Missouri ACP 2015 Abstract Winners

October 11, 2016

The abstracts below represent the winners in the Residents and Medical Students categories at the 2015 Missouri ACP Chapter meeting.

Winner, Resident Poster Contest Missouri ACP 2015

Outcomes of Acute Myeloid Leukemia Induction with Addition of Cladribine. Martin W. Schoen, MD, MPH; James Braun Pharm.D; Susan Woelich Pharm.D. BCOP; Reshma Ramlal MD; Carl E. Freter MD, Ph.D; FACP; Jack M. Lionberger MD, Ph.D

Introduction: A standard regimen for acute myeloid leukemia (AML) includes seven days of cytarabine and three days of an anthracycline (7+3). At Saint Louis University (SLU), our preferred regimen is cytarabine 200mg/m^2 by continuous infusion, idarubicin 12mg/m^2 daily, and five days of cladribine 5mg/m^2 daily (IAC or '7+3+5'). This regimen was derived from a Polish Adult Leukemia Group (PALG) study that included patients ≤60 years old. The impact of IAC on older patients is important to review considering cladribine adverse effects and outcomes in this population have not been previously reported. **Methods**: Retrospective analysis of patients who started IAC from July 2012 to August 2014 at SLU with follow-up until September 2015. Mortality, disease response, and adverse events were analyzed, with stratification by age and NCCN risk classification. **Results**: Of 44 patients identified, 27/44 (61%) were ≥60 years old, 6/44 (14%) had abbreviated therapy (missing or reduced doses). Thirty-eight of 44 (86%) patients survived to hospital discharge, and 5 deaths occurred before day 28. Additionally, 5/6 of these early deaths occurred in patients aged 60 or older. NCCN stratification showed 7/44 (16%) favorable; 17/44 (39%) intermediate; and 20/44 (46%) poor risk cases. Complete response (CR) occurred in 68% after first induction while 7% required a second round, for a total CR rate of 75%. One-year overall survival was 26/44 (59%). Significantly more deaths (15/18 or 83%) occurred among patients ≥60 years old (OR 5.8, 95% CI 1.4-25), and among higher NCCN risk classes. No deaths occurred in favorable risk group, but 7/44 (41%) and 11/44 (55%) occurred in intermediate and high-risk strata, respectively (p=0.039 by Chi-Square test). Adverse events: Diarrhea occurred in 34/44 (77%) patients, 26/44 (59%) developed rash, and 14/44 (32%) experienced mucositis/stomatitis. Intensive care unit admission occurred in 14/44 patients (32%). Fever was documented in 43/44 (98%) patients, of which 23/44 patients (52%) had a documented infection. For patients surviving to discharge (38/44), median hospitalization was 32 days, neutrophil recovery (ANC>500) occurred at a median of 28 days, and platelet recovery (>50,000) at 29 days. **Conclusions**: Addition of cladribine to cytarabine and idarubicin is an effective induction regimen for AML with similar rates of CR and treatment-related mortality compared to historical studies. In patients ≥60, this regimen deserves further study and could be an effective option in those with favorable prognosis and limited co-morbidities. Continued survival analyses and investigation

of adverse events will help define the role of this regimen in induction chemotherapy for AML.

***Candida parapsilosis* prosthetic valve endocarditis presenting as ST elevation myocardial infarction.** Ian Ross MD, Jaime Bolda MD, Gerome Escota MD. Washington University in St. Louis. **Introduction**: Fungal prosthetic valve endocarditis is an uncommon disease, accounting for only 1.3-6% of all cases of infectious endocarditis1. Candida albicans is the most common causative pathogen, and Candida parapsilosis is the most common non-albicans species2. Fungal endocarditis embolizes more frequently than bacterial endocarditis and can rarely present as an ST elevation myocardial infarction. **Case Description**: A 57-year-old male with a history of aortic bileaflet mechanical prosthetic valve and intravenous drug use presented to the ER with complaints of chest pain, syncope, and abdominal pain. An ECG showed 2 mm ST elevations in the inferior leads. Immediate cardiac catheterization was aborted due to coagulopathy. The patient's myocardial infarction was managed medically. Echocardiography showed a 1.4×0.8 cm echogenic mass on the anterior leaflet of the mechanical aortic valve. Subsequent imaging showed hemoperitoneum, superior mesenteric artery and splenic mycotic aneurysms, as well as renal infarcts. Blood cultures grew Candida parapsilosis. The patient was treated with micafungin and fluconazole and underwent valve replacement. His aneurysms and hemoperitoneum were treated surgically. **Discussion**: Candida parapsilosis is an important pathogen in fungal endocarditis, and is especially prevalent in intravenous drug users3. Coronary septic embolism is a rare cause of ST elevation myocardial infarction and was first described by Virchow4. It is estimated to occur in only 0.5-10% of cases of infective endocarditis, and the left anterior descending artery is most commonly affected. Fungal endocarditis is associated with a higher incidence of embolic events than bacterial endocarditis. Elements in the history and presentation that can aid in diagnosis include a history of intravenous drug use, valve replacement, or concurrently observed embolic/hemorrhagic phenomena. Combined medical and surgical therapy is the mainstay of treatment, with isolates usually susceptible to amphotericin and azole antifungals.

Winner: 2015 ACP-Missouri Chapter Medical Student Competition

Acid-sensing ion channels are required for amphetamine sensitization. Comron Hassanzadeh, Qian Jiang, Xiangping Chu. *Department of Basic Medical Science, School of Medicine, University of Missouri-Kansas City, Kansas City, MO 64108*

Drug addiction is a persistent mental illness and there is no effective therapy for patients. The precise mechanisms underlying addictive responses have not been completely deciphered. Increasing evidence has been shown that ion channels in the brain reward circuits are believed to play a vital role in drug addiction. Recently, protons are identified as neurotransmitter and one of the candidate for sensing proton is acid-sensing ion channels (ASICs). ASICs are highly expressed in brain reward circuits with ASIC1a and ASIC2 channels being the predominant subtypes. These channels are enriched at synaptic sites and are critical for the regulation of normal synaptic transmission. Moreover, increasing evidence has indicated that ASICs contribute to the neuropsychiatric disorders. We and others have shown that ASICs are involved in cocaine addiction. Here, we hypothesized that amphetamine (AMPH), a psychostimulant similar to cocaine, may also impact the function of ASICs. Following IACUC

approval, adult wild-type (WT) C57BL/6J, ASIC1a and ASIC2 knock-out (KO) mice were placed in individual test chambers to allow accommodation to novel environment for 60 minutes. They then received a single intraperitoneal (i.p) injection of AMPH and their locomotor activities were recorded for 150 minutes. The experiment was repeated daily for a total of 5 days. After a 2-week withdrawal period, the mice were brought back to the behavioral chamber followed by a final challenge i.p injection of AMPH at half dosage of pretreatment. Locomotor activity to this challenge dose was measured for 150 min. Acute AMPH injection (1.0, 1.5, 2.0, and 3.0 mg/kg) induced a typical dose-dependent increase in locomotor activities in WT, ASIC1a and ASIC2 KO mice. However, the increase in locomotor activities were attenuated in ASIC1a, but not ASIC2 KO mice as compared to WT mice. Repeated exposure of AMPH resulted in a progressive and persistent enhancement of locomotor response in all genotypes. All WT, ASIC1a and ASIC2 KO mice showed sensitization to AMPH. However, either ASIC1a or ASIC2 KO mice showed higher behavioral sensitization to AMPH than WT mice. Our data provides new understanding of the complex genetic and molecular mechanisms of ASICs in response to AMPH exposure. Thus, targeting ASICs might represent a novel therapeutic strategy for drug addiction. **Acknowledgement**: This work was supported by NIH grant DA031259 to XPC.