President Raymond Vanholder took over ERA-EDTA Presidency in 2011. In an interview, he talks about the latest developments within the society.

Prof. Vanholder, the number of ERA-EDTA’s scientific working groups has been growing over the last years. Some of them such as the Immunonephrology Working Group or EURECA-m have been active already for four or five years; others, e.g. DESCARTES or the MBD-CKD Working Group started last year. Are you satisfied with the scientific output of these groups?

Prof. Vanholder: Our concept of working groups proved to be very successful over the years. Each group is presenting its research programme and then it will be decided, what should be implemented. We may also consider the possibility that some of these work groups will stop their activity after a certain period of time. Up to now, however, they have been very productive: they publish a lot of papers, essentially position statements. Some of them started systematic scientific studies – think about the VALIGA study of the Immunonephrology Working Group, which gathered a huge number of data on IgAN patients from all over Europe. In addition, there are many exciting ideas and results, which will be presented and discussed during the next days.

Do you plan to install additional working groups?

Prof. Vanholder: There is a new one pending called “Diabetes”, which is an artificial word unifying diabetes and obesity. We still didn’t decide whether to install it.

Last year the European Renal Best Practice group, ERBP, increased their capacities by a number of scientists who provide expertise in the design of clinical studies as well as guidelines and their implementation. Did this effort pay off?

Prof. Vanholder: Yes, certainly so. The figures speak for themselves: in 2011, the ERBP group produced three monographs. In 2012 instead, eight monographs were generated and a full guideline is out now. In addition, two other full guidelines are on the verge to be published, and a fourth one is in the pipeline. In addition, we are talking to other guidance bodies, especially with KDIGO, but also with the Australian CARI group, to achieve better harmonisation of guidelines.

Looking at the congress programme I see quite a lot of joint symposia with other scientific societies.

Prof. Vanholder: That is true. We’ll have, for example, a joint symposium with the Chinese Society of Nephrology about the epidemiological aspects of renal diseases. We are about to intensify our network with national renal societies, and will have a forum to introduce renal care in countries that usually do not get much opportunities to present their situation in our congresses, e.g. Eastern European countries. We set up a joint symposium with the American Society of Nephrology covering the highlights of the latest ASN Congress in Philadelphia – in exchange they will give us the opportunity to present the results of five of our working groups at their next conference. You also might have noticed the joint CME sessions with the European Society of Paediatrics, the Australian CARI group, to achieve better harmonisation of guidelines.

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Continued on page 2

It’s time for action!

Low sodium diet should be broadly implemented... page 17

Renoprotection

ACE inhibitors act by moderating progenitor cell activation... page 8

The LUST study

Lung ultrasound may improve outcomes in haemodialysis... page 10

Developing nephrology

Learn more about renal care in Eastern Europe... page 10

From CONTRAST to ESHOL

Studies show benefits for online haemodiafiltration... page 15
Continued from page 1

Is this type of international networking beyond the classical ERA-EDTA member states a general trend within your society?

Prof. Vanholder: Absolutely, yes. I think we are facing a new wave of globalisation which forces us to look for good contacts also outside of Europe. Therefore, we built a specific Commission for International Affairs, or ComIA, led by Ziad Massy. ComIA is in charge of following all the initiatives related to countries outside our traditional area, i.e. Europe and the countries bordering Europe and the Mediterranean. ComIA is also responsible for proposing new initiatives and updating the Council accordingly.

How big is the influence of the ERA-EDTA on public health issues in Europe?

Prof. Vanholder: It is very important to create awareness for the burden of chronic kidney disease and the socio-economical impact of dialysis and transplantation in Europe.

With our commitment to the European Kidney Health Alliance we try to sensitise politicians and the media, for example, to achieve better harmonisation of reimbursement and stimulate the use of ‘alternative strategies’ in dialysis and transplantation. This is a long way, but I think we are really making progress. We have a very good lobbying group that is helping a lot and we are coming closer to the core of the European Community.

What about the participation of young nephrologists in the ERA-EDTA activities?

Prof. Vanholder: Last year, the Young Nephrologists’ Platform was installed and very recently their Board was constituted; our plan is to have them involved in all major decision-making within the ERA-EDTA. The YNP is a success from the very beginning; it has now already more than 100 members.

A successful opening

The ERA-EDTA calls for more public awareness of chronic kidney disease.

Chronic kidney disease (CKD) is a major health problem that deserves more public attention than it currently receives, according to ERA-EDTA President Raymond Vanholder and Congress President Gultekin Suleymanlar. Both underlined their message by presenting epidemiological data at this year’s ERA-EDTA opening press conference: Approximately 500 million patients worldwide are affected by chronic kidney disease, corresponding to one in every ten adults. While proceeding to end-stage renal disease, their treatment poses a considerable economic burden to public healthcare systems. Not only the ethnic, racial and genetic variations but also diseases such as diabetes and hypertension are considered to play a major role in their etiology. “Actually, the 21st century has been the most diabetogenic era in the history of human beings, due to changes in nutrition and lifestyle,” stated Gultekin Suleymanlar. In addition, estimated numbers of hypertensive individuals amount to 1.5 billion worldwide.

Hypertension and salt

With 15 million affected people, high blood pressure is also a major health risk in Turkey, according Congress Secretary Cengiz Utas. At the opening press conference, he drew the attention to the link between hypertension and the high salt consumption in his home country: “A per-capita intake of 15 to 18 g salt per day is record-breaking, compared to other countries. Daily consumption of bread alone contributes with 7.2 g of salt per day to this huge amount, while the recommended quantity to prevent hypertension is 5 to 6 g per day.” Long-term changes of these habits can only be achieved through the concerted action of physicians, healthcare politics, food industry and the media – not only in Turkey, but in other countries as well.

Focus paediatric nephrology

ESRD conditions requiring dialysis or renal transplantation are 20 times less frequent in children than in adults. However, recent registry data indicate an increase in renal replacement therapies in patients younger than 15 years. “This difference can reflect an improved reporting of children on dialysis, but it is most likely due to increasing survival rates of children with chronic kidney disease in early childhood,” explained Professor Rosanna Coppo, Head of the ERA-EDTA Scientific Committee. “Nevertheless we have to do any possible effort to prevent the loss of renal function in these young patients.” Therefore, the ERA-EDTA decided to establish a special track dedicated to paediatric nephrology, which started already yesterday during the Working Group Fair with a CME session which was highly welcomed by attendees – as were the other pre-congress CME courses.

Where do you see the challenges for the ERA-EDTA in the coming years?

Prof. Vanholder: Many of our activities, for example the development of guidelines, are financed by our own financial resources. To a certain extent, however, money comes from the industry, either via unrestricted grants or indirectly, for example from renting exhibition space during our annual meeting. We have to convince the industry that we are using their money for useful projects for the benefit of patients and renal care. So, I think we need more transparency in our communication towards the industry.

Thank you very much.
Growing new kidneys from embryonic cells

In his keynote lecture, Giuseppe Remuzzi will be presenting the most recent advances in renal tissue engineering.

Introducing Giuseppe Remuzzi to an audience of nephrologists seems to be redundant. The ISN President from 2013–2015 is a pioneer in nephrology, has received several prizes and is known for various achievements in this field including contributions on the understanding of the pathophysiology of haemolytic uraemic syndrome, the role of protein trafficking in renal disease progression, kidney self repair in chronic kidney disease, therapy approaches for improved graft tolerance and the prevention of renal and cardiovascular damage in diabetes.

Remuzzi is fascinated by the potential of stem cells and he comes to Istanbul to present results from a recent study on in vivo maturation of functional renal organoids formed from embryonic cell suspensions. Unprecedented findings elucidate the potential of tissue-engineered kidney as an answer to the known shortage of organs for transplantation.

A functional tissue-engineered kidney replacing a moribud one is still a vision far ahead. However, Remuzzi and his co-workers from Ospedali Riuniti di Bergamo and the local Mario Negri Institute for Pharmacological Research managed to construct renal organoids from single cell suspensions of murine embryonic kidneys. These newly formed kidney tissues were able to carry out physiological functions after transplantation into the rat host and developed glomerular-like structures and well-formed tubuli.

VEGF is vital for glomerulogenesis

Compared to previous experiments, Remuzzi’s team established a more advanced protocol of organoid construction. They started from a large cell aggregate culture, and Remuzzi emphasises that this is “of utmost methodological importance to achieve the formation of viable nephrons.” Another crucial modification pays attention to the assumed role of Vascular Endothelial Growth Factor (VEGF) for glomerulogenesis.

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RRT in ANCA-associated vasculitis

Registry data suggest that limited access of AAV patients to renal transplantation is not justified.

ANCA-associated vasculitides (AAV), particularly granulomatosis with polyangiitis (GPA, formerly referred to as Wegener’s granulomatosis) and microscopic polyangiitis (MPA) are relatively rare but potentially life-threatening autoimmune diseases that have been recognised as the leading cause of rapidly progressive glomerulonephritis. Despite advances in the therapeutic management of AAV, about 20–30% of AAV patients with renal involvement develop end-stage renal disease (ESRD) within five years.

New drugs (e.g. rituximab for the induction of B cell depletion) recently introduced into the armamentarium of AAV therapies seem to better maintain remission and increase remission rates in relapsing AAV patients compared to standard treatments. The impact of these new treatment regimens on the long-term outcome of AAV patients, especially on the risk of progression to ESRD, is still uncertain.

Overall mortality rates in AAV patients requiring renal replacement therapy (RRT) have been reported to be similar to those in non-AAV non-diabetic patients, both for the dialysis and transplant subgroups, but such data are mostly based on small single centre reports. Recent data from 228 patients with GPA and 221 patients with MPA from the Australian and New Zealand Registry (ANZDATA) demonstrated similar survival of AAV patients on dialysis, but somewhat worse outcome of 46 MPA patients after renal transplantation (in terms of both patient and graft survival).

The ERA-EDTA Registry represents a unique large database providing data on the outcome of patients on RRT with different primary renal diagnoses. In the current study we aimed to describe the incidence and outcomes of European patients on RRT for ESRD due to AAV. Altogether, data from 2,371 vasculitis patients (1,650 patients suffering from GPA and 721 with MPA, over five times the number available in ANZDATA) were available for analysis – they had been identified among 195,826 incident RRT patients from 12 renal registries providing their data to the ERA-EDTA Registry for at least 16 years between 1991 and 2010.

Incidence of RRT for AAV was thus 1.01 per million population (ppm) for GPA (predominating in the northern countries) and 0.44 ppm for MPA (prevailing in the south). Renal transplantation was performed in 360 cases of GPA (21.8%) and in 139 with microscopic polyangiitis (19.3%). Compared to patients with other primary renal diseases a higher percentage of GPA patients recovered independent renal function within 90 days after the start of RRT compared to all patients (6.7% vs 1.5%, P<0.0001).

The ten-year survival probability since day 91 after the start of RRT was 34.2% (95% confidence interval 30.9–37.5%) in granulomatosis with polyangiitis and 25.7% (21.5–30.2%) in microscopic polyangiitis. We found that survival of RRT patients on dialysis and survival after kidney transplantation did not differ between AAV and non-vasculitis, non-diabetic patients.

Graft survival adjusted for age and sex was even better in granulomatosis with polyangiitis than in non-vasculitis non-diabetic patients. In a large number of patients we were unable to confirm the worse patient and graft survival of transplanted MPA patients. Reasons for the differences between the registries are not clear; the basic demographics of patient populations were similar and the percentage of living donors with a known better outcome was even higher in ANZDATA than in the ERA-EDTA Registry.

Data available from the ERA-EDTA Registry do not provide information on the putative extrarenal activity of AAV on dialysis and after renal transplantation. Comparable outcome of dialysed and transplanted AAV patients to matched non-diabetic patients without systemic disease (e.g. primary glomerulonephritis) suggest that extrarenal activity, if present, has no significant impact on patient and graft survival.

In conclusion, the ERA-EDTA Registry provided data on the outcome of RRT of the so far largest cohort of patients with end-stage renal disease due to AAV (both granulomatosis with polyangiitis and microscopic polyangiitis). Especially the data on the good outcome of renal transplantation in these subjects are very important and suggest that any limitation of the access of the AAV patient to renal transplantation is not justified.

Vladimir Tesar and Zdenka Hruskova, Charles University, Prague, Czech Republic, on behalf of V.S. Steh, K.J. Jager, C. Wanner, ERA-EDTA Registry and the national/regional registry representatives in Europe

S4: ERA-EDTA Registry
Room Anadadolu
Date: 19-05-2013
From: 8:45 to 10:15

Acidosis and progression of chronic kidney disease

Sodium bicarbonate is associated with slowing the rate of decline of renal function.

Chronic kidney disease causes metabolic acidosis by progressively impairing the ability of kidneys to excrete the normal burden of hydrogen ions. Experimental evidence suggested that metabolic acidosis can accelerate the progression of chronic kidney disease which has been confirmed by clinical studies published recently. Moreover, in patients with advanced chronic kidney disease (estimated glomerular filtration rate < 30 ml/min) a randomised controlled study has suggested that the correction of acidosis by sodium bicarbonate is associated with slowing the rate of decline of renal function, reduction in the incidence of end-stage renal disease and improvement of nutritional parameters. In the light of current evidence it appears that correction of acidosis by sodium bicarbonate which is a cheap and simple strategy and is in line with current renal recommendations has the potential of significant economic and clinical benefits in an ever increasing cohort of patients with chronic kidney disease.

References
Two critical decisions in treating elevated serum phosphorus:

WHEN & HOW

Renvela®: right from the start™ in your chronic kidney disease patients new to dialysis.

To learn more, visit booth #Q11 at the European Renal Association – European Dialysis and Transplant Association Congress May 18 – May 21.

Product Summary: Renvela 800 mg film-coated tablets. Renvela 2.4 g powder for oral suspension. Active substance: sevelamer carbonate. Subject to medical prescription. Composition: Each tablet contains 800 mg sevelamer carbonate. Each tablet also contains microcrystalline cellulose, sodium chloride and zinc stearate. The tablet coating contains hypromellose and diacetylated monoglycerides. The printing ink contains iron oxide black (E172), propylene glycol, isopropyl alcohol and hypromellose. Each sachet contains 2.4 g sevelamer carbonate. The powder contains propylene glycol alginate, citrus cream flavour, sodium chloride, sucrose, ferric oxide (E172). Therapeutic indications: Renvela is indicated for the control of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis. Renvela is also indicated for the control of hyperphosphataemia in adult patients with chronic kidney disease not on dialysis with serum phosphorus > 1.78 mmol/l. Renvela should be used within the context of a multiple therapeutic approach, which could include calcium supplement, 1,25-dihydroxy Vitamin D3 or one of its analogues to control the development of renal bone disease. Contraindications: Hypersensitivity to the active substance or to any of the excipients. Hypophosphataemia. Bowel obstruction. Possible side effects: The safety of sevelamer (as either carbonate and hydrochloride salts) has been investigated in numerous clinical trials involving a total of 969 haemodialysis patients with treatment duration of 4 to 50 weeks (724 patients treated with sevelamer hydrochloride and 245 with sevelamer carbonate), 97 peritoneal dialysis patients with treatment duration of 12 weeks (all treated with sevelamer hydrochloride) and 128 patients with CKD not on dialysis with treatment duration of 8 to 12 weeks (79 patients treatment with sevelamer hydrochloride and 49 with sevelamer carbonate). The most frequently occurring (≥5% of patients) undesirable effects possibly or probably related to sevelamer were all in the gastrointestinal disorders system organ class. Most of these adverse reactions were mild to moderate in intensity. Data possibly or probably related to sevelamer from these studies are listed by frequency here next. Gastrointestinal disorders: nausea, vomiting, upper abdominal pain, constipation (very common) and diarrhoea, dyspepsia, flatulence, abdominal pain (common). The reporting rate is classified as very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000), including isolated. Post-marketing experience: During post-approval use cases of pruritus, rash, intestinal obstruction, ileus/subileus and intestinal perforation have been observed in patients during treatment with sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate. Product licence holder: Genzyme Europe BV, Gooimeer 10, 1411 DD Naarden, The Netherlands. Date of revision of text: September 2010. Attention: Please see full prescribing information.
Anti-PLA2R in membranous nephropathy

Antibodies to the phospholipase A(2) receptor in podocytes are highly associated with disease activity.

Primary (idiopathic) membranous nephropathy (MN) is a common cause of non-diabetic nephrotic syndrome in adults. It has characteristic immunopathological findings on kidney biopsy and a variable clinical course. Some patients remit spontaneously, some progress to end-stage renal disease (ESRD), and others have persistent nephrotic syndrome unless treated with immunosuppressive drugs. In patients who progress to end-stage renal disease and undergo kidney transplantation, there is a relatively high rate of recurrence of MN in the allograft. Until recently, the diagnosis could only be made by kidney biopsy and assessment of disease activity has relied on the presence of proteinuria.

In 2009 Beck and colleagues from the Salant laboratory at Boston University Medical Center reported that the major target antigen in primary MN is the M-type receptor for phospholipase A2 (PLA2R). They also found that a high proportion of patients with primary, but not secondary MN have circulating anti-PLA2R autoantibodies that contribute to the sub-epithelial immune deposits that characterise MN. Since that report, other investigators have confirmed the initial findings, and it is now apparent that up to 80% of patients from various ethnic groups with active primary MN have circulating anti-PLA2R, and that PLA2R can be detected in the immune deposits along with the antibodies on immunohistology in a similarly high proportion of cases. Early studies have also documented that the presence of high levels of anti-PLA2R at the time of transplantation is associated with recurrence of MN in the allograft. Studies from Europe and Asia have also found strong associations between the risk of primary MN and variations in the genes encoding PLA2R and a specific class II MHC immune response receptor. From a practical clinical perspective, this discovery has enabled the development of high-throughput immunassays for anti-PLA2R that will aid in the serological diagnosis of primary MN, distinguish it from secondary MN, and determine immunological activity and perhaps the likelihood of disease recurrence after transplantation.

Members of the Beck and Salant lab at Boston University. Standing (from the left): Laurence Beck, Hong Ma, Nuria Perez, Rivka Ayalon. Sitting: Dana Sandor, David Salant.

Immunofluorescence micrograph of a kidney biopsy from a patient with primary membranous nephropathy showing colocalisation of IgG4 and PLA2R.

©Bernard Collins, Massachusetts General Hospital

Immunosuppression in 2013

New immunosuppressive regimen currently are evaluated in phase I and II studies.

The unaccomplished goal of immunosuppressive regimen in renal transplant recipients is to selectively minimise the alloimmune response to the graft, without interfering with the systemic host defence against external pathogens. Graft survival is usually used as proxy for the first goal and patient survival for the latter. Efficacy of immunosuppressive cocktails is commonly evaluated in short-term randomised controlled trials (RCTs) with a combined outcome including biopsy confirmed rejection, GFR, graft loss or death. Given the low BCAR rates which are in the single digits nowadays, graft patency rates of more than 90% after one year and annual attrition rates of 5-6%, superiority study designs are no longer feasible. The success over the last years could be attributed to improved one-year graft survival (see figure).

It is unlikely that future RCTs of novel drugs in transplantation will be designed to show differences in graft and patient survival. Thus all new/upcoming immunosuppressive drugs are evaluated in non-inferiority trials. This trial design, however, has several limitations. If superiority of a novel regimen is no longer an option, other issues such as health-related quality of life (HRQL) due to fewer side effects have to be considered.

Currently, there are new immunosuppressive regimens evaluated in phase I and II studies. Examples are the ITN trial evaluating donor stem cells in paediatric allograft recipients (NCT01446484), or a trial testing the TLR-2 blocker in subjects with increased risk for DGF (NCT01794663). However, data of these trials will not be available soon. Thus, until the data of larger phase III studies has been presented, well-tolerated and effective standard immunosuppressive regimen remain the gold standard of immunosuppression in renal transplantation.

Rainer Oberbauer, Elisabethinen Hospital, Linz, Austria

S 18: Immunosuppression: when not enough, when too much
Room: Rumeli A
Date: 19-05-2013
From: 16:15 to 17:45

Graph showing deceased donor kidney transplant attrition rates in the United States (n = 164,480).
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The fostering role of ACE inhibitors

ACE inhibitors restore glomerular architecture by moderating progenitor cell activation.

The incidence of kidney diseases is increasing worldwide, and these conditions are emerging as a major public health problem. Renal outcomes are mostly unfavourable in patients with progressive kidney disease, showing the limited capacity of the kidney to repair chronic damage.

However, pharmacological interventions that halt the inexorable tendency of patients with chronic kidney disease to progress to end-organ damage and renal replacement therapy are available. It has been reported that eight years of therapy with angiotensin-convert- ing enzyme (ACE) inhibitor stabilised kidney function in six patients with type 1 diabetes\(^1\). Findings from the “Ramipril Efficacy in Nephropathy (REIN)” study showed that ramipril compared with conventional therapy reduced the rates of renal function loss in patients with non-diabetic chronic nephropathies by 50\%\(^2\). These studies provided evidence that progressive loss of kidney function can be prevented in patients with severe chronic kidney disease, and underlined the possibility of kidney repair in this population.

Evidence of remission of renal disease and regression of renal lesions in humans was deepened by animal studies. The three-dimensional reconstruction of glomerular capillary tufts based on kidney serial section analysis demonstrated that ten weeks of ACE inhibitor treatment in rats genetically programmed to develop glomerulosclerosis allowed the recovery of glomeruli free of sclerosis at an extent higher than that observed in the tissue when the treatment was started\(^3\). ACE inhibitors induced regression of glomerulosclerosis and new formation of glomerular tissue\(^4\).

Recent evidence shed light on the underlying mechanism of renoprotection by ACE inhibitors. In normal kidney the presence of a population of NCAM+ renal progenitor cells within the Bowman’s capsule of adult rat kidney was documented\(^5\). Chaotic migration and proliferation of the Bowman’s capsule progenitor cells pave the way to crescent formation and subsequent sclerosis. By moderating progenitor cell activation, ACE inhibitors restored glomerular architecture and prevented renal disease progression\(^6\). This phenomenon occurs in patients, too.

Understanding the mechanisms of action of already available renoprotective drugs is crucial to unravel novel pathways that are possibly relevant to renal repair. Insights from human genetics and mechanistic studies on renoprotection will be key to design new molecules targeting genes relevant to the renal regeneration. The final goal, if any, would lead to no more dialysis or renal transplantation.

References

Ariela Benigni, IRCCS - Istituto di Ricerche Farmacologiche Mario Negri, Bergamo, Italy

S39: Benefits and risks when pushing renal regeneration
Room: Anadadolu
Date: 21-05-2013
From: 8:00 to 9:30

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Understanding glomerular disease

The pathogenesis of crescentic nephritis and FSGS involve activated parietal epithelial cells.

Activation of glomerular parietal epithelial cells (PECs) has been recognised as common pathomechanism in two seemingly very different glomerular diseases: crescentic nephritis (CN) and focal and segmental glomerulosclerosis (FSGS). These novel insights may fundamentally change our concept and treatment strategy in both diseases.

CN is characterised by uncontrolled proliferation of cells within Bowman’s space. If not treated in time, these cellular crescents may ultimately progress to block the urinary flow into the tubule. Blockade of urinary flow results in degeneration of the tubule and irreversible loss of the entire nephron. This mechanism accounts for the rapid and often irreversible loss of renal function in CN. Recently, it has been shown by cell fate tracing that cellular crescents are derived from PECs and to a lesser extent also from podocytes. The first event in cellular crescent formation is “activation” of PECs: activated PECs express novel marker molecules, change their shape, proliferate and/or migrate. In animal models, early cellular crescents are derived purely from activated PECs and podocytes. This finding was confirmed in human biopsies.

FSGS may occur as primary disease; however, much more frequently it occurs as final common pathway for all glomerular diseases that may ultimately progress into chronic renal insufficiency. So far, glomerulosclerosis has been regarded as an unspecific passive degenerative scarring process. However, cell fate tracing in transgenic mice has again proven that PECs are also activated in this disease. Rather than proliferating in situ as observed in CN, activated PECs invade segments of the glomerular tuft via adhesion from the Bowman’s capsule. From this entry site, activated PECs continue to spread across the glomerular tuft, depositing foreign matrix and thus potentially driving the chronic progressive loss of renal function in a self-perpetuating process. In as yet unpublished studies, we found that PECs participate in all forms of primary or secondary FSGS lesions. We therefore regard glomerulosclerosis as an active process, which is mediated by a specific cell type: the activated PEC.

Activated PECs show specific differences also at the molecular level, such as de novo expression of receptors and activation of signalling pathways. Therefore, it should be possible to inhibit activated PECs pharmacologically. Recently, PDGF receptor inhibition has already been described as an effective therapeutic approach in both CN and FSGS. Future research may offer the exciting perspective of developing novel therapies to develop more specific and potentially effective therapies for these glomerular diseases.

References

Marcus J. Moeller, RWTH Aachen, University Hospital, Aachen, Germany

S39: Benefits and risks when pushing renal regeneration
Room: Anadadolu
Date: 21-05-2013
From: 8:00 to 9:30

The delicate balance of divalent cations

In his lecture, Joost Hoenderop will highlight the characteristics of Mg2+ influx channels.

Magnesium is of great physiological importance in its function in neural excitability, muscle contraction, bone formation, hormone secretion and enzyme activity. The human body is equipped with an efficient negative feedback system counteracting variations of the magnesium balance. This divalent is maintained within a narrow range by the small intestine and kidney which both increase their fractional (re)absorption under conditions of deprivation. Rapid progress has recently been made in the identification and characterisation of magnesium transport proteins which contribute to the delicate balance of divalent cations. Genetic studies in families with a disturbed magnesium balance revealed novel gatekeeper proteins that belong to the super family of the transient receptor potential (TRP) channels.

The epithelial magnesium channel (TRPM6) forms the prime target for hormonal control of active magnesium flux from the urine space or intestinal lumen to the blood compartment. The renal distal convoluted tubule (DCT) has an essential role in maintaining systemic magnesium concentration. The segment is the final determinant of plasma magnesium levels, as the more distal nephron segments are largely impermeable to magnesium. In the past decade, positional candidate strategies in families with inherited forms of hypomagnesaemia have led to the identification of genes involved in magnesium handling. The characteristics of the newly identified transporters and regulatory factors will be discussed and in particular the distinctive molecular regulation of TRPM6 in (patho)physiological situations will be highlighted.

Joost Hoenderop, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

S28: A novel actor – hypo- and hypermagnesaemia
Room: Rumeli B
Date: 20-05-2013
From: 14:30 to 16:00
Lung ultrasound for refining prognosis

US-B lines are powerful predictors of death and cardiovascular complications in end-stage renal disease patients.

Volume overload is a leading risk factor for death and cardiovascular events in end-stage renal disease patients maintained on chronic dialysis, particularly in those with myocardial ischemia and heart failure which represent a substantial fraction of this population. Early identification of volume overload may prevent cardiovascular sequel in these patients, but clinical signs of volume expansion are unsatisfactory to reliably identify patients at risk and monitor them over time. On the other hand, however, reliable standard techniques for measuring extracellular or circulating (blood) volume do not convey information on fundamental heart function parameters that determine the individual haemodynamic tolerance to volume excess and the response to ultrafiltration, i.e. left ventricular (LV) filling pressure and LV function.

Extravascular lung water critically depends on these parameters and represents a proxy of both, circulating volume and LV filling pressure and function; it may therefore be a better criterion to identify patients at a higher risk of volume-dependent adverse clinical outcomes and to monitor the effect of therapy for preventing these outcomes. Recently, a fast (<5 min), easy-to-learn, simple and non-expensive technique has been validated in dialysis patients. By using standard ultrasound (US) machines, this technique quantifies extra-vascular lung water based on the number of US-B lines detected in the whole lung area.

In a multicentre study, 392 haemodialysis patients were enrolled in 11 renal units (Zoccali C et al., JASN 2013, accepted for publication). Moderate to severe lung congestion (US-B lines score 15-60) was detected in 175 patients (45%) and severe congestion (US-B lines >60) in 56 patients (14%). Most patients with moderate to severe lung congestion (71%) were asymptomatic or showed mild effort dyspnoea. During the follow-up period (median 2.1 years) 96 patients died and 90 patients had incident cardiac events that were fatal in 43 cases. Independently of NYHA class and other risk factors, the risk of death (HR: 4.2, 95% CI: 2.4–7.2) and cardiac events (3.20, 1.75–5.88, p<0.001) increased parallel to the BL-US score, being 4.2 times and 3.2 times higher in those with severe lung congestion compared to those with mild or no lung congestion (P<0.01, see figure). The independent predictive power of BL-US for these outcomes was consistent across age, gender, diabetes, hypertension, smoking and background cardiovascular events strata. Prognostic models including US-B lines increased the explained variation in study outcomes of models based on standard risk factors related to CKD and NYHA classification (mortality: from 24% to 30%; cardiac events: from 17% to 22%; both P<0.001). Furthermore, including the BL-US score in the model significantly improved the risk reclassification for cardiac events by 10% (P<0.015).

Lung ultrasound detects pulmonary congestion at a preclinical stage in a substantial number of patients with chronic kidney disease (CKD) stage 5D; it is a strong, independent predictor of death and cardiac events which improves risk reclassification in this population. This technique may be applied for refining prognosis and for designing trials which aim at counteracting lung congestion in this high risk population.

The LUST study, funded by the ERA-EDTA, is set up to test whether a treatment policy (including intensification of ultrafiltration) guided by US-B lines may help to improve clinical outcomes in haemodialysis patients.

Cardiovascular damage in paediatric CKD

Surrogate markers in children may change with age and height.

Chronic kidney disease (CKD) and in particular CKD stage 5 are rare paediatric conditions, with an incidence of about ten per million of the age-related population. CKD is a major factor contributing to cardiovascular (CV) morbidity and mortality in adults, with the highest risk in patients on dialysis. Renal transplantation decreases the cardiovascular risk; however, it still remains definitely higher than for the general population. As large multicentre and longitudinal studies are difficult to perform in children, and given the scarcity of cardiovascular events in paediatrics, surrogate markers should be assessed to characterise cardiovascular damage in this particular population. The appropriate estimation of cardiovascular risk is important not only to identify potential modifiable risk factors but also to evaluate the effect of treatments aimed to reduce risk.

Non-invasive methods of measuring vascular changes and circulating biomarkers are available to assess the presence and severity of cardiovascular damage. Many of these surrogate markers of future cardiovascular events and death are well validated in adult CKD patients, but need technical adaptation, standardisation...
Practical challenges in managing Thrombotic Microangiopathies (TMAs)

Chairman: Professor Oguz Soylemezoglu
Ankara, Turkey

Monday, May 20th 2013, Emirgan Room /ICC-B2

12:45 - 12:50 Introduction
Professor Oguz Soylemezoglu
Ankara, Turkey

12:50 - 13:15 Considerations in diagnosing TMAs
Professor Franz Schaefer
Heidelberg, Germany

13:15 - 13:40 Treatment of aHUS in native and non-native kidney
Professor Neil Sheerin
Newcastle, United Kingdom

13:40 - 13:45 Closing remarks
Professor Oguz Soylemezoglu
Ankara, Turkey
Treating nephropatic cystinosis

The development of a slow-release cysteamine preparation would be important for cystinosis patients.

Since its first description by the Swiss chemist Abderhalden in 1903, nephropathic cystinosis has remained a challenge for (paediatric) nephrologists because of its rarity, laborious treatment and progressive course in the majority of patients. Pioneering studies by Schneider and Gahl in the 1960s-1970s revealed lysosomal cystine accumulation being the cornerstone of cystinosis and the discovery of the cystinosis gene cystinosin (CTNS) in 1999 unravelled the genetic and biochemical background of cystinosis. Cysteamine treatment introduced in the 1980s was a major advantage for improving renal and extrarenal prognosis of patients. In their publication, Marcello et al. clearly showed that the administration of cysteamine before the age of two years and a regular dose adjustment based on the measurement of cystine levels in white blood cells could postpone or even prevent the deterioration of glomerular filtration rate in patients. Wide use of cysteamine therapy in Europe resulted in an increase of age at start of renal replacement therapy, especially in patients treated in specialised centres. Moreover, cysteamine appeared to be protective for extra-renal organs and delayed the development of hypothryoidism, swallowing difficulties and diabetes. Cysteamine lowers lysosomal cystine accumulation via a disulfide exchange reaction with cystine and resulting in the formation of cysteamine and a cysteine-cysteamine mixed disulfide that uses an alternative to the cystine transporter to exit lysosomes. The transporter of the latter disulfide belonging to the P-gp loop family of transporters is therefore a promising alternative for treating cystinosis patients.

One of the major problems using surrogate markers in children is that normal values of a given parameter may change with age. Furthermore, children with chronic diseases known to cause arterial stiffening as CKD frequently suffer from growth retardation. In all population-based paediatric studies, age and height were found to be the major determinants of IMT, ABPM and PWV (see figure), emphasising the need to consider height rather than chronological age in patients with growth deficit. Thus age- and height-specific normal values and percentile curves have been established for these parameters. Based on these data, individual values should be expressed as standard deviation score (SDS) values in paediatric patients to allow comparison between different ages and growth deficits. This offers the possibility for use in longitudinal interventional studies. Thus, some promising methods are available; however, with our current state of knowledge, in paediatric patients these should be reserved for research studies. Scarce clinical resources may better be utilised for preventative strategies to reduce the modifiable risk factors for calcification from early stages of chronic kidney disease.

References:

George S. Reusz, First Department of Paediatrics, Semmelweis University, Budapest Hungary

S34: Cardiovascular disease in children with CKD
Room: Beylerbeyi
Date: 20-05-2013
From: 16:15 to 17:45

Mini Lecture: Improvement in the renal prognosis in nephropathic cystinosis
Room: Beylerbeyi
Date: 20-05-2013
From: 14:30 to 16:00
Chronic kidney disease (CKD) is a growing health problem that leads to end-stage kidney disease and cardiovascular complications in Turkey as well as worldwide. A population-based, national survey in Turkey on populations aged over 18 years, the so-called CREDIT study, was performed to determine the prevalence of CKD, and to evaluate relationships between CKD and cardiovascular risk factors. A cluster sampling technique was used to select study participants. A sampling frame was defined as the seven geographical regions of Turkey which included 81 cities. The study sample was comprised of 23 cities. A total of 10,872 participants were included in the study. A low glomerular filtration rate (GFR) (<60 ml/min/1.73 m²) was present in 5.2% of the subjects who were evaluated for GFR, while microalbuminuria and macroalbuminuria were observed in 10.2% and 2.0% of the subjects, respectively. The estimated prevalence of CKD was 15.7% in the Turkish adult population. The prevalence rates for CKD stages 1, 2, 3, 4, and 5 were 5.4%, 5.2%, 4.7%, 0.3% and 0.2%, respectively. The majority of subjects presented with CKD stage 1-3. CKD was significantly more common in women than in men (18.4% vs. 12.8%, p<0.001). Moreover, the prevalence of CKD increased with increasing age of the subjects. The odds ratios of CKD ranged from 1.45 to 2.18 for every ten years of increase in age for subjects over 30 years. The prevalence of CKD was found to be 11.5% in the population aged <60 years, while it was as high as 38.3% in subjects aged 60 years or older. Stage 3 CKD was especially more common among subjects aged over 60 years (1.6% vs. 21.5%). CKD prevalence was slightly higher among subjects living in rural areas than in those in urban areas (16.8% vs. 15.2%). CKD prevalence was highest among subjects from the Marmara region (19.7%) followed by Southeastern Anatolia (18.6%), the Black Sea (16.1%), East Anatolia (14.2%), the Aegean (13.8%), Central Anatolia (12.6%), and the Mediterranean (11.7%) regions.

In the general population, the prevalence rates for hypertension, diabetes, dyslipidaemia, obesity, and metabolic syndrome were 32.7%, 12.7%, 77.0%, 20.1%, and 32.3%, respectively. The prevalence of hypertension was higher in subjects with CKD than in those without CKD (56.3% vs. 31.0%). Similarly, the prevalence rates of diabetes (26.6% vs. 10.1%), dyslipidaemia (83.4% vs. 75.8%), obesity (29.2% vs. 20.0%), and metabolic syndrome (46.0% vs. 29.8%) were significantly higher in subjects with chronic kidney disease compared to subjects without CKD. Furthermore, the prevalence of these cardiovascular risk factors gradually increased in subjects having advanced stages of the disease. Thus, chronic kidney disease was found to be strongly associated with these cardiovascular risk factors.

The prevalences of decreased GFR and microalbuminuria were higher in subjects having these risk factors, particularly in those having hypertension and diabetes. The prevalence of chronic kidney disease among subjects with and without hypertension was 25.3% and 10.6%, respectively. Similarly, chronic kidney disease was significantly more common in subjects with diabetes than in subjects without diabetes (32.4% vs. 13.0%). In conclusion, similar to many other countries, CKD is a major health problem in Turkey. Associations between CKD and several cardiovascular risk factors emphasise that this is a major public health problem, and a major predictor of overall morbidity and mortality. The population examined in the present study is currently being followed up in a longitudinal study, and results will be evaluated after five years.

Reference

Gultekin Suleymanlar, Akdeniz University Medical School, Antalya, Turkey, Congress President of the ERA-EDTA and President of the Turkish Society of Nephrology

CKD & Its Stages in Turkey

Cardiovascular risk factors were significantly more prevalent in CKD patients, according to the Turkish CREDIT study.
Developing nephrology

A special symposium on Monday is dedicated to renal care in various countries of Eastern Europe and Maghreb.

In the past 20 years, dramatic political and economic changes have occurred in Eastern Europe and the Maghreb which also had a positive impact on renal care in these regions. Although the availability and the outcome of renal replacement therapy in many of these states have become comparable with what is seen in more developed Western Europe, large differences between individual countries exist.

Congress attendees are cordially invited to visit a special symposium on the developing nephrology in 14 countries of Eastern Europe and Maghreb. For a first impression, read more about renal replacement therapy (RRT) in Russia and transplantation in Bosnia and Herzegovina.

Russia – past and present of RRT

The territory of Russia covers more than 17 million square kilometers and is home for about 143 million people. With an average income per capita of 19,240 US dollars (PPP adjusted), the total health spendings amount to 998 US dollars (PPP adjusted) per capita per year. 1.7 million deaths occur in Russia due to non-communicable diseases (NCD), with an age-standardised NCD death rate as high as 1108.6 and 561.8 per 100,000 males and females, respectively. Russia consists of 83 territorial entities; each is administrated by its own regional government, and local healthcare budgets and policies are determined by regional authorities. Interregional health expenditures depend on the economic status accounting for fourfold differences between distinct regions, while life expectancy at birth can vary within almost 20 years. The Russian Registry of Renal Replacement Therapy was established as one of the most important activities of the Russian Dialysis Society founded in 1998; the registry provides comprehensive data about treated end-stage renal disease (ESRD) patients in all regions. RRT prevalence rates increased from 55.9 pmp in 1998 to 142.3 pmp in 2007 and to 195.7 pmp in 2011. RRT treatment is provided in 341 facilities around the country (almost 13% more than five years ago). By the end of 2011 the total number of patients on RRT had reached 27,989 (almost 38.5% more than in 2007). Of these, 5,932 (21.2%, 41.5 pmp) were living with a functioning kidney graft, 20,214 (72.2%, 141.3 pmp) were treated with haemodialysis (HD), and only 1843 (6.6%, 12.9 pmp) received peritoneal dialysis (peritoneal dialysis, mainly continuous ambulatory peritoneal dialysis). Despite of this tremendous increase, RRT rates in Russia still remain much lower than in Central and Western Europe. Depending on the regional economic status, RRT prevalence rates range from 30 pmp to 350 pmp, with highest rates in Saint Petersburg and Moscow. In recent years, RRT development and economic growth in many regions made these inequalities less pronounced. However, national RRT programmes throughout the whole country are still missing. While dialysis is supported only by regional authorities, kidney transplantation is the only RRT modality supported by federal government, and transplantation rates almost doubled from 465 operations in 1998 (3.2 pmp) to 975 in 2011 (6.8 pmp). Nevertheless, the urgent need for more kidney transplantations remains.

Due to the lack of HD stations, Russian patients on RRT differ from patients in Europe and USA in many aspects. The mean age of prevalent dialysis patients in 2011 was 50.8 years, with 14% being older than 65 years. 42.3% of ESRD cases on dialysis could be attributed to chronic glomerulonephritis (although rarely proved by biopsy), 12.5% to diabetic nephropathy, 11.9% to polycystic kidney disease, 11.6% to chronic tubulointerstitial nephritis and pyelonephritis, and 6.1% to hypertensive glomerulonephritis.

The mean age of patients with kidney graft was 43.1 years; 5.1% were older than 65 years; 4.8% were diabetics. Quality of treatment improved substantially over the past years, as shown by an increase of HD patients with urea reduction rates of more than 65 from 55.5% in 2001 to 85.1% in 2011. Moreover, the prevalence of anaemia (haemoglobin <100 g/l) in HD patients decreased from 70% in 2000 to only 30% in 2011; in addition, the rate of prevalent HD patients with a systolic blood pressure of more than 160 mm Hg decreased from 27.5% in 2000 to 18.6% in 2011. The five-year average annual mortality rate was 7.1 per 100 patient-years for HD, 8.5 for PD and 1.6 for kidney transplant recipients.

Russia is the largest country on earth in terms of surface area with an extremely non-uniform distribution of its population spread and considerable regional differences with regard to economic conditions. Nevertheless, RRT has been developing rather quickly in recent years with substantial improvement in the quality of treatment. The future development of ESRD care depends a lot on the implementation of a state-funded programme including screening for chronic kidney disease and nephroprotection in high risk populations.

Transplantation in Bosnia and Herzegovina

Health care in Bosnia and Herzegovina is not guided by one common ministry. Instead, responsibility lies in the hands of two health ministries representing the two political entities, the Federation of Bosnia and Herzegovina and the Republic of Srpska, and a third health department for the Brcko District. On the country level, the Ministry of Civil Affairs is responsible for coordinating activities between these ministries, although on a limited level.

![Natalia Tomilina](Tomiлина(2))

![Halima Resic](Resic)
Data related to organ transplantation in Bosnia and Herzegovina are scarce and mostly available to a small number of people concentrated in medical centres. Therefore, public awareness of organ donation in Bosnia and Herzegovina society is virtually non-existing and organ transplantation plays a minor role in RRT.

Although a waiting list for cadaveric kidney transplants in the Federation of Bosnia and Herzegovina has been existing since 2006, it includes only 180 registered patients from the Federation of Bosnia and Herzegovina. According to the Bosnia and Herzegovina Renal Registry, however, the number of candidates waiting for cadaveric renal transplantation amounted to 600 patients in 2011. Between 2006 and 2012, a total of 23 cadaveric transplantsions of kidney, liver and eye cornea have been performed in three transplant centres in Tuzla, Sarajevo and Banja Luka.

Systems to identify potential donors and recipients are missing in Bosnia and Herzegovina. Nevertheless, efforts to raise public awareness have been undertaken by the Donor Network of Bosnia and Herzegovina and the Donor Network of Canton Sarajevo; they resulted in 9000 signed donor cards in Canton Sarajevo, but these cards are not obligatory.

In the field of healthcare, Bosnia and Herzegovina has adopted several strategic documents to assure adjustments to international obligations. One of these documents is a Resolution of Health Policy for all Bosnian citizens stating the necessity of building a health care system that is compatible with other European countries. Both Ministries of Health and the Brcko District Department of Health have adopted their legislation regarding organ transplantation.

Identification of potential donors and the consent of potential donors and/or their families to donation are key elements for organ transplantation. Appointment brain death coordinators in hospitals would be the first step to improve the donation process.

Constant public education and additional efforts to raise public awareness and educate health care professionals must also be included. Thus, Bosnia and Herzegovina needs better organisation in this field, central coordination and a central authority for transplantation.

From CONTRAST to ESHOL

Studies suggest that high volume online haemodiafiltration provides significant survival benefit.

Despite advances in dialysis therapy, both overall and cardiovascular mortality rates in patients treated with conventional haemodialysis (HD) are much higher than those seen in the non-uraemic population. Retention of middle or large middle-sized molecules is considered to impact the pathogenesis of cardiovascular disease (CVD). It is therefore reasonable to assume that dialysis treatment modalities increasing the removal of middle molecules may reduce the incidence of CVD and thereby contribute to improved patient survival. Removal of larger uraemic retention solutes, commonly referred to as uraemic toxins, is limited in conventional HD therapies. Online haemodiafiltration (OL-HDF), which combines diffusive and convective transport, is superior to conventional HD in terms of clearance of small solutes, such as urea and middle molecules, like α-2 microglobulin. It has been suggested that OL-HDF (utilising biocompatible high-flux membranes and ultrapure dialysis fluids) may improve clinical outcomes through enhanced small, middle and larger protein-bound uraemic solute clearance, better intradialytic haemodynamic stability, reduced inflammation, anaemia correction and improved phosphate control compared with conventional HD. The Dialysis Outcomes and Practice Patterns Study (DOPPS) found that high-efficiency OL-HDF treatment (high-volume substitution 15–25 l) was associated with better survival compared to low-flux HD. The prospective, observational RISCAVID study and a retrospective analysis also suggested OL-HDF to be associated with better survival.

Recently, three randomised controlled trials (RCT) investigated the effect of OL-HDF on survival. The CONTRAST study randomised 714 prevalent patients to low-flux HD or OL-HDF. The primary outcome measure was all-cause mortality during three years of follow-up. Although target convection volume was 24 l per session, median convection volume achieved was 19.8 l. No significant survival difference was found, however, there was a 39 % decrease in mortality risk in patients treated with a convection volume over 21.95 l after an extensive adjustment for determinants of convection volume and mortality.

The second one, the Turkish Haemodiafiltration Study, randomised 782 prevalent patients to high-flux HD and OL-HDF. Primary outcome was a composite of overall mortality and new cardiovascular events; secondary outcomes included overall and cardiovascular mortalities. The median replacement volume and convection volume reached were 17.4 l and 20.7 l, respectively, and were thus higher than in the CONTRAST study. Despite a trend favouring OL-HDF for primary and secondary outcomes, the difference was statistically not significant. Similarly to the previous study, the subgroup of OL-HDF patients treated with a median substitution volume over 17.4 l showed better cardiovascular (p=0.002) and overall survival (p=0.03) compared to the high-flux group. In adjusted Cox-regression analyses, high volume OL-HDF was superior, too.

The ESHOL study randomised 906 prevalent patients to high-flux HD and to OL-HDF. Primary outcome was overall mortality during a mean follow-up of 1.91±1.1 years. This RCT achieved much higher convection volumes than the other two trials; the median quarterly replacement volume and convective volume during the study ranged from 20.8 to 21.8 l/session and 22.9 to 23.9 l/session, respectively. ESHOL showed that OL-HDF provides a 30 % lower risk of all-cause mortality (p=0.01), a 33 % lower risk of cardiovascular mortality (p=0.06), and a 55 % lower risk of infection-related mortality (p=0.03). Additionally, OL-HDF reduced intradialytic hypotension and hospitalisation rates.

The results of these studies demonstrate that postdilution OL-HDF is a safe, well-tolerated treatment method and high volume OL-HDF provides significant survival benefit.
Improving intradialytic hypotension

Intradialytic biofeedback control systems may offer improved haemodynamic stability.

The progressive increase in the mean age of patients on haemodialysis and the growing number of comorbidities, especially cardiovascular diseases and diabetes, have significantly worsened tolerance to conventional haemodialysis treatment. Attempts to correct extracellular fluid expansion in “frail” patients result in intradialytic hypotension (IDH) which affects up to 40% of all haemodialysis sessions and is associated with morbidity and mortality. The first step towards improving the haemodynamic management of dialysis is the utilisation of non-invasive sensors to continuously monitor haemodynamic or biochemical parameters involved in cardiovascular stability, such as blood volume (BV), blood temperature (BT), blood pressure (BP), heart rate and electrolytes.

A second step is the use of so-called biofeedback control systems, which may exert a more direct control. The biofeedback concept is synonymous with a closed-loop control of biological variables; apart from the continuous measurement of a variable, it presupposes evaluation by an expert system, the so-called controller, and a series of tools, the actuators, that allow to regulate the behaviour of a variable that we wish to control (figure). In clinical practice, different biofeedback systems emerged which address the control of BV (figure), BT and BP. The application of BV biofeedback to haemodialysis involves a clinically significant reduction in the frequency of symptomatic IDH. A recent meta-analysis1 has confirmed a substantial reduction (10%, CI 8-13%) of hypotension episodes with biofeedback haemodialysis in comparison with conventional haemodialysis. Apart from BV, intradialytic haemodynamics can be improved using a BT monitor. The thermal exchange processes between blood and heated dialysate during haemodialysis may have a negative impact on several haemodynamic parameters (i.e. peripheral vascular resistances, myocardial contractility) of patients on haemodialysis. This additional cardiovascular stress can be avoided by adapting dialysate temperature to individual patient needs. The availability of microprocessor-controlled equipment allows for the development of a biofeedback (closed-loop control) to influence the extracorporeal thermal balance in a predefined way according to the medical prescription.

A prospective study (on 95 hypotension-prone patients)2 documented the haemodynamic benefits by showing reduction of the IDH of isoe energetic haemodialysis (patient temperature was kept constant throughout the treatment) as compared with the thermo-neutral treatment mode (no temperature changes in the extracorporeal study).

Lastly, biofeedback can also be based on both BP measurement throughout the haemodialysis session and the automatic counter-regulation of ultrafiltration rates. The system is based on a fuzzy controller allowing for the modulation of ultrafiltration proportionally to the variation trend in BP. So, small variations in BP are matched by small variations in ultrafiltration or the maintenance of constant ultrafiltration rates, while large BP reductions are matched by large variations in ultrafiltration. A clinical randomised controlled trial, based on the application of this system, has shown its efficacy in improving symptomatic IDH.3 However large and well-designed randomised trials on these biofeedback systems are needed to assess the effects on survival, hospitalisation and quality of life.

References


Antonio Santoro, Policlinico S. Orsola-Malpighi, Bologna, Italy

S8: Common dialysis problems – new solutions

Room: Harbyle
Date: 19-05-2013
From: 14:30 to 16:30

Towards the best possible guideline

Meet at the booth of the European Renal Best Practice group in Istanbul.

The European Renal Best Practice (ERBP) group is committed to offering guidance to the nephrology community. Last year, five young nephrologists joined the ERBP group to work on guidelines and provide methods support. Reinforcing the team already paid off: the guideline on kidney transplant management is in production and an online version will be available at the congress – ERBP chair Professor Wim Van Biesen of the University Hospital Ghent appreciates the useful input of ERA-EDTA members after the draft was sent to them. Moreover, the hyponatraemia guideline is almost finalised after the manuscript was evaluated in a CME session in March 2013. At the ERBP booth in Istanbul, congress attendees can participate in a quiz on both topics and win fancy prizes such as an iPod Touch. In addition, short format versions of the transplant guideline and diagnostic flowcharts for hyponatraemia are available there.

Another change refers to the renal guidance section in the Nephrology Dialysis Transplantation journal. Van Biesen explains: “We currently
have six papers covering aspects that can be of interest when producing guideline. These papers will be published in the coming months and I think they will provide an ideal starting point to discuss on the future concept of guidelines. The publication of van Biesen refers to will be entitled:
- Mission Statement of ERBP: deals with what guidelines should be or not, according to ERBP, and introduces the concept of shared decision making as an important aspect during guideline production.
- Is there a place for health economic considerations in guideline formation: discusses pros and cons of introducing health economic aspects in guideline formation.
- Providing guidance in the dark – orphan renal diseases and guideline: refers to the specific problem of providing guidance for diseases for which not much evidence is available.
- Bridging the gap between what we know and what we do in renal medicine: deals with problems to get available knowledge implemented in daily clinical practice.
- The importance of correct outcome selection and reporting in studies for guideline production: will be an introduction to both the problem of ‘outcome selection’, and also to the planned ‘SONG initiative’, a collaborative effort together with the Sydney-based Cochrane Renal Centre.
- Towards the best possible guideline: describes the procedure and methodology ERBP will use to produce its guidelines.

Wim Van Biesen also gives an outlook on future ERBP activities: “We expect to finalise our guideline on the management of diabetes in patients with advanced CKD early next year.

In addition, we have identified new guideline topics. These will address vascular access, management of frail patients with advanced chronic kidney disease, such as the elderly, and pre-emptive transplantation. We furthermore plan to expand our section on patient information as I think this is crucial to increase shared decision making.”

As the involvement of nephrologists is essential for the tasks ERBP has set for itself, the ERBP chair encourages nephrologists to participate actively: “Our team is happy to provide methods support for those who'd like to learn more about guidelines and evidence-based medicine.”

It's time for action!

Low sodium diet should be the basic approach to CKD-related hypertension.

A large body of evidence supports the validity of lowering blood pressure (BP) to prevent cardiovascular disease in the general population. This issue becomes even more critical in chronic kidney disease (CKD) patients because they carry a greater cardiovascular risk across the entire spectrum of CKD stages.

In these patients, achievement of lower BP levels also is fundamental to limit the progression of renal damage, especially in the presence of significant proteinuria. Although guidelines have repeatedly recommended in the last decade to intensively decrease BP in CKD, management of hypertension in renal patients still remains inadequate.

Armed with the knowledge of the extreme salt-sensitivity of BP in CKD, it is reasonable to hypothesise that low salt diet should be the basic approach to CKD-related hypertension. Indeed, besides the well known lower effectiveness of diuretic therapy in the presence of unrestricted salt intake, normal sodium diet also precludes optimal control of BP during pharmacological treatment with vasodilating agents (Fig. 1). Furthermore, about one out of four hypertensive patients with non-dialysis CKD have resistant hypertension (RH): persistence of office BP ≥130/80 mmHg despite adherence to ≥3 full-dose antihypertensive drugs including a diuretic or ≥4 drugs regardless BP level. This condition, that markedly increases the risk of cardiovascular and renal events, is more common in patient not adhering to a low salt regimen (Fig. 2).

Unfortunately, although abundant literature has evidenced that dietary sodium restriction decreases BP not give up with low salt diet prescription but rather make all the efforts to broaden implementation of this indispensable non-pharmacological intervention in their hypertensive patients.

Luca De Nicola, Second University of Naples, Italy

S32: Sodium in kidney failure patients: new open questions
Room: Rumeli B
Date: 20-05-2013
From: 16:15 to 17:45
Where East meets West

Palaces and imperial mosques line Istanbul's hills as visible reminders of the city's cultural heritage.

For nearly sixteen centuries, Istanbul, formerly known as Constantinople, served as the capital of four empires: the Roman, the Byzantine, the Crusader and the Ottoman Empire. Today, it is among the largest cities in Europe with an estimated number of 14 million inhabitants. Located at both sides of the Bosphorus, Istanbul stands on two different continents.

Europe and Asia. Although the Republic of Turkey established its capital in Ankara, palaces and imperial mosques still line Istanbul’s hills as visible reminders of the city’s cultural heritage.

Attraction not to be missed

- **Topkapi Palace (Topkapi Sarayi):** residence of Ottoman rulers. The palace hosts numerous Ottoman treasures and offers one of Istanbul’s most beautiful views, incorporating the Bosphorus, the Golden Horn, the two shores and the sea of Marmara. Bab-i Hümayün Caddesi (Sultanahmet tram stop); www.topkapisarayi.gov.tr

- Bosphorus boat trip

Departure is from Eminönü in the immediate vicinity of the Galata Bridge. You may plan for a stop in one of the many villages along the route and schedule dinner at one of the fish restaurants with a breathtaking view over the Bosphorus. www.wittistanbul.com/magazine/what-bosphorus-cruise-tour-to-take-in-istanbul/

- **Shopping**

- The Grand Bazaar (Kapali Çarsı): a must of each visit to Istanbul. You may enter the bazaar for example through the Carsi Gate (Beyazıt tram stop). Monday to Saturday, 9:00 to 19:00. Closed on Sunday. www.grandbazaaristanbul.org

- Nisantasi: Doubtlessly the most important shopping and fashion centre of Istanbul. The quarter forms the background to several novels by Nobel laureate Turkish novelist Orhan Pamuk, who is a local resident. One of the most popular avenues of Nisantasi is Abdi İpekçi Caddesi, ten minutes walk from Osmanbey metro station.

- **Dining in Istanbul**

360° Istanbul

A breathtaking view high above the rooftops of Istanbul! The restaurant, located in an Art Nouveau building, was chosen in 2006 as the most beautiful place to eat in Istanbul. By reservation only. Istiklal Cad. 311 | Misir Apt. (Beyoğlu), www.360istanbul.com

Changa

Excellent fusion cuisine. Through a glass floor, guests can watch the chef de cuisine at work. Siraselviler Cad. 47 (Taksim), www.changa-istanbul.com

Balıklı Sabahattin

Excellent seafood and mezes close to the Blue Mosque. Seyit Hasan Kuyu Sokak 1, (Fatih), http://balikcisabahattin.com

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Attractions not to be missed

- **Blue Mosque (Sultanahmet Camii):** a superb building in the classical Ottoman style and one of the most famous monuments in the Islamic world. It owes its name to the roughly 20,000 blue and white ceramic tiles that line the inside of the entire walls and ceiling. Meydan Sokak 17, Sultanahmet (Sultanahmet tram stop), www.3dmekanlar.com/blue_mosque.htm

- Hagia Sophia (Ayasofya): built in the sixth century by the Emperor Justinian it was one of the largest domed basilicas in the Christian world. Later, the Ottomans converted it into a mosque. Now a museum, the Hagia Sophia shows a unique selection of coexisting Islamic and Christian religious art works. Hagia Sophia Square, Sultanahmet (Sultanahmet tram stop), www.ayasofyamuzesi.gov.tr

- Basilica Cistern (Yerebatan Sarıncı). Remember the scene in one of the early James Bond movies “From Russia With Love”, when Sean Connery is rowing in a small boat through a forest of marble columns? That scene was filmed in Yerebatan, a giant underground cistern built by Roman Emperor Justinian in 532 to provide water to the city in cases of siege. Yerebatan Caddesi 13, Sultanahmet (Sultanahmet tram stop); www.yerebatan.com

- Spices at the bazaar.

- Pastry: don’t think only of baklava and Turkish delight; there is also a variety of puddings, and künefe, a grilled dessert made from wheat, cheese, and sugar syrup.

- Kebab: the traditional Turkish response to fast food; try for example Fistik kebab, made of minced lamb and chopped pistachios, or Cag kebab, which originates in the eastern Anatolian province of Erzurum.

- Fish: if you love to eat fish, Istanbul is paradise on Earth. In May, sea bass, mullet, sole and swordfish are still very good. Shrimp and lobster are also available.

- Parast: do not think only of baklava and Turkish delight; there is also a variety of puddings, and künefe, a grilled dessert made from wheat, cheese, and sugar syrup.

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The results of five path-breaking clinical trials will be presented during the ‘late-breaking clinical trial’ session on Sunday morning. Please read more about the trial results in tomorrow’s ERA-EDTA Daily Congress Newspaper.

Soluble ferric phosphate in HD
Dr. Ajay Gupta et al., Wixom, Michigan, U.S.A.: Soluble ferric phosphate (SFP) is a unique iron compound delivered to the haemodialysis patient via dialysate. The PRIME Study examined the efficacy of SFP on the doses of erythropoiesis stimulating agents used to maintain Hgb levels in a target range of 95 to 115 g/l in dialysis patients.

Prophylaxis of catheter-related infections in PD
Dr. Carolyn van Eps, Brisbane, Australia: Unfortunately, there is a paucity of high level clinical evidence available to guide the optimal strategy for preventing exit site infection (ESI) and peritonitis in peritoneal dialysis (PD) patients. In her study, the author tested the effects of antibacterial honey in this indication.

Restoring estrogen receptor and anti-oxidant levels in diabetic kidney disease
Prof. Gary Striker et al., New York, U.S.A.: Expression of the estrogen receptor α (ERα) is reduced in diabetic kidney disease (DKD), a fact that may explain the increased risk of cardiovascular disease in these patients. In their study the authors asked the question if sevelamer carbonate can improve this situation.

The effectiveness of atorvastatin in chronic HD
Dr. Guenther Silbernagel et al., Bern, Switzerland: Low density lipoprotein (LDL) cholesterol lowering with atorvastatin can improve this situation.

Prognostic effects of HDL cholesterol and apolipoproteins
Prof. Winfried März et al., Mannheim, Germany: High-density lipo-protein (HDL) cholesterol has been suggested to be dysfunctional in end-stage renal disease. In their study, the authors investigated the impact of HDL cholesterol and the major protein components of HDL, namely apolipoproteins A1, A2, and C3 on the outcome in diabetic patients on haemodialysis.

Late-breaking clinical trials
Join today’s morning session to catch up with the latest hot topics in clinical nephrology.

In the spirit of the 50th anniversary of the ERA-EDTA congress, we have been looking back at changes in haemodialysis (HD) care since the start of the Dialysis Outcomes and Practice Patterns Study (DOPPS) in 1996. Results of this review will be presented at the symposium ‘International practices and improved dialysis outcomes: the DOPPS’.

Since 1996, the DOPPS programme has expanded across the world; currently, data are being collected from over 500 dialysis units in 21 countries. There are over 70,000 patients in these units, and a random sample of over 18,000 of these patients is being studied in great detail. These data give us a representative picture of HD in these countries. The large sample of units and patients increases the observable variation in practices and outcomes. By adjusting for demographics and comorbidities, we are able to identify associations between practice patterns and outcomes such as mortality, hospitalisation and quality of life. As in all observational studies, it is not possible to determine cause and effect from these associations. However, by studying practices at the level of the dialysis unit, we are able to reduce bias caused by the link between individual patients’ characteristics and their indications for particular treatments.

In large part, the DOPPS was established in response to the great differences in mortality observed by dialysis registries among patients in the United States, Europe and Japan. The DOPPS has confirmed these differences and has highlighted the major role of vascular access, in particular HD catheters, in explaining them. Since 1996, there have been large changes in the use of catheters in many countries, not always for the better. Although the HD population of patients in 2012 is older and more likely to have diabetes than in 1996, this does not explain all of these changes. During the symposium we will discuss how the treatment of anaemia and mineral and bone disorder (MBD) has changed over the last 17 years. The impact of payment changes and new guidelines on anaemia and MBD will be discussed.

The primary aim of DOPPS is to both ‘add years to life’ and ‘life to years’ for HD patients. To identify practices that lead to an improved quality of life we have studied patient-reported outcomes in the DOPPS. Recent analyses have shown how the simple question “How long does it take you to recover from a dialysis session” can help identify those patients with a poor quality and life and increased risk of hospitalisation and mortality. We look forward to seeing you at the DOPPS symposium!

References
1 Robinhood BM et al. CJASN 04940512; published ahead of print October 25, 2012, doi:10.2215/CJN.04940512

Hugh C. Rayner, Birmingham Heartlands Hospital, Birmingham, UK

S30: International practices and improved dialysis outcomes: DOPPS
Room: Harbiye
Date: 20-05-2013
From: 16:15 to 17:45
OUR NAME HAS CHANGED.
OUR COMMITMENT TO
NEPHROLOGY ENDURES.

The partner you once called Abbott is now AbbVie. Our name has changed but our commitment to join you in improving patient care has not. We stand by our promise to develop and deliver innovative medicines and work with you to elevate the standard of care in the treatment of kidney disease.

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