunction with MMF and daclizumab may be beneficial in comparison with standard-dose CsA-based immunosuppression. The study aimed at demonstrating improved renal function while at the same time providing an acceptable rate of acute rejection and a favourable safety profile.

Symphony is the largest ever prospective study in de novo renal transplant patients. In the Symphony study, 1645 adult patients were randomised to receive one of the following treatments: standard-dose CsA (target trough level 150-300 ng/ml for 3 months, 100-200 ng/ml thereafter), 1g bid MMF and corticosteroids (Group A), or daclizumab induction (2mg/kg followed by 4 x 1mg/kg every 2 weeks), 1 g bid MMF and corticosteroids in combination with either low-dose CsA (50-100 ng/ml; Group B), low-dose TAC (3-7 ng/ml; Group C) or low-dose SRL (4-8 ng/ml; Group D).

Differences in glomerular filtration rate (GFR) and biopsy-proven acute rejection (BPAR) were statistically significant among the 4 groups (p < 0.0001). The low-dose TAC group was significantly superior to all other groups with respect to mean calculated GFR, as measured by Cockcroft-Gault (65.6 ml/min compared with 56.7-59.7 ml/min) at 12 months. The lowest incidence of BPAR at 12 months (12% compared with 24-37%) was also observed in the low-dose TAC group. In addition, 12-month graft survival was significantly better in this treatment group than in the standard-dose CsA (94% vs 89%, p = 0.0108) and the low-dose SRL groups (94% vs 89%, p = 0.0115). No significant differences in patient survival were observed between the 4 treatment groups. The safety profile was similar between the treatment groups with no significant differences in most of the parameters measured. In patients receiving low-dose TAC, significantly higher incidences of diarrhoea (26% vs 15-22%, p = 0.0003) and diabetes mellitus (11.5% vs 5.7-8.6%) were observed, whereas in patients receiving low-dose SRL a significantly higher incidence of lymphoceles (12.9% vs 3.6-6.0%, p < 0.0001) was detected.

The Symphony study proves that MMF with low-dose TAC maximises the function and longevity of the organ. This combination protects the patient by providing the best balance between efficacy and toxicity available to date.

**References**

2 Ekberg H. World Transplant Congress 2006, Boston, USA.
Bart D. Maes, MD, PhD

Bart Maes is currently Nephrologist at the Heilig Hartziekenhuis of Roeselare, Belgium. His research interests include immunosuppressive therapy in transplantation and glomerulonephritis, metabolic and gastrointestinal disorders in transplantation, and hepatic and gastrointestinal metabolism of immunosuppressive drugs (CYP3A4 and P-glycoprotein system). His articles on these subjects appear in a variety of peer-reviewed journals. Dr. Maes received his MD and PhD (gastric motility) from the Catholic University of Leuven.

Severe diarrhea in renal transplant patients: Results of the DIDACT Study

Bart D. Maes, MD, PhD

Abstract

Diarrhea is common in transplant recipients. While the majority of cases are mild and transient, some are severe and prolonged, which can threaten graft survival through dehydration. While it is known that some immunosuppressive agents can elicit diarrhea, there does not appear to be any consensus on the role that other non-immunosuppressive causes can play in transplant patients. The aim of the DIDACT-study - an open, non-randomized, multicenter study - was to identify non-immunosuppressive factors involved in severe diarrhea in renal transplant patients. Patients (n=108) with severe diarrhea (≥3 stools/day for ≥7 days) were enrolled from 16 Belgian transplant centers. Patients were diagnosed according to an agreed flowchart that consisted of identification of possible infections, followed by changes in empirical and immunosuppressive treatment. Approximately 50% of patients experienced resolution of severe diarrhea following treatment for infections, dietary problems or diarrhea-causing concomitant medications. In conclusion, a large proportion of the severe diarrhea observed in renal transplant recipients is not associated with immunosuppressive therapy and can be treated through anti-infectives, changes to concomitant medication and other empirical treatments. Correct diagnosis of the cause of severe diarrhea in such patients should help to protect graft survival in transplant recipients.
Tomas Reischig, MD

Born on March 4, 1972 (Pilsen)

Education
- 9/90 – 6/96 (Degree Doctor of Medicine in 6/96) - School of Medicine in Pilsen, Charles University (Honored by Dean’s Award for the study results)
- 4/99 1st Degree in Internal Medicine (postgraduate)
- 4/03 2nd Degree in Nephrology (postgraduate)

Professional Experience
- 9/96–up to now Charles University Teaching Hospital, Department of Internal Medicine I, Department of Nephrology, Transplant Centre. During the period 1996 – 1997 I was working on nephrology department (inpatient care) and hemodialysis centre. Since 1998 I have been working as a transplant nephrologist. I was designated as a head of Division of nephrology in September 2006.

Research
- At the beginning my research activity was focused on anemia in end-stage kidney patients. Later on I started with studies on the impact of infectious complications after kidney transplantation, particularly cytomegalovirus infection. I presented our research data at major transplant meetings such as ATC, ESOT and TTS congresses. Results of our clinical studies were published in prestigious transplant journals. In 2006 I was awarded by The Czech Transplantation Society for the publication in the Transplantation journal.

Full Text Publications in Journals with Impact Factor

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Tomáš Reischig, MD
Indirect effects of cytomegalovirus infection after solid organ transplantation

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Abstract

Cytomegalovirus (CMV) is one of the most common pathogens causing opportunistic infections in patients after solid organ transplantation. The adverse impact of CMV infection is all the more important as it causes not only direct viral syndromes (CMV disease) but, also, indirect long-term effects. The latter include an increase in the risk for acute and chronic rejection and the onset of other opportunistic super-infections. CMV may be involved in the pathology of acute rejection by several mechanisms, including up-regulation of adhesion molecules, increased expression of MHC class II antigens on allograft tissue, and release of variety of cytokines. Direct infection of arterial smooth muscle cells and endothelial cells accelerates the development of allograft vasculopathy. CMV-encoded chemokine receptor US28 has the ability to induce smooth muscle cell migration. Moreover, CMV abrogates the vascular protective effects of endothelium-derived nitric oxide system. Some studies have demonstrated an association between CMV and subsequent development of cardiovascular complications or new-onset diabetes mellitus following renal transplantation. Hence, it comes as no surprise that CMV infection and disease have an adverse impact on the long-term patient and graft survival.

Given the medical and economic consequences, wide application of preventive measures aimed at reducing the incidence of CMV disease is clear to understand. The two main current strategies include universal prophylaxis and preemptive therapy. Considering the drawbacks of intravenous administration, the most common option includes prophylaxis with oral ganciclovir, valganciclovir, and valacyclovir with well-established efficacy in randomized trials. Also preemptive therapy approach leads to a significant reduction in the incidence of CMV disease. Prophylaxis may have some benefit in the prevention of CMV indirect effects. Nevertheless, late-onset CMV disease and ganciclovir resistance after prophylaxis are of a concern.