Aktivitäten des Suisse ADPKD Kompetenzzentrums

Schweizer ADPKD Symposium

Zürich, 7. November 2019

Prof. Dr. Stefan Russmann

ADPKD Forschung

Database management with outcomes and safety analyses for a patient cohort with autosomal dominant polycystic kidney disease (ADPKD)

Analysis of efficacy and safety data of tolvaptan treatment in patients with autosomal dominant polycystic kidney disease

Master thesis conducted by Emiri Grimes[1],

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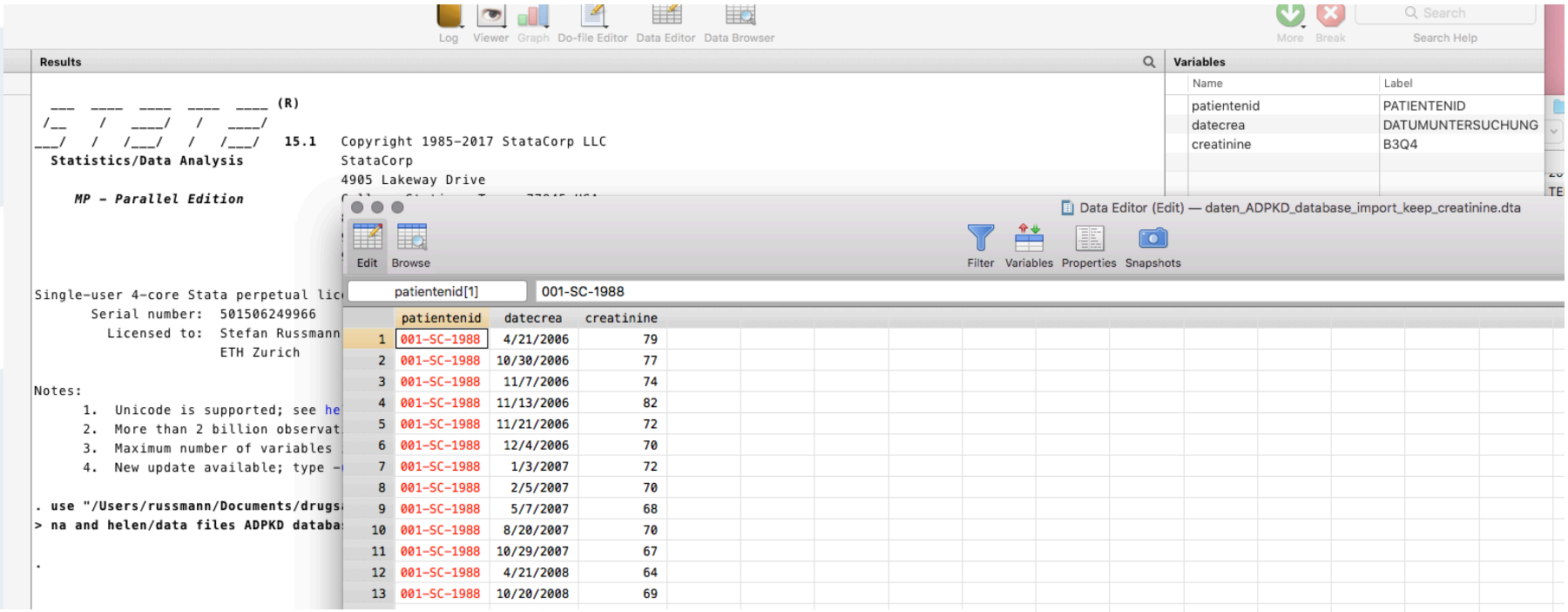

Cyst Infections in Patients with Autosomal Dominant Polycystic Kidney Disease

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Background and objectives: Cyst infection is a complex diagnostic and therapeutic issue in patients with dominant polycystic kidney disease (ADPKD); however, published data regarding the diagnosis and the managem infections in patients with ADPKD are sparse.

ADPKD Sprechstunde

ADPKD Sprechstunde

DRUGSAFETY.CH

- Tolvaptan-Therapie
- Monitorisierung von Leberwerten

AUSTRALIAN PRODUCT INFORMATION
JINARC® (TOLVAPTAN) TABLETS

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Idiosyncratic hepatic toxicity

Tolvaptan has been associated with idiosyncratic elevations of blood alanine and aspartate aminotransferases (ALT and AST) with infrequent cases of concomitant elevations in bilirubin-total (BT).

In postmarketing experience with tolvaptan in ADPKD, acute liver failure requiring liver transplantation has been reported.

WARNING: RISK OF SERIOUS LIVER INJURY

- **JYNARQUE (tolvaptan) can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported**
- **Measure transaminases (ALT, AST) and bilirubin before initiating treatment, at 2 weeks and 4 weeks after initiation, then monthly for the first 18 months and every 3 months thereafter. Prompt action in response to laboratory abnormalities, signs, or symptoms indicative of hepatic injury can mitigate, but not eliminate, the risk of serious hepatotoxicity.**
- **Because of the risks of serious liver injury, JYNARQUE is available only through a Risk Evaluation and Mitigation Strategy program called the JYNARQUE REMS Program**

Curr Hypertens Rev. 2013 Feb;9(1):2-11.

Cardiovascular complications in autosomal dominant polycystic kidney disease.

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Abstract

Cardiovascular complications are a major cause of morbidity and mortality in patients with autosomal dominant polycystic kidney disease (ADPKD). Hypertension is a common finding of ADPKD occurring in 50-70% of patients before the impairment of renal function. Stimulation of the renin-angiotensin-aldosterone system plays a major role in the development of hypertension in ADPKD. Hypertension is associated with an increased rate of progression to end-stage renal disease and is the most important potentially treatable variable in these patients. Left ventricular hypertrophy, a major cardiovascular risk factor, is also common in patients with ADPKD. Both hypertension and left ventricular hypertrophy play a crucial role in the development of cardiovascular complications in these patients. Furthermore, endothelial dysfunction, impaired coronary flow velocity reserve, biventricular diastolic dysfunction, increased carotid intima-media thickness, and arterial stiffness are present even in young normotensive patients with ADPKD who have well-preserved renal function. These findings suggest that cardiovascular involvement starts very early in the course of ADPKD. Intracranial and extracranial aneurysms and cardiac valvular defects are other potential cardiovascular problems in patients with ADPKD. A multifactorial approach aiming at all cardiovascular risk factors, such as hypertension, smoking, dyslipidemia and obesity is extremely important in these patients. Early diagnosis and treatment of hypertension, with drugs that block the renin-angiotensin-aldosterone system, has the potential to decrease the cardiovascular complications and slow the progression of renal disease in ADPKD.

PMID: 23971638

Kidney Blood Press Res. 2017;42(6):1290-1302. doi: 10.1159/000486011. Epub 2017 Dec 15.

Early Markers of Cardiovascular Risk in Autosomal Dominant Polycystic Kidney Disease.

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Abstract

BACKGROUND/AIMS: Cardiovascular disease is the most frequent cause of morbidity and mortality in autosomal dominant polycystic kidney disease (ADPKD) patients, often before the onset of renal failure, and the pathogenetic mechanism is not yet well elucidated. The aim of the study was to identify early and noninvasive markers of cardiovascular risk in young ADPKD patients, in the early stages of disease.

METHODS: A total of 26 patients with ADPKD and 24 control group, matched for age and sex, were enrolled, and we have assessed inflammatory indexes, mineral metabolism, metabolic state and markers of atherosclerosis and endothelial dysfunction (carotid intima media thickness (IMT), ankle brachial index (ABI), flow mediated dilation (FMD), renal resistive index (RRI), left ventricular mass index (LVMI)) and cardiopulmonary exercise testing (CPET), maximal O2 uptake (V'O2max), and O2 uptake at lactic acid threshold (V'O2@LT).

RESULTS: The ADPKD patients compared to control group, showed a significant higher mean value of LVMI, RRI, homocysteine (Hcy), Homeostasis Model Assessment-insulin resistance (HOMA-IR), serum uric acid (SUA), Cardiac-troponinT (cTnT) and intact parathyroid hormone (iPTH) ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p=0.007$, $p=0.019$; respectively), and a lower value of FMD and 25-hydroxyvitaminD (25-OH-VitD) ($p<0.001$, $p<0.001$) with reduced parameters of exercise tolerance, as V'O2max, V'O2max/Kg and V'O2max (% predicted) ($p<0.001$, $p<0.001$, $p=0.018$; respectively), and metabolic response indexes (V'O2@LT, V'O2 @LT%, V'O2@LT/Kg,) ($p<0.001$, $p=0.14$, $p<0.001$; respectively). Moreover, inflammatory indexes were significantly higher in ADPKD patients, and we found a positive correlation between HOMA-IR and C-reactive protein (CRP) ($r=0.507$, $p=0.008$), and a negative correlation between HOMA-IR and 25-OH-VitD ($r=-0.585$, $p=0.002$).

CONCLUSION: In our study, ADPKD patients, in the early stages of disease, showed a greater insulin resistance, endothelial dysfunction, inflammation and mineral metabolism disorders, respect to control group. Moreover, these patients presented reduced tolerance to stress, and decreased anaerobic threshold to CPET. Our results indicate a major and early cardiovascular risk in ADPKD patients. Therefore early and noninvasive markers of cardiovascular risk and CPET should be carried out, in ADPKD patients, in the early stages of disease, despite the cost implication.

ADPKD Sprechstunde

- CV Risikofaktoren
  - Blutdruckeinstellung

DRUGSAFETY.CH

ADPKD SYMPOSIUM
Klinik Hirslanden, 4. Oktober 2016

SICHERE UND ERFOLGREICHE BLUTDRUCKTHERAPIE BEI ADPKD

Prof. Dr. med. Stefan Russmann

ESC European Society of Cardiology

European Heart Journal (2019) **00**, 1–78
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ESC/EAS GUIDELINES

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

Authors/Task Force Members: François Mach* (Chairperson) (Switzerland), Colin Baigent* (Chairperson) (United Kingdom), Alberico L. Catapano[1]* (Chairperson) (Italy), Konstantinos C. Koskinas (Switzerland), Manuela Casula[1] (Italy), Lina Badimon (Spain), M. John Chapman[1] (France), Guy G. De Backer (Belgium), Victoria Delgado (Netherlands), Brian A. Ference (United Kingdom), Ian M. Graham (Ireland), Alison Halliday (United Kingdom), Ulf Landmesser (Germany), Borislava Mihaylova (United Kingdom), Terje R. Pedersen (Norway), Gabriele Riccardi[1] (Italy), Dimitrios J. Richter (Greece), Marc S. Sabatine (United States of America), Marja-Riitta Taskinen[1] (Finland), Lale Tokgozoglu[1] (Turkey), Olov Wiklund[1] (Sweden)

ADPKD Sprechstunde

- CV Risikofaktoren
  - Blutdruckeinstellung
  - Hypercholesterinämie

ADPKD Sprechstunde

- CV Risikofaktoren
  - Blutdruckeinstellung
  - Hypercholesterinämie
  - Rauchen

ADPKD Sprechstunde

- Gicht
  - Allopurinol
  - Febuxistat (Adenuric®)
  - Rasburicase (Fasturtec®)

ADPKD Sprechstunde

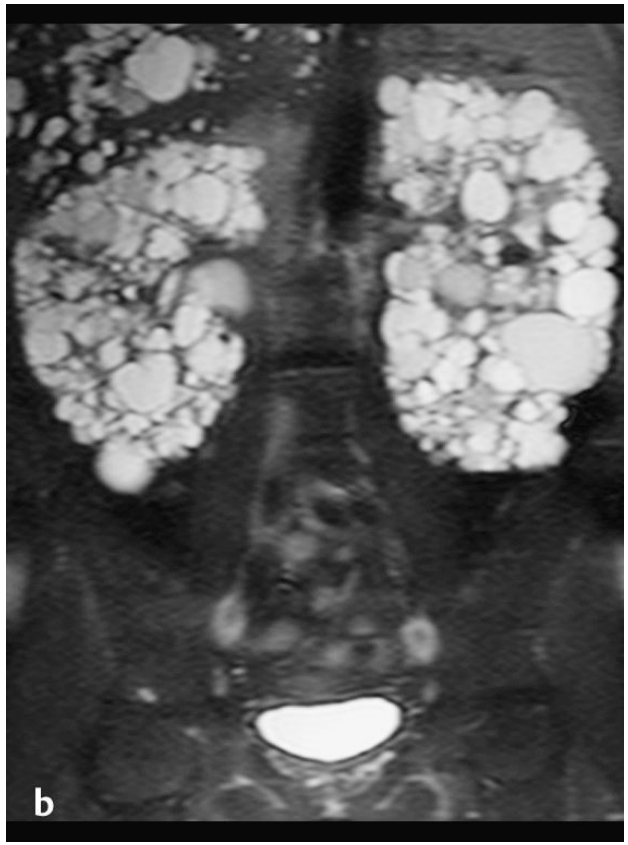
- Valsartan (Verunreinigung)
- HCT (Haut)

Vier Schweizer Medikamentenhersteller rufen Tabletten zurück, die den Wirkstoff Valsartan enthalten. Grund ist das Risiko, dass einzelne Chargen der betroffenen Generika mit einem wahrscheinlich krebserregenden Stoff verunreinigt sein könnten.

Das Heilmittelinstitut Swissmedic veröffentlichte am Mittwoch Rückrufe von jeweils mehreren Chargen von Spirig HealthCare, Axapharm, Helvepharm und Mepha Pharma. Betroffen vom europaweiten Rückruf sind Arzneimittel, die Valsartan des chinesischen Herstellers Zhejiang Huahai Pharmaceutical enthalten.

ADPKD Sprechstunde

- Leberzysten
  - Lanreotid (Somatuline Autogel®)



ADPKD Sprechstunde

- Nebenerkrankungen
- Sonstige Pharmakotherapie

Stationäre Betreuung ADPKD Patienten

- Bei Komplikationen

Betreuung vor und nach Nierentransplantation

- Ziel: Dialyse vermeiden !

HIRSLANDEN

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