January/February 2011

Winter Issue

# Gulf Coast Society of Health-System Pharmacists

Has your contact information changed? Please send all changes to Katy Hanzelka at khanzelka@mdanderson.org

## *President's Report*

**Jennifer Nguyen, PharmD, BCPS**

Happy New Year fellow colleagues. This will be my last newsletter as President, so I would like to acknowledge that it has been an honor to work with all of the members of the GCSHP Board of Directors.

We are proud of our contributions and accomplishments this past year, some of which include: sponsoring events / meetings for our local student chapters, developing and funding two new scholarships, sponsoring the TMC Residency Council, participating with the Houston Read Commission, as well organizing a few CE events.

GCSHP still has work that needs to be done as far as increasing membership, organizing another annual seminar, and increasing involvement with the community to name a few.

As we look forward to the installation of new officers this spring, please continue to send any comments to jennifer.nguyen@va.gov regarding chapter ideas, future programming, or new opportunities in health-system pharmacy.

Thank you again for continuing to support our society and our profession.

Best wishes!

*Jennifer Nguyen*

*Texas Medical Center*

**Inside this issue:**



## 2011 TSHP Annual Seminar San Antonio, TX April 14-17

See details on page 3

# January 2011

| Sun | Mon | Tue | Wed | Thu | Fri | Sat |
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## Schedule of Events

- January 1
  Happy New Year 2011!
- January 17
  MLK Observance
- January 27
  UH/TSU 6th Annual Residency Mentoring Social
- January 30
  Houston READ Commission Fundraiser
- February 18-20
  TSU COPHS hosts SNPhA Regional Conference
- April 14-17
  TSHP 2011 Annual Seminar

# February

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# 2011 Annual Seminar
# April 14 - 17, 2011
# The Westin La Cantera
# San Antonio, Texas


## 63rd Annual Seminar & Exhibit

## of the Texas Society of Health-System Pharmacists

### EDUCATION

The overall educational goal of the TSHP Annual Seminar is to provide information and instruction on a variety of topics to enable the pharmacy practitioner to provide quality patient care. Individuals will participate in a variety of programs that include lectures and case studies in addition to interactive, audience-participation programming.

These Knowledge– and Application– based continuing professional education programs provide up to **18.5 contact hours** (1.85 CEUs) of continuing pharmacy education. To receive a Statement of Participation, individuals must register for the meeting.

### Featured Activities

Clinical Track
Management Track
Technician Track
New Practitioner Track
Student Track
Reception and Social Events
Exhibits

### Hotel Information

Westin La Cantera
16641 La Cantera Parkway
San Antonio, TX 78256
Fax: (210) 558-2400

Room Rate:
Single/Double $195

Reservations:
Visit the online reservations site (preferred method)
or call 1-888-627-8396

**Mention TSHP to received discounted rate**
**Reservation deadline for discount is March 21, 2011**

# STUDENT SECTION

## Texas Southern University SSHP
## Kingsley Nwogu, President

As the holidays have ended and the spring semester begins, TSU-SSHP would like to thank everyone that made the fall semester an exciting semester.

During Pharmacy Week, all of the organizations within the College of Pharmacy came together and orchestrated an event for all pharmacy students. They were able to relax from exam week and mingle with students they may not normally see. Also for Pharmacy Week, an article was sent to the school newspaper to inform students about health-system pharmacy and its importance.

TSU-SSHP would like to recognize Derek Kimani and Christopher Njigha for winning the Clinical Skills Competition during the fall semester at Texas Southern University COPHS. And we also want to thank everyone that participated and helped make the competition a success this semester. We definitely supported Derek and Chris as they traveled to the ASHP Midyear Clinical Meeting to compete in the national competition and represent the College of Pharmacy proudly.

TSU-SSHP would like to commend all the students who attended ASHP Midyear Clinical Meeting in hopes of attaining a residency/fellowship position. As the field of pharmacy continues to become more clinical, we are quite sure that these students are making great decisions to continue to build upon their clinical skills. All in all, we had a good fall semester with new members and guest speakers.

TSU-SSHP looks forward to starting 2011 very strong. One of the main events for the spring semester is the Residency Mentoring Social (RMS) that we are co-hosting along with the University of Houston College of Pharmacy. Students will have valuable face time with residency directors and residents from around the area. TSU-SSHP also looks forward to the various speakers, community service projects, and TSHP Annual Seminar.

***TSU COPHS will be hosting the SNPhA Regional Conference this year in Houston, February 18-20, 2011 at the Intercontinental Hotel. Please show your support!***

I would like to wish all students a successful and productive spring semester!

*Kingsley*

## University of Houston SSHP
## Avani Desai, President

Welcome back to a new spring semester to all pharmacy students! Hoping everyone had a bright and cheery holiday season and I wish happiness and success to all!

The annual UH Residency Showcase was held on November 5 from 2:30 – 5:00 PM at the Trevisio Conference Center in the Texas Medical Center. This event was open to all pharmacy students in the Houston area. It afforded them the opportunity to meet and interact with residency directors and residents in a smaller venue similar to the ASHP Residency Showcase.

Thirty-two facilities provided information for over 40 different PGY1 and PGY2 residency programs and fellowships. Programs from Texas (the Houston area; Dallas-Fort Worth area; San Antonio; Austin; and Temple), Louisiana, and New Jersey participated in the event. Current residents, preceptors, and/or the program director represented the facilities. Approximately 200 students, from 6 colleges of pharmacy (UH, TSU, UT, TAMU, TTU, Incarnate Word), attended. The majority of the students were in the P4 year, but there were also P1, P2, and P3 students present.

UH SSHP would like to thank Dr. Jessica Cottreau for organizing this exceptional event this year. Additionally, we heartily recognize the Gulf Coast Society of Health Systems Pharmacists (GCSHP) for their generous financial support in organizing the Residency Showcase every year for pharmacy students across Texas.

This December, ASHP Midyear was a wonderful experience for UH students interested in discovering post-graduate training opportunities across our nation. Many of our students participated in the poster presentations, residency showcases, as well as enjoying the city of Anaheim, CA! UH SSHP wishes all P4 students the best of luck in their interviews and match process coming up!

Our next big event will be our annual ***Residency Mentoring Social held on January 27th in conjunction with TSU SSHP.*** As a tradition for the past six years, GCSHP has generously supported our students once again in a dinner and networking opportunity for local area residency programs in the Texas Medical Center. ***Dr. Catina Brimmer from Harris County Hospital District*** will be our keynote speaker on the Pharmacy Practice Model Initiative! We are excited to host this event once again and look forward to seeing everyone soon!

*Avani*

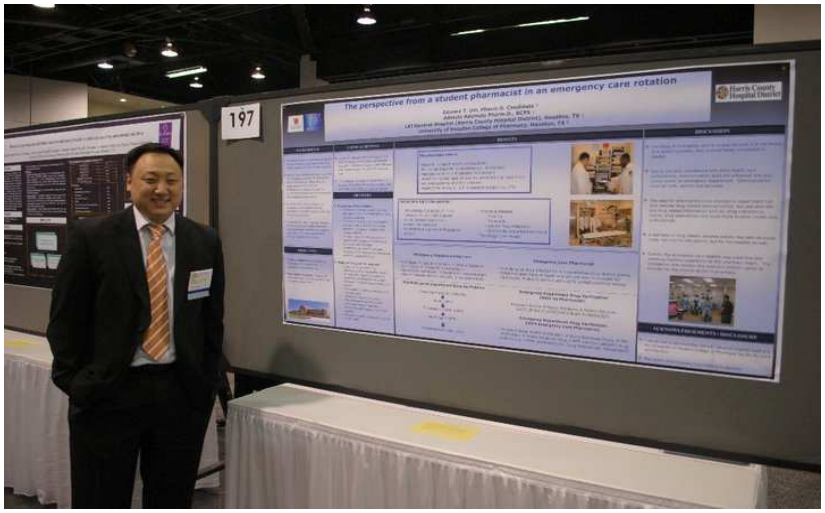
# STUDENT SECTION


Natalie Lee, Vicky Do, Michelle Roberts, Tara Thompson

## University of Houston

## College of Pharmacy Students make their mark on the

## ASHP Midyear Clinical Meeting in Anaheim, California

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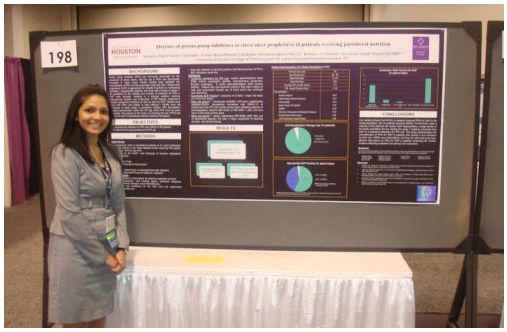
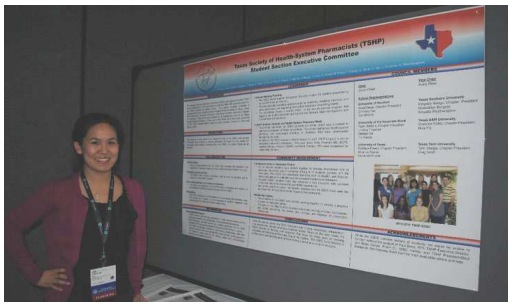



Khushbu Patel


Mabel Truong




Christina Tan


Tara Thompson

# STUDENT SECTION

## Hypertonic Saline vs. Mannitol for the Treatment of Increased Intracrainial Pressure

**Meredith Grant, Pharm.D. Candidate 2011**

University of Houston College of Pharmacy

### Background

There are various clinical options available for the treatment of cerebral edema due to traumatic brain injury, acute ischemic stroke, brain tumor resection, etc. One of the more important aspects for optimizing patient outcomes in patients with neurotrauma is to decrease raised intracranial pressure (ICP) to a controlled level. Osmotherapy is usually implemented for this task; however, the optimal agent for this has become controversial. Current adult guidelines from the Brain Trauma Foundation and the American Stroke Association recommend mannitol for progressively increasing ICP values due to lack of data on the dosing, safety, and effectiveness of hypertonic saline. Alternatively, the World Federation of Pediatric and Critical Care Societies recommend using hypertonic saline for controlling ICP in pediatric patients with head injuries. There are very few studies, especially large clinical trials, directly comparing mannitol to hypertonic saline for ICP control; however, more recent studies show evidence that hypertonic saline is a better agent than once thought.

### Studies

In a prospective, randomized clinical study by Harutjunyan, et al., the safety and efficacy of bolus 7.2% hypertonic saline hydroxyethyl starch 200/0.5 (7.2% NaCl/HES 200/0.5) was compared with 15% mannitol in 32 neurotrauma patients with increased ICP > 20mmHg. 7.2% NaCl/HES 200/0.5 achieved an ICP < 15mmHg within 6.0 (1.2–15.0) minutes, and mannitol within 8.7 (4.2–19.9) min ($p < 0.0002$). 7.2% NaCl/HES 200/0.5 caused a larger decrease in ICP than mannitol (57% versus 48%; $p < 0.01$). The cerebral perfusion pressure (CPP) was increased above 70 mmHg to 72 (54–85) mmHg from 60 (39-78) mmHg by infusion with 7.2% NaCl/HES 200/0.5 ($p < 0.0001$), while CPP only increased to 70 (50–79) mmHg from 61 (47-71) mmHg with mannitol ($p < 0.0001$). The mean effective dose that achieved an ICP < 15 mmHg was 1.4 (0.3–3.1) ml/kg for 7.2% NaCl/HES 200/0.5 versus 1.8 (0.45–6.5) ml/kg for mannitol ($p < 0.05$).

A pediatric, retrospective review by Peterson, et al., intended to determine the effects of continuous infusions of 3% hypertonic saline on ICP control and describe the physiological effects of the treatment on 68 children with closed head injury. All of the patients enrolled had similar Injury Severity Scores and the treatment effectively lowered ICP to < 20 mmHg in these patients and was under good control over 90% of the time during the study. Only three of the patients (4%) died of uncontrolled elevation of ICP. None of the adverse effects that could be attributed to hypertonic saline, such as renal failure, pulmonary edema, or central pontine myelinolysis, were reported.

Wu, et al. is a more recent prospective, double-blinded, randomized clinical trial compared the effects of 3% hypertonic saline and 20% mannitol with on brain relaxation during brain tumor removal. 238 patients were given an equiosmolar dose of one or the other study medications just prior to surgical opening. The hypertonic saline group had superior brain relaxation conditions (soft/adequate/tight, n = 58/43/21) in comparison to the mannitol group (soft/adequate/tight, n = 39/42/35; P = 0.02). Serum sodium levels dropped to hyponatremic levels (Na< 135mEq/L) in the mannitol group; however the levels were not increased to a hypernatremic level in the hypertonic saline group (Na > 150mEq/L). The average urine output in the mannitol group (707 mL) was higher than it was in the hypertonic saline group (596 mL) (P < 0.001). There were no significant differences in fluid input, or the duration of ICU and hospital days between the 2 groups.

### Conclusion

Despite the potential side effects, hypertonic saline is proving itself to be at least as safe and efficacious, if not more so, than mannitol for the lowering and maintenance of ICP. Adult guidelines should include hypertonic saline as an alternative osmotic agent to mannitol for neurotrauma patients with increased ICP. However, more large-scale clinical trials are required to prove hypertonic saline as the superior agent for osmotherapy.

### References

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Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons, Joint Section on Neurotrauma and Critical Care. Guidelines for the management of severe traumatic brain injury. II. Hyperosmolar therapy. J Neurotrauma 2007;24(1):S14-20.

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Harutjunyan L, Holz C, Rieger A, et al. Efficiency of 7.2% hypertonic saline hydroxyethyl starch 200/0.5 versus mannitol 15% in the treatment of increases intracranial pressure in neurosurgical patients- a randomized clinical trial. Crit Care 2005;9:530-540.

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*The CGSHP website is linked to the TSHP website!*

*Log on to the TSHP website at www.tshp.org*

*Under the Links tab, click GCSHP!!!!*

# STUDENT SECTION

## Disseminated Intravascular Coagulation Therapy: Current and Investigational Treatments

**Mabel Truong, Pharm.D. Candidate 2011**

University of Houston College of Pharmacy

Disseminated intravascular coagulation (DIC) is a secondary disorder caused by a variety of clinical conditions. The most common underlying disorders are sepsis, trauma, malignancies, and obstetrics[1]. DIC results from cytokine mediation of coagulation activation, impairment of anticoagulant mechanisms, and inhibition of fibrinolysis. This hemostatic imbalance leads to microvascular thrombosis, the inflammatory process, and consumption of coagulation factors that lead to hemorrhage. These problems can eventually lead to ischemia, massive blood loss, and multiple organ failure[2]. DIC diagnostic criteria was created by the International Society of Thrombosis and Haemostasis (ISTH) in 2001 using an algorithm based on platelet count, fibrin markers, prothrombin time, and fibrinogen levels to assess patients for overt DIC[4]. Higher scores for overt DIC have been associated with increased mortality rates. DIC has also been shown to be an independent risk factor for patients with infection and decreased mortality rates have been associated with DIC resolution.[5,7,8].

Treating the underlying disease associated with DIC is the first line of therapy and may result in the spontaneous resolution of the coagulation disorder[1]. When this is not immediately possible, supportive measures such as fluids and vasopressors can be utilized in addition to replenishment of blood products. Heparin can often be used, but has not been proven to decrease mortality in DIC. Prophylactic or treatment doses may be appropriate for patients with predominating thrombosis or critically ill patients without active bleed[4].

Alternative treatments have been investigated based on the current understanding of coagulation pathway dysfunction in DIC[3]. The first target is thrombomodulin, a thrombin receptor that helps in the activation of protein C in the coagulation pathway and is depleted in DIC. The efficacy of recombinant human soluble thrombomodulin (ART-123) compared to low dose heparin is investigated in Saito et al. in a phase III, randomized, double-blind clinical trial including 234 patients with DIC associated with hematologic malignancy or infection[6]. Difference in DIC resolution rates for the ART-123 group compared to the heparin group were 66.1% and 49.9% (95% CI 3.3 -29.1). Mortality rates for ART-123 and heparin groups were 17.2% and 18% (95% CI -14.2%-12.5%) for malignancy, 28% and 34.6% (95% CI -24.5-11.3) for infection.

The second target in the pathway is the restoration of activated protein C and the use of drotrecogin alfa (activated) (DrotAA) as discussed in Dhainut et al[5]. This retrospective study contained 454 patients pulled from the PROWESS trial (*n=1690*) classified with DIC using a modified ISTH scoring system split into a placebo group and DrotAA group to assess efficacy in severely septic patients with DIC. Results showed an overall reduction in mortality with DrotAA compared to placebo (29% vs. 18%), but this was not statistically significant. Overt DIC patients treated with DrotAA had an absolute reduction in mortality of 12.5%, but this was also not statistically significant.

Antithrombin (AT) is another important component as a regulator of coagulation through inhibition of thrombin and factor Xa. In DIC, antithrombin levels are low because it is rapidly degraded, consumed, and synthesis is impaired. In Kienast et al., high dose AT was used in a retrospective placebo-controlled, randomized trial based on the KyberSept study testing its efficacy in 229 patients compared to placebo with documented sepsis and DIC[8]. A significant decrease in mortality was seen in DIC patients with AT treatment compared to placebo at 28 days (25.4% vs. 40%, *P=0.024*) and 90 days (34.3% vs. 50.4%, *P=0.015*). In addition, patients with DIC had higher mortality compared to patients with no DIC at 28 days (40% vs. 22.2%, *P=0.004*) and 90 days (50.4% vs. 32.9%, *P=0.002*).

Managing DIC in critically ill patients has been shown to decrease mortality[6]. Investigated strategies in therapy using DrotAA, ART -123, or ATIII have merit based mechanistically in regulating defects of anticoagulant pathways in DIC. Although the trials above have shown some benefit, more studies for safety and efficacy need to be conducted along with cost considerations and risk assessment before application into practice. It is also important to stress the necessity of appropriate uniform diagnosis based on both laboratory information and clinical observation to maximize patient outcomes.

### References

Zeerleder S, Hack CE, et al. Disseminated intravascular coagulation in sepsis. Chest 2005; **128**: 2864-2875.

Levi, Marcel. Disseminated intravascular coagulation. *Critical Care Medicine* 2007; **35**: 2191-2195.

Levi M, de Jonge E, et al. Rationale for restoration of physiological anticoagulant pathways in patients with sepsis and disseminated intravascular coagulation. *Critical Care Medicine* 2001; **29**: S90-S94

Levi M, Toh CH, et al. Guidelines for the diagnosis and management of disseminated intravascular coagulation. *British Journal of Haematology* 2009; **145**: 23-33.

Dhainaut JF, Yan SB, et al. Treatment effects of drotrecogin alfa (activated) in patients with severe sepsis with or without overt disseminated intravascular coagulation. *Journal of Thrombosis and Haemostasis* 2004; **2**: 1924-1933.

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Fourrier F, Chopin C, et al. Double-blind, placebo-controlled trial of antithrombin III concentrates in septic shock with disseminated intravascular coagulation. *Chest* 1993; **104**: 882-888.

Kienast J, Juers M, et al. Treatment effects of high-dose antithrombin without concomitant heparin in patients with severe sepsis with or without disseminated intravascular coagulation. *Journal of Thrombosis and Haemostasis* 2006; **4**: 90-97.

# STUDENT SECTION

## The Macrovascular Effects of Intensive Blood Glucose Control in Type 2 Diabetes

**Lori Krustchinsky, PharmD Candidate 2011**

University of Houston College of Pharmacy

### Background:

Sustained hyperglycemia in type 2 diabetics as measured by hemoglobin A1C or plasma glucose levels increases the risk for multiple health problems including cardiovascular disease (CVD) and microvascular issues like kidney failure, blindness, peripheral neuropathy, and early cognitive decline[4]. CVD is the main cause of morbidity and mortality in those with type 2 diabetes and the relative risk for its development is nearly doubled compared to those without type 2 diabetes.[3]

In the past, glucose lowering guideline recommendations were based on epidemiological studies and limited clinical trials that demonstrated that many of the macrovascular and microvascular complications were directly associated with the degree of hyperglycemia. Several clinical trials have demonstrated a graded relationship between CVD and A1C levels and thus suggested that a reduction in the A1C levels would decrease cardiovascular outcomes. This hypothesis has recently been tested in several adequately powered randomized clinical trials. Surprisingly, the results were inconsistent among each trial.[3]

### Studies:

In 2001, a 5.6 year randomized, placebo controlled clinical trial called The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial set out to determine whether targeting an A1C level less than 6% in those with type 2 diabetes and either established CVD or with CVD risk factors would reduce the incidence of cardiovascular events compared with an A1C goal of 7.0-7.9%. The study was terminated early after 3.5 years due to the increased rate of death from cardiovascular causes (HR 1.35, 95% CI 1.0-1.76, P=0.02) and an increased rate of death from any cause (HR 1.22, 95% CI 1.01-1.46, P=0.04) in the intensive-therapy group. The results also demonstrated a greater benefit with intensive glucose lowering in those with a lower A1C (<8%) and those without CVD[4].

The ADVANCE study was a randomized, placebo controlled trial that assigned patients with type 2 diabetes to undergo either standard (A1C 7%) or intensive (A1C<6.5%) glucose control in order to study the effects on vascular outcomes. The primary outcome of combined microvascular and macrovascular events was significantly reduced in the intensive therapy group (HR 0.9, 95% CI 0.82-0.98, P=0.01) although the results were primarily due to a significant reduction in microvascular events. There was no significant reduction in macrovascular outcomes alone.[5]

The Veterans Affairs Diabetes Trial (VADT) randomized patients with type 2 diabetes to receive intensive glucose control (A1C<6%) or standard control with a planned A1C separation of at least 1.5%. The primary outcome of composite CVD events was not significantly lower in the intensive therapy group (HR 0.88, 95% CI 0.74-1.05, P=0.12). The rate of cardiovascular death was higher in the intensive therapy group compared to the standard therapy arm (40 deaths vs. 33 deaths) although it was not statistically significant.[1] Post hoc analysis of the results demonstrated that intensive glucose lowering in those with a long duration of type 2 diabetes resulted in more negative effects than those with newly diagnosed diabetes. In addition, prior CVD and recent hypoglycemic events seemed to blunt the benefits of intensive glucose control[2].

### Conclusion:

Although the microvascular benefits of intensive glycemic control is well established, the effect on macrovascular events is still questionable. These studies suggest that there may be more benefit of intensive glucose control in those with a shorter duration of diabetes, absence of known CVD, and a lower baseline A1C. This demonstrates the importance of lifestyle and medication management in newly diagnosed diabetics. Macrovascular events in diabetics are due to multiple metabolic problems like hyperlipidemia, hyperglycemia, hypertension, and hypercoagulability and must all be adequately addressed. Patients with type 2 diabetes should be evaluated independently and given individualized A1C targets. Until more conclusive evidence is obtained, an A1C as close to normal as possible seems reasonable if it can be safely achieved in the patient given individual risk factors and overall health.

### References

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Duckworth, William C. VA Diabetes Trial Update. Webcast presented at: ADA 69th scientific session. 2009; Louisiana, New Orleans.

Meigs, James B. Epidemiology of type 2 diabetes and cardiovascular disease: Translation from population to prevention. Diabetes Care. 2010 Aug; 33(8):1865-71.

The Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in Type 2 diabetes. N Engl J Med. 2008 Jun 12; 358(24):2545-59.

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**SAVE THE DATE**

UH/ TSU 6th Annual Residency Mentoring Social
Thursday January 27, 2011
5:00pm - 8:00pm

UH Alumni Center- O'Quinn Great Hall on the UH Main Campus. 3100 Cullen Blvd, Houston, TX 77204

Keynote Speaker:
Catina Brimmer, PharmD, MBA

# RESIDENT SECTION

## Harris County Hospital District Residency Programs

Kristine Aquino
PGY1 Resident

Ogechi Eshleman
Residency Programs Coordinator

Ali Shah-Mohammadi
PGY2 Resident



Kandi Icenhower-PGY1 Resident


Ogechi Eshleman-Residency Programs Coordinator
Tam Nguyen-Operations Manager
Shahana Quadri—PGY2 Resident

*..some time for fun at Universal Studios!*

# RESIDENT SECTION

## Tribenzor™ Drug Monograph

**Ali-Reza Shah-Mohammadi, PharmD PGY -2 Health-System Pharmacy Administration Resident**
Harris County Hospital District

Xavier Brager Pharm.D. Candidate
Texas Southern University

Maria Elioku Pharm.D. Candidate
Texas Southern University

The combination medication Olmesartan Medoxomil, Amlodipine, and Hydrochlorothiazide (Tribenzor ™), marketed by Daiichi Sankyo Inc, is the newest FDA-approved agent for the treatment of hypertension that is not adequately controlled with combination of two of the following classes of medications: angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs) or diuretics. Hypertension is characterized as blood pressure (BP) that is greater than or equal to 140/90 mmHg and is one of the most prevalent disease-states worldwide contributing to comorbidities and disease burdens including coronary heart disease[1]. There are a multitude of risk factors that can lead to hypertension including increased dietary sodium intake, obesity, and excessive alcohol consumption[2-4]. It is estimated that over 50 million Americans warrant treatment for their elevated BP but despite treatment available, there is still a high prevalence of this disease-state[5].

### Mechanism of Action/Pharmacology

Tribenzor ™ is comprised of three medications. The first component is Olmesartan Medoxomil (OM) which is an ARB that acts by displacing angiotensin II from the $AT_1$ receptor. This action antagonizes the effects of $AT_1$ including vasoconstriction, aldosterone release, catecholamine release, arginine vasopressin release, water intake and hypertrophic responses. The second component is Amlodipine (AML) which is a CCB that blocks the "slow channels" of vascular smooth muscle and myocardium during depolarization producing a relaxation of coronary smooth muscle and coronary vasodilation. The final component is Hydrochlorothiazide (HCTZ) which is a diuretic that inhibits sodium reabsorption in the distal tubules causing increased excretion of sodium and water as well as potassium and hydrogen ions.

### Clinical Trials

The role of triple combination therapy with OM, AML, and HCTZ compared to dual combinations of these components in patients with moderate to severe hypertension was evaluated in a multicentered, randomized, double-blinded, parallel-group study termed the TRINITY (Triple Therapy with Olmesartan Medoxomil, Amlodipine Besylate, and Hydrochlorothiazide in Adult Patients with Hypertension) study. This was a 12-week study involving 2492 patients 18 years or older randomized to either receive the triple combination of OM 40 mg, AML 10 mg and HCTZ 25 mg as compared to dual combination of the individual components (OM 40 mg/AML 10 mg, OM 40 mg/HCTZ 25 mg and AML 10 mg/HCTZ 25 mg). At the end of the 12-week study period, there was significant mean reduction in seated blood pressure (SeBP) in the group that received triple combination therapy as compared with dual combination therapy. The seated diastolic blood pressure decreases observed with triple combination therapy versus dual combination therapy were -21.8 versus -15.1 to -18.0 mmHg, $p < 0.001$; seated systolic blood pressure: -37.1 versus -27.5 to -30 mmHg, $p < 0.001$[6]. In the open-label extension (OLE) of the COACH (Combination of Olmesartan Medoxomil and Amlodipine Besylate in Controlling High BP) cohort, the long-term use of combination OM and AML with or without HCTZ in specified subgroups (based upon age, race and diabetes status) was evaluated. This study was a 44-week OLE of an 8-week multicentered, randomized, double-blinded, placebo-controlled, factorial designed study. Both Black and non-Black subgroups had clinically relevant SeBP decreases from baseline. The average in reduction of blood pressure in Blacks and non-Blacks at week 52/early termination were 30.8/18.7 and 33.0/20.0 mmHg, respectively. Those patients who were titrated from OM and AML to the addition of HCTZ also showed a greater SeBP reduction. Likewise those patients that presented with diabetes showed a better decrease in average SeBP than those without. When both diabetic and non-diabetic patients received the up-titration form of OM and AML to the addition of HCTZ, they showed an improvement in both groups' ability to reach goal SeBP. The OLE study did not identify any safety concerns that had not previously been identified in the COACH double-blind study.[7]

### Dosing

The dosing of OM, AML, and HCTZ is a daily dose of 20 – 40 mg, 5 – 10 mg, and 12.5 – 25 mg, respectively. Doses to be available are 40 mg/5 mg/25 mg, 40 mg/10 mg/25 mg, 20 mg/5 mg/12.5 mg, 40 mg/5 mg/12.5 mg and 40 mg/10 mg/12.5 mg of OM/AML/HCTZ. The strengths may be titrated upwards after 2 weeks. OM reaches peak levels in 1 – 2 hours and its half-life is 13 hours. AML reaches peak levels from 6 – 12 hours with a half-life of 30 – 50 hours. Lastly, HCTZ reaches its peak effects in 4 – 6 hours and its half-life is 6 – 15 hours.

### Contraindications, Warnings, and Precautions

Common side effects of Tribenzor ™ include dizziness (9.9%), peripheral edema (7.7%) headache (6.4%), nasopharyngitis (3.5%) and muscle spasms (3.1%). Hypokalemia (0.7%) is a more serious side effect that is occasionally seen. Contraindications of use include individuals with hypersensitivity to sulfonamide-derived drugs as well as those with anuria. Tribenzor ™ has not been studied in patients with impaired renal function however it should be avoided in patients with severe renal impairment (estimated creatinine clearance ≤ 30 mL/min). No clinical trial has been conducted to determine the dosing for hepatic insufficiency. It is not known whether OM or AML are ex-

# RESIDENT SECTION

creted in human milk, but thiazides appear in human milk and OM is secreted at low concentration in the milk of lactating rats. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother. Tribenzor is an FDA pregnancy category risk C.

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## The Need for Qualified Pharmacy Leaders During an Era of Health Care Reform and Beyond


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Harris County Hospital District


Six years ago, Sara White, MS, Pharmacy Leadership Consultant, posed a thought-provoking concern regarding a pharmacy leadership crisis. Today, the uncertainties of health care reform and the concern for trained leaders to guide our profession remains an obstacle.[1]

Recently, Steven H. Berger, CPA, FACHE, FHFMA president, Healthcare Insights LLC and a financial expert stated labor and supply chain are two major expense areas that need to be evaluated to properly reduce costs. Prior to analyzing such data, leaders need to assess the baseline knowledge of their managers. Often, hospital managers do not comprehend the basic principle which is understanding how revenue is generated and where the expenses are incurred. Berger stated, "There are many managers who weren't trained to be managers. They were the best radiology technician or the best floor nurse who was promoted into management. And if they received any training prior to their promotion, it was usually just a few hours' worth which is not even close to the amount of training that is needed."[2]

Our profession faces these challenges to a greater extent. The lack of adequate succession planning and a true career ladder within our profession combined with the continuous challenge to either establish or maintain representation at the C-suite level creates a sense of discomfort in an era of health care reform and the future. Now is the time for our leaders to engage to a greater degree in building the framework for concepts such as Accountable Care Organizations (ACOs) and how we as pharmacy leaders may contribute to such models. As healthcare transitions from a volume-based operation to one that values and rewards quality, our profession needs to proactively participate on how we can improve quality and better manage our costs.[3] A prime example of this action was recently communicated by The National Association of Chain Drug Stores (NACDS). The NACDS declared the need to include pharmacy as a key stakeholder in the ACO governing structure and recommended medication therapy management to be a component of cost savings in the ACO model.[4]

As we plan ahead for our future, it is imperative that we produce leaders who are knowledgeable and willing to work outside of their comfort zone and their so-called silos. We must foster a culture of mentoring and promote ideas such as advanced degrees in administration and residencies that will bridge the gap between our current and future leaders.

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# RESIDENT SECTION

## Fecal Transplantation: Alternative Treatment for Chronic Clostridium Difficile

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*Clostridium Difficile* Infection (CDI) is a stubborn infection that causes uncontrolled diarrhea in many patients who are treated with antibiotics at home or in the hospital. *Clostridium difficile (C. difficile)* is a spore forming, anaerobic gram positive bacillus.[1] It produces toxins that are responsible for gastrointestinal conditions such as pseudomembranous or ulcerative colitis. *C.difficile* can survive under harsh environmental conditions, can withstand antibiotic treatment, and may be transmitted by person-to-person contact. CDI can recur in patients with significant comorbidities (i.e. diabetes, CHF, etc.). Particularly in patients over the age of 65 years old due to the likelihood of decreased immunogenicity. A common dilemma with CDI is the frequency of relapse noted in up to 40% of patients experiencing at least one recurrence.[2] Patients with multiple relapses may have difficulties in clearing the infection due to prolonged periods of antibiotic therapy. Silverman et al[2] demonstrated that patients with multiple relapses of CDI have strains that are less susceptible to metronidazole.

Silverman et al[2] hypothesized that CDI develops because of secondary disruption of the normal bowel flora; therefore, restoration of normal bacterial flora may be an alternative therapeutic strategy for the treatment of CDI and pseudomembranous or ulcerative colitis. In 1958, Eisman et al[3] first used the administration of human feces in individuals who failed other treatments. This new alternative treatment was called fecal bacteriotherapy, also known as fecal transplantation. Fecal transplantation is a therapeutic procedure for patients with CDI or pseudomembranous or ulcerative colitis conditions. Fecal transplantation procedure may involve 5 to 10 days administration of healthy human donor feces via nasogastric tube, enema, or colonoscopy.

To ensure a safe fecal transplantation, recipients are required to have laboratory testing (i.e. stool culture) and prescribed maintenance therapy with oral vancomycin (125 mg four PO times daily) or metronidazole (500 mg PO three times daily) plus oral *S. boulardii* (Florastor) 500 mg PO twice daily to ensure they are asymptomatic, defined as being afebrile for 24 to 48 hours prior to the procedure.[2-3] Donors are screened for *C. difficile* toxins, parasites, blood borne viruses (i.e. HIV), and syphilis prior to stool donation. Potential donors are usually family members or close relatives.

Fecal transplantation procedure via 3 different types of administration:[1-3]

A. Nasogastric (NG) tube

Stop vancomycin or metronidazole 24 to 48 hours prior to fecal transplantation.

Continue *S. boulardii* during transplant, then 60 days afterwards.

Obtain fresh solid stool sample (~30 grams) from the donor no later than 6 hours prior to fecal transplantation.

Add 150 to 200 ml of 0.9% Normal Saline (NS) to the stool sample, and mix in the blender until it liquefies to a "milkshake" consistency.

Filter the stool suspension using a filter paper, and then administer it to the patient.

Flush the tube with 0.9% NS and immediately remove the tube after transplantation.

B. Enema Bag

Follow steps 1 through 4 (as described in section A).

Pour the mixture (~ 250 ml) into the enema bag, and then administer it to the patient.

Patient should hold the infusate as long as possible and lie still to prevent defecation. If diarrhea recurs within 1 hour, the procedure may be repeated immediately

C. Colonoscopy

The day before the fecal transplantation, whole bowel irrigation is performed using polyethylene glycol and electrolytes.

Inject the stool sample into the colon through a colonoscope.

Silverman et al[2] conducted a case series (n=7) of fecal transplantation where 100% clinical success, define as negative *C.difficile* toxin testing and no recurrence of chronic diarrhea, was attained in treating patients with CDI. In this case series, 1 patient developed irritable bowel syndrome and 2 patients developed urinary tract infection after transplantation, but none of these patients were positive C.difficile and no episode of chronic diarrhea. No patient had recurrent CDI and no side effects related to the transplantation. Yoon et al[4] reported 12 cases that were successfully treated with fecal transplantation into the colon via colonoscopy. All 12 patients experienced durable therapeutic response to fecal transplantation. No side effects were identified from fecal transplantation.

The role of fecal transplantation in the management of recurrent CDI continues to evolve. Fecal transplantation may be an efficient and potentially economical approach for patients with recurrent CDI. As this approach is made more available in the healthcare setting, this therapy may facilitate quicker recovery for patients and allow them to return back to their normal daily activities. However, further studies are warranted to further recommend this alternative treatment.

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# RESIDENT SECTION

## U-500 Insulin: Doing More with Less

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The prevalence and clinical consequences of diabetes mellitus (DM) are both staggering and on the rise. Approximately 26.3 million people in the United States alone have DM, accounting for 7.8% of the total population of the country, and the prevalence has increased 16.5% since 2004. Over $174 billion per year in direct and indirect medical expenses is spent on DM management. Chronic hyperglycemia is associated with macrovascular complications such as coronary artery disease, peripheral artery disease, and stroke and microvascular complications such as retinopathy, nephropathy, and neuropathy.

Insulin resistance is becoming more common in patients with type 2 DM, and large doses of insulin are frequently required to attain good glycemic control. U-500 insulin is a viable treatment option in diabetic patients with severe insulin resistance, defined as requiring >200 units of insulin per day. U-500 insulin is five-fold more concentrated (500 units/mL) than U-100 regular insulin (100 units/mL), allowing patients to inject a smaller volume of insulin per injection. This strategy minimizes insulin leakage, poor absorption from the injection site, and patient discomfort and subsequently improves patient compliance with treatment.

The human form of U-500 insulin has been available in the United States since 1997 and is the only stable form of concentrated insulin. The onset (30 minutes), peak (1-3 hours), and duration of action (up to 24 hours) are similar to NPH insulin. Secondary hypoglycemia may be observed 18-24 hours after injection, attributable to delayed absorption of U-500 insulin from the injection site. No universal dosing guidelines exist, although the American Diabetes Association and multiple institutions have made dosing recommendations. Subsequently, clinicians should develop individualized strategies to initiate and titrate U-500 insulin regimens. As a guide, the total daily U-100 insulin requirement should be used to calculate the potential U-500 insulin requirement. The conversion dose may be increased or decreased by a percentage based on the HbA1c level and treatment goals, and the total daily dose should be divided throughout the day. As a rule of thumb, patients requiring <300 units should have their dose divided twice daily, patients requiring 300-599 units divided three times daily, and patients requiring ≥600 units divided four times daily.

Multiple prescribing considerations should be addressed when utilizing U-500 insulin to manage type 2 DM. First, always verify that your patient is injecting the correct insulin. U-100 insulin may easily be confused with U-500 insulin due to similar packaging, which may contribute to hypo- or hyperglycemia. Second, ensure that your patient is using the correct syringe to inject, as U-500 insulin is administered via tuberculin syringes instead of U-100 insulin syringes. A tuberculin syringe is marked in milliliters from 0.1 to 1 mL. Patients will typically draw up insulin according to the number of milliliters ordered. When transitioning a patient from U-100 to U-500 insulin, adequate education is required to ensure proper insulin draw-up technique.

U-500 insulin is an effective and convenient treatment for insulin-savvy patients with severe insulin-resistant type 2 diabetes. Patient compliance and subsequent glycemic control may be improved with U-500 insulin, as patient satisfaction and an ability to titrate insulin dosages increases with concentrated insulin. Patient education and evaluation of compliance prior to initiating U-500 insulin is necessary to ensure safety and efficacy of therapy. Pharmacists can play a major role in patient education and diabetes management in highly insulin-resistant type 2 diabetic patients.

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The GCSHP Elections will be held in the next couple of weeks. When you receive your ballot, please do not hesitate to exercise your right to vote as a member.

Please consider nominating a colleague or yourself for a GCSHP Board position and send those names to Jennifer Nguyen at Jennifer.Nguyen@va.gov

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-Perform the duties of the office of the President whenever the President shall be unable to do so

-Represent the Board of Directors and serve as its Vice-Chair

-Serve in an oversight role for the Society's Annual Seminar

-Serve as a member of TSHP and shall represent GCSHP through service as a member of the TSHP Board of Directors

-One year term

Director

-Represent the general membership on the Board of Directors

-First-year director shall serve as the vice-chair of the Society's Annual Seminar

-Two year term

Membership Secretary

-Maintain membership records

-Prepare and distribute ballots for all Society elections

-Prepare and distribute proposed changes to the Constitution and Bylaws to the membership for approval

-Distribute GCSHP newsletters and meeting notices to the membership

-Two year term

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