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Medications for Diabetes and Its Complications: a Case-Based Approach

A Live and Archived Webcast
Sponsored by Community Health Association of Mountain/Plains States (CHAMPS)
Presented by Laura Shane-McWhorter, PharmD, BCPS, FASCP, CDE, BC-ADM
Wednesday, January 16, 2008

Community Health Association of Mountain/ Plains States

Supplementary Information Packet

Contents:

Learning Objectives

Upon completion of this program, participants should be able to:

1. Describe the current controversy surrounding glitazone use.
2. Describe use of newer agents for diabetes including inhaled insulin and DPP-IV inhibitors.
3. List new American Heart Association target blood pressures for specific disease states.
4. Review information regarding the direct renin inhibitor, aliskiren.
5. Discus priorities in hyperlipidemia treatment in patients with diabetes.

Continuing Education Statements

This live webcast has been reviewed and is acceptable for up to 1.5 Prescribed Continuing Medical Education (CME) credits by the American Academy of Family Physicians (AAFP). Application for 1.5 hours of Prescribed CME credit for the archived version of this webcast will be filed immediately after the live event. The AAFP invites comments on any activity that has been approved for AAFP CME credit. Please forward your comments on the quality of this activity to cmecomment@aafp.org.

The University of Colorado Denver School of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This program has been accredited 1.5 contact hours and assigned the ACPE numbers: 008-999-08-004-L01-P (live webcast) and 008-999-08-004-H01-P (archived webcast). To receive CE credit, participants must complete the evaluation and post-questions. CE credit will issued within 6 weeks. Initial release 1-16-2008; archived webcast expires 1-16-2009.

Laura Shane-McWhorter has disclosed that she is on the Speaker's Bureau for Pfizer, Astro-Zeneca, and Roche. She has no other real or apparent conflicts of interest to disclose.

Biography of Laura Shane-McWhorter, PharmD, BCPS, FASCP, CDE, BC-ADM

Laura Shane-McWhorter is a clinical Professor at the University of Utah College of Pharmacy, where she teaches therapeutics, including lectures on diabetes, psychiatry, complementary products, and OTC products to undergraduate and graduate pharmacy students, physician assistant students, and nurse practitioner students. She provides clinical support at a Community Health Center, offering patient education to underserved patients, particularly in the areas of diabetes, hypertension, and hyperlipidemia. She also provides drug therapy consultation services to health care providers. Laura received her Doctor of Pharmacy degree from the University of Utah in 1988, and completed a Post-Doctoral Residency in Geriatic Pharmacy. She has worked on several diabetes collaborative projects at the local, state, and national level, and has several publications in the area of diabetes, depression, complementary therapies and women's health. Laura is also an experienced lecturer on topics including diabetes, depression, geriatrics, hypertension, hyperlipidemia, women's health, and complementary therapies, and is a regular presenter at national American Association of Diabetes Educators meetings. She served as first author for the chapter, "Biological Complementary Therapies in Diabetes" in *A Core Curriculum for Diabetes Education, Fourth Edition,* published in 2001 by the American Association of Diabetes Educators, and her book, "Complementary and Alternative Medicine Supplements for Diabetes: A Clinicians Guide" was introduced in June 2007 at the Scientific Sessions of the American Diabetes Association.

Description of CHAMPS

CHAMPS, the Community Health Association of Mountain/Plains States, is a non-profit organization dedicated to providing a coordinating structure of service to the community, migrant, and homeless health centers serving the medically indigent and medically underserved of Region VIII (CO, MT, ND, SD, UT, WY) as well as Region VIII's State Primary Care Associations (CCHN, MPCA, CHAD, AUCH, and WYPCA). Currently, CHAMPS programs and services focus on education and training, collaboration and networking, policy and funding communications, and the collection and dissemination of regional data. For more information, please visit http://www.champsonline.org or call (303) 861-5165.

Medications for Diabetes and Its Complications

Sponsored by Community Health Association of Mountain/Plains States (CHAMPS)

www.CHAMPSonline.org

Laura Shane-McWhorter, PharmD, BCPS, FASCP, CDE, BC-ADM, Professor (Clinical), University of Utah College of Pharmacy Department of Pharmacotherapy

Wednesday, January 16, 2007
11:30am – 1:00pm Mountain Time

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Objectives

Using patient cases, the participant will be able to:

- Discuss the current controversy surrounding glitazone use
- Describe use of newer agents for diabetes including DPP-IV inhibitors
- List new American Heart Association target blood pressures for specific disease states
- Review information regarding the direct renin inhibitor, aliskiren
- Discuss priorities in hyperlipidemia treatment in patients with diabetes

Laura Shane-McWhorter, PharmD

Diabetes: The Statistics

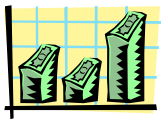
- Persons with diabetes:
  - 20.8 million persons –
    - 7.0% of the population
  - Diagnosed: 14.6 million people
  - Undiagnosed: 6.2 million people
- Pre-diabetes: 54 million people

Source: American Diabetes Association. National Diabetes Fact Sheet, 2005. Available at: http://www.diabetes.org/diabetes-statistics.jsp

Laura Shane-McWhorter, PharmD

Diabetes Statistics…

- 1.5 million new cases of diabetes were diagnosed in people aged 20 years or older in 2005.
- Costs of diabetes in the US:
  - Total: $132 billion
  - Direct medical costs
    - $92 billion
  - Indirect medical costs
    - $40 billion
    - Disability, work loss, premature mortality



Source: American Diabetes Association. National Diabetes Fact Sheet, 2005. Available at: http://www.diabetes.org/diabetes-statistics.jsp

Laura Shane-McWhorter, PharmD

Trends in Type 2 Diabetes: 1988 - 2000 NHANES

- Mean A1C ↑ from 7.7% to 7.9%
  - Glucose control (A1C <7.0%) decreased from 44.5% to 35.8% (21% decrease)
    - A1C > 8.0% in > 37%
- Average BMI ↑ from 30.4 to 32.3 kg/m^2

Laura Shane-McWhorter, PharmD

Trends in Type 2 Diabetes: 1988 - 2000 NHANES

- Medication Trends
  - Oral agents only ↑ from 45.4% to 52.5%
  - Diet-only decreased from 27.4% to 20.2%
  - Insulin-only ↓ from 24.2% to 16.4%
  - Insulin + oral agents increased from 3.1% to 11.0%

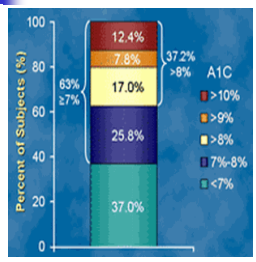
Laura Shane-McWhorter, PharmD

How many persons with diabetes have A1C, blood pressure, and cholesterol controlled?

- 5%
- 7%
- 10%
- 25%

Laura Shane-McWhorter, PharmD

Most Diabetes Patients NOT At A1C Goal of <7%



- 7% of adults with diabetes achieved all 3 targets:[1]
  - A1C <7%
  - BP <130/80 mm Hg
  - Total Cholesterol <200 mg/dL
- Each 1% ↑ in A1C represents a 28% ↑ in risk of death[2]

[1] JAMA. 2004;291:335-342.
[2] BMJ. 2001;322:1-6.

Laura Shane-McWhorter, PharmD

Diabetes Chronic Complications

- Macrovascular Complications
  - Cardiovascular disease
  - Cerebrovascular disease
  - Peripheral vascular disease
- Microvascular Complications
  - Diabetic Neuropathy
  - Diabetic Retinopathy
  - Diabetic Nephropathy

Laura Shane-McWhorter, PharmD

Case - JS

- JS is a 45 y/o overweight female recently diagnosed with type 2 DM. Her A1c is 8.5% and FPG is 160 mg/dL and 2 random PPG values are 220 and 190 mg/dL. Cr is 1.5 mg/dL. ALT is 38 U/L. Fasting lipids are normal. Notable allergies are penicillin and sulfa.

Laura Shane-McWhorter, PharmD

Case - JS

- What agent(s) may be considered to start treatment in JS?
  - Glyburide
  - Metformin
  - Nateglinide
  - Rosiglitazone
  - Acarbose

Laura Shane-McWhorter, PharmD

Case - JS

- JS' primary care provider has decided to start a glitazone.
- What considerations should be evaluated before starting a TZD (glitazone) in JS?

Case - JS

- What considerations should be evaluated before starting a TZD (glitazone) in JS?
  - Recommendations from AHA and ADA
  - Circulation 2003;108:2941-8
  - Diabetes Care 2004;27:256-63

Case - JS

- What considerations should be evaluated before starting a TZD (glitazone) in JS?
  - Evaluate whether JS has underlying cardiac disease
    - Previous MI
    - Other evidence of CHD
    - Prior CHF episodes
    - Significant aortic or mitral valve disease

Case - JS

- What considerations should be evaluated before starting a TZD (glitazone) in JS?
  - ✓ Evaluate whether JS has underlying cardiac disease
  - Is JS taking any drugs that → fluid retention?
    - NSAIDs, Cox-2 inhibitors
    - Vasodilators
  - Is JS taking any drugs that → pedal edema?
    - Calcium channel blockers

Case - JS

- What considerations should be evaluated before starting a TZD (glitazone) in JS?
  - ✓ Evaluate whether JS has underlying cardiac disease
  - ✓ Is JS taking any drugs that → fluid retention or pedal edema?
  - If JS does not have CHD but has edema, TZD use is not contraindicated
  - Does JS have any SOB, particularly with exertion due to cardiac or other causes ?
    - Have adequate assessment of baseline Sx and monitor
  - Review most recent ECG for CHF risk factors
    - Silent MI?
    - LVH?

Case - JS

- When starting a TZD in persons with one or more risk factors for CHF?
  - Consider risk factors for CHF
    - H/O heart failure
    - H/O prior MI or symptomatic CHD
    - HTN
    - LVH
    - Aortic/mitral valve disease
    - Age > 70
    - Preexisting edema or tx with loop diuretics
    - Development of edema or weight gain on TZD
    - On insulin
    - Creatinine > 2 mg/dL

Case - JS

- When starting a TZD in persons with one or more risk factors for CHF?
  - Consider risk factors for CHF
  - Start at LOW DOSES and ↑ dose slowly

Case - JS

- When starting a TZD in persons without CHF but with a depressed ejection fraction (< 40%)?
  - Start at LOW DOSES and ↑ dose only after several months

Case - JS

- What about using a TZD in symptomatic heart disease?
  - Use cautiously in Class I or II NYHA CHF
  - Start at LOW DOSES
  - Observe for weight gain with gradual dose escalation
  - DO NOT USE in Class III or IV NYHA CHF

Case - JS

- What patient education should be provided when starting a TZD (glitazone) in JS?
  - Report any new sign or symptom
    - Weight gain > 3 kg
    - Pedal edema (especially if onset is acute and amount progresses rapidly)
    - Report SOB or fatigue without any other cause
  - Provider should then determine if CHF is present
  - If CHF is present, D/C TZD and make sure patient is on ACE Is, or ARBs, or diuretics, etc.

Case - JS

- Why does edema occur with TZDs?
  - TZDs ↑ BP
  - ↓ renal excretion of sodium
  - ↑ sodium retention
  - ↑ free water retention

Case - JS

- What agents have been shown to diminish mild edema that occurs with TZDs?
  - Furosemide?
  - HCTZ?
  - Chlorthalidone?
  - Spironolactone?

Case - JS

- How should edema be managed?
  - Preliminary evidence that spironolactone 50 mg/day or HCTZ 25 mg/day (but not furosemide) may help in mild edema

J Am Soc Nephrol 2006;17:3482-90

Case - JS

- JS has heard that glitazones may cause heart attacks. What is the evidence surrounding glitazone use and cardiovascular effects?

Does Rosiglitazone Increase Risk of MI and CV Mortality?

N Engl J Med 2007;356:2457-71

- Meta analysis of 42 trials
  - N=15,560 pts on rosiglitazone
  - N=12,283 on other drugs
- MI (OR was 1.43; p=0.03)
  - 86 in rosiglitazone group
  - 72 in control group
- Death from CV causes (OR 1.43; p=0.06)
  - 39 in rosiglitazone group
  - 22 in control group

Does Rosiglitazone Increase Risk of MI and CV Mortality?

- Issues
  - 42 trials pooled that were not originally intended to explore CV outcomes; e.g. not powered to discern differences (if present)
  - Total # of events was small
  - Study could not control for previous risks of heart disease or prior CV events
  - Confusion regarding stats – should have absolute risk increase; calculation not possible with info given (if one crunches the numbers, there is higher absolute risk of MI in the control group (0.618% vs 0.598%)

Does Rosiglitazone Increase Risk of MI and CV Mortality?

- New interim analysis of RECORD (Rosiglitazone evaluated for cardiac outcomes and regulation of glycemia in diabetes)
  - 2220 pts assigned to receive add on rosiglitazone
  - 2227 to receive combo of metformin + SU
  - Primary end point: hospitalization or death from CV disease
  - Mean F/U: 3.75 yrs

N Engl J Med 2007;357:28-38

Does Rosiglitazone Increase Risk of MI and CV Mortality?

- Results (HR 1.08; CI 0.89-1.31; pending adjudication HR: 1.11; CI 0.93-1.32)
  - 217 in rosi group achieved primary endpoint
  - 202 in control group achieved primary endpoint
- No significant differences between groups regarding MI and death from CV causes
- More pts with HF in rosi group (HR 2.15; CI 1.3-3.57)
- Interim findings are inconclusive regarding effect on overall risk of hospitalization or death from CV or all causes

N Engl J Med 2007;357:28-38

Do Glitazones Increase Risk of Fractures?

- In women, glitazones may increase risk of fractures
- What part of the body?
  - Humerus, hand, ankle, foot – rosiglitazone
  - Forearm, hand, wrist, tibia, fibula, foot, ankle - pioglitazone
- Not the same as postmenopausal fractures
  - Hip and spine fractures more common in postmenopausal women
- How common is it?
  - 2.7 fractures/100 pt years (rosiglitazone)
  - 1.9 fractures/100 pt years (pioglitazone)
  - Overall, 1 more fracture per 100 women taking a glitazone for one year

Pharmacist's Letter April 2007

Laura Shane-McWhorter, PharmD

Do Glitazones Increase Risk of Fractures?

- Potential mechanism?
  - Glitazones may inhibit bone formation by activating receptors that turn off bone growth
- The bottom line
  - Suggest bone density scans in women at risk for falls or fractures

Pharmacist's Letter April 2007

Laura Shane-McWhorter, PharmD

AJ

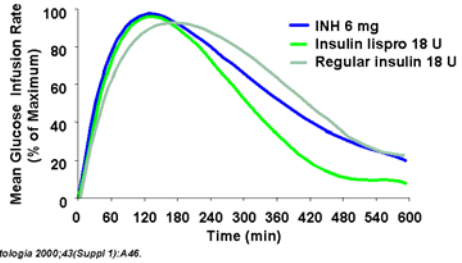
- AJ is a 23 y/o female with Type 1 diabetes who had been injecting insulin, using the following regimen:

  2 mg of Exubera 3 times a day with meals

  18 Units of Lantus at bedtime
- AJ is interested in continuing inhaled insulin but finds out it is now discontinued; she wants to know how it compares to Humalog and how many units she should use

Laura Shane-McWhorter, PharmD

Inhaled, Lispro, Regular Insulins



Diabetologia 2000;43(Suppl 1):A46.

Laura Shane-McWhorter, PharmD

Inhaled vs SC Insulin: T1 DM

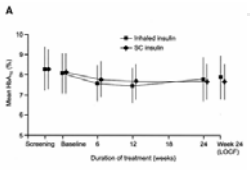
- Patients assigned to:
  - Inhaled insulin tid + UL (N=170)
  - SC Reg insulin bid-tid + NPH bid (N=164)
- Duration – 24 weeks

Quattrin et al: Diabetes Care 2004;27:2622-27

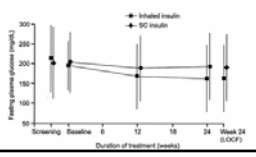
Laura Shane-McWhorter, PharmD

Inhaled vs SC Reg Insulin in T1 DM

8.1% to 7.9%
8.1% to 7.7%



194 to 159 mg/dL
203 to 193 mg/dL



Diabetes Care 2004;27: 2622-27

Laura Shane-McWhorter, PharmD

AJ

- AJ wants to know how many units she should use of Humalog?
  - 2 Units 3 times a day with meals?
  - 3 Units 3 times a day with meals?
  - 4 Units 3 times a day with meals?
  - 6 Units 3 times a day with meals?

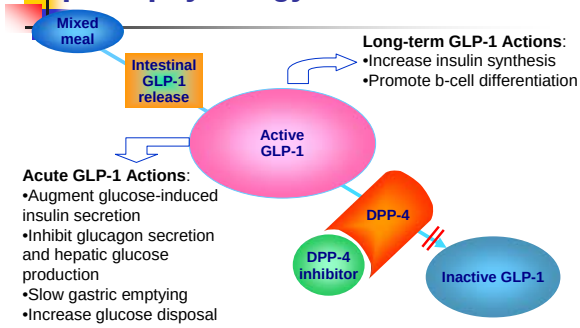
AJ

- AJ wants to know how many units she should use of Humalog?
  - 2 Units 3 times a day with meals?
  - 3 Units 3 times a day with meals?
  - 4 Units 3 times a day with meals?
  - 6 Units 3 times a day with meals? ✓
- Are the doses of Novolog or Apidra the same?
  - Yes ✓

JT

- JT is a 5'10" 88 kg, 68 y/o male with Type 2 DM. He is currently on the following:
  - Glipizide/Metformin 5/500 mg – 2 tablets twice daily
- He is adherent to his medication, MNT, and exercise regimen (30 min walking 4-5 days/wk)
- Labs:
  - A1C is 7.8%
  - SCr 1.0 mg/dL
  - ALT 43 IU/L
- JT refuses to "take any needle medicine" and he does not want to take a TZD because he is afraid of a "heart attack"
- What regimen is best to add to his oral regimen?

Glucagon Like Peptide 1 pathophysiology



Adapted from Rothenberg P. *Diabetes*. 2000;49(suppl 1):A39
Drucker DJ. *Diabetes Care* 2003;26:2929-2940.

DPP-IV Inhibitors

- Sitagliptin (Januvia®)
- Vildagliptin (Galvus ®)

DPP-IV Inhibitors

- Mechanism of action
  - Inhibit breakdown of GLP-1 and GIP
  - Hence, levels of GLP-1 and GIP rise, especially in response to meals
    - This inhibits glucagon
    - Stimulates endogenous insulin secretion when glucose is highest
  - Since these agents increase only glucose-stimulated insulin secretion, there is little risk of hypoglycemia

Sitagliptin (Januvia®)

- Side effects
  - Headache
  - Nasopharyngitis
  - URI
  - What about effects on the immune system?
    - Other DPP-IV substrates include growth factors and cytokines
    - DPP-IV may affect T-cell activity
    - Thus far, no problems

Laura Shane-McWhorter, PharmD

Sitagliptin

- Drug Interactions
  - Studied in combination with SUs, metformin, pioglitazone
  - 38% protein bound
  - Does not inhibit or induce isoenzyme systems
    - Minor metabolism through CYP 3A4 and 2C8
  - Small ↑ in digoxin SDCs (11-18%)

Laura Shane-McWhorter, PharmD

Sitagliptin

- Dose 100 mg daily with or without food
- No dose adjustment in mild-moderate hepatic insufficiency
  - Not studied in severe hepatic impairment
- Dose adjustment in renal impairment
  - Cr Cl $\geq$ 30 to < 50 mL/min is 50 mg daily
    - Males: Cr > 1.7 to $\leq$ 3 mg/dL
    - Females: Cr > 1.5 to $\leq$ 2.5 mg/dL
  - Cr Cl < 30 mL/min is 25 mg daily
    - Males: Cr > 3 mg/dL
    - Females: Cr > 2.5 mg/dL
    - On dialysis

Laura Shane-McWhorter, PharmD

Sitagliptin

- Effects on A1c, BG, Weight
  - If A1c is ~8-9%
    - A1c ↓ 0.6 to 0.8%
  - If A1c is 9-10%
    - A1c ↓ 1.4%
  - FBG ↓ ~16 to 22 mg/dL
  - PPG ↓ ~ 47 to 56 mg/dL
  - Weight neutral
- Combination with metformin (Janumet®)
  - Dosed twice daily

Laura Shane-McWhorter, PharmD

Vildagliptin (Galvus®)

- Primarily hepatically metabolized
  - In severe dysfunction, AUC increases 30%, but not half life
  - No adjustment needed for severe hepatic dysfunction

Laura Shane-McWhorter, PharmD

Vildagliptin

- Side effects
  - Cough, nasopharyngitis, 0.6% experience hypoglycemia
  - Rash in monkeys at high doses?
- Drug interactions
  - ???

Laura Shane-McWhorter, PharmD

Vildagliptin

- Efficacy
  - Similar to metformin and rosiglitazone
- Studied as monotherapy, in combo with metformin, and in combo with insulin
- Dose?
  - 50-100 mg daily
- Weight neutral

Laura Shane-McWhorter, PharmD

JT

- JT is a 5'10" 88 kg, 68 y/o male with Type 2 DM. He is currently on the following:
  - Glipizide/Metformin 5/500 mg – 2 tablets twice daily
- He is adherent to his medication, MNT, and exercise regimen (30 min walking 4-5 days/wk)
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- JT refuses to "take any needle medicine" and he does not want to take a TZD because he is afraid of a "heart attack"

Laura Shane-McWhorter, PharmD

JT

- What regimen is best to add to his oral regimen?
  - Sitagliptin
- Cr Cl = 73 mL/min
- Dose?
  - 100 mg?
  - 50 mg?
  - 25 mg?

Laura Shane-McWhorter, PharmD

JT

- What regimen is best to add to his oral regimen?
  - Sitagliptin
- Cr Cl = 73 mL/min
- Dose?
  - 100 mg? ✓
  - 50 mg?
  - 25 mg?

Laura Shane-McWhorter, PharmD

What About New Reported Side Effects of Exenatide (Byetta®)

- WHAT ABOUT PANCREATITIS?
  - 30 reports thus far
  - Most of these patients had other risk factors for pancreatitis such as:
    - Alcohol use
    - Very high triglycerides
    - Gall stones
    - Does this occur because it's derived from Gila monster saliva and bites from this lizard may lead to pancreatitis?
  - Bottom line: Ask patients to report unexplained severe abdominal pain (± nausea/vomiting)

Laura Shane-McWhorter, PharmD

HP

- HP is a primary care provider who hears that there are some new blood pressure guidelines published by the American Heart Association
  - What do the new guidelines say?

Laura Shane-McWhorter, PharmD

New 2007 AHA BP Targets

Indications	BP Goal (mm/Hg)	Initial Tx	Beta-blockers
Low CAD Risk	<140/90	ACEI, ARB, CCB, thiazide	Not first line
High CAD Risk	<130/80	ACEI, ARB CCB, thiazide	Not first line
With CAD	<130/80	BB and ACEI or ARB	Use first line
Heart failure	<120/80 if possible	BB, ACEI or ARB, diuretics, and aldosterone antagonist	Use first line

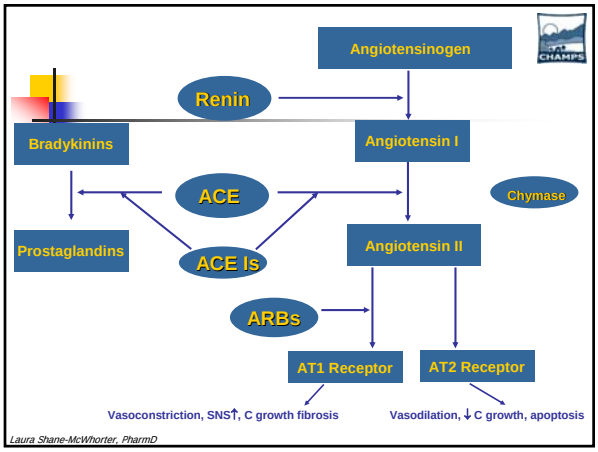
Circulation 2007;115:2761-88.

Laura Shane-McWhorter, PharmD

PF

- PF is a 42 y/o female with Type 2 DM who has had trouble controlling her BP. Her BP tends to be ~ 145/95 mm Hg. Currently she is on the following:
  - Valsartan HCT 160/12.5 mg – 1 tablet daily
  - Metoprolol 100 mg – 1 tablet twice daily
- Are there any new antihypertensives that may be used?

Laura Shane-McWhorter, PharmD



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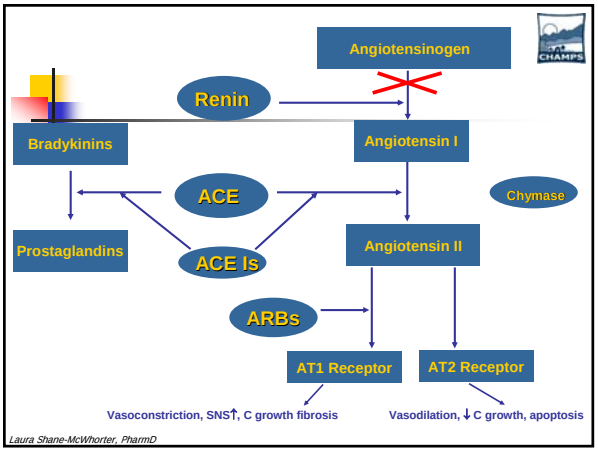


Laura Shane-McWhorter, PharmD

Direct Renin Inhibitors (DRIs)

- New class
- Aliskiren (Tekturna®)

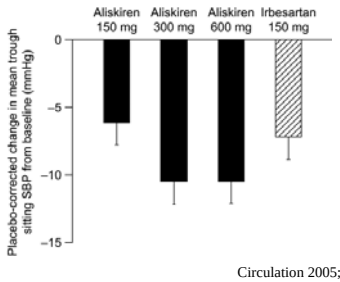
Laura Shane-McWhorter, PharmD

Direct Renin Inhibitors (DRIs)

- MOA
  - Directly inhibits renin
    - Renin is secreted in response to decreased blood volume and renal perfusion
    - Renin controls first step of the RAAS – cleaving Angiotensinogen to Angiotensin I
    - Inhibits renin from cleaving Angiotensinogen to Angiotensin
      - This ↓ circulating levels of Angiotensin II
  - Reaches steady state in about one week

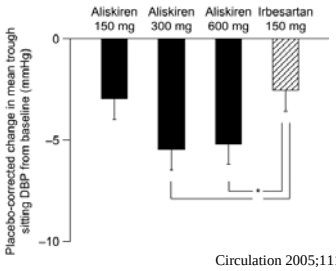
Laura Shane-McWhorter, PharmD

Direct Renin Inhibitors (DRI)



Circulation 2005;111:1012-18

Direct Renin Inhibitors (DRI)



Circulation 2005;111:1012-18

Direct Renin Inhibitors (DRIs)

- ADRs
  - Diarrhea (at higher dose and in women and elderly)
  - Cough – less common
  - Rash – less common
  - Angioedema (Rare)
  - Teratogenicity

Direct Renin Inhibitors (DRIs)

- Mainly metabolized through CYP3A4
  - Hence theoretical induction or inhibition by inducers or inhibitorsI
- Drug Interactions
  - Irbesartan ↓ aliskiren Cmax by up to 50%
  - Atorvastatin ↑ aliskiren Cmax by 50%
  - Ketoconazole ↑ aliskiren SDCs by 80%
  - Aliskiren ↓ AUC and Cmax of furosemide by 30% and 50% (respectively)
  - No significant interactions with lovastatin, atenolol, cimetidine, warfarin, or celecoxib

Direct Renin Inhibitors (DRIs)

- Common example
  - Aliskiren (Tekturna®)
  - Dose – 150 mg daily; may ↑ to 300 mg daily
- May be used as monotherapy or combined with HCTZ 25 mg or amlodipine 5 mg to ↑ antihypertensive efficacy
- Has also been studied in combination with ACEIs and ARBs – jury is out as to potential combination recommendations
  - Most experience in combination is with diuretics and ARBs

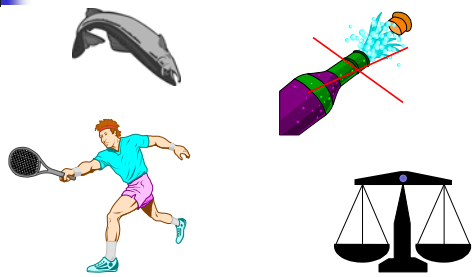
Direct Renin Inhibitors (DRIs)

- Place in therapy
  - Not known yet
  - Being studied in combination with other drugs, including ACEIs and ARBs
    - May see increased K
  - More complete inhibition of RAAS than ACEIs or ARBs
  - DM or renal disease?

Direct Renin Inhibitors (DRIs)

- Monitoring
  - BP
  - Electrolytes, etc. if combined with HCTZ
  - K, if combined with ACEIs or ARBs (especially in patients with DM)
    - Not adequately studied with max doses of ACEIs
  - High fat meals decrease absorption – establish routine time for taking aliskiren

Don't Forget Lifestyle Modification



Life-Style Modification

- Stop Smoking!!!
- Reduce Cholesterol/saturated fat intake (low-fat)
- Reduce sodium intake (NTE 100 mmol/day [2.4 g of Na of 6 g of NaCl])
- Increase physical aerobic activity (walk 30"/day)
- Weight loss if overweight
- Adequate intake of K^+ (fruits, vegetables) Ca^{++}, Mg^{++}
- Restrict alcohol (Males: NTE 1 oz ETOH: 24 oz beer, 10 oz wine, 3 oz 100-proof whiskey; females: 1 drink/day)

JNC 7, 2003

Life-Style Modification

- How much can systolic/diastolic pressure be lowered with a 10 lb weight loss?
  - 10/9?
  - 8/7?
  - 7/6?
  - 6/5?

Lifestyle Modification to Lower Blood Pressure

Modification	Potential ↓ in Systolic/Diastolic Blood Pressure (mmHg)
10-lb weight loss	**7/6**
Dietary Approaches to Stop Hypertension diet (DASH)	**11.4/5.5**
Restriction of alcohol consumption **Men: ≤ 2 drinks/day** **Women: ≤ 1 drink/day**	**3.9/2.4**
Exercise: 30-60 minutes/day, 4-7 days/week	**4.9/3.7**
Restrict dietary sodium to < 1.4 g/day	**3.4/1.9**

JAMA 2002;288:1882-8.

Priorities in Hyperlipidemia Treatment

Case - QE

- QE is a 50 y/o male with the following:
  - HTN, treated with HCTZ 12.5 mg qd
  - Diabetes, treated with metformin, 2000 mg/day
  - Hyperlipidemia, treated with atorvastatin 10 mg/day
  - Gastric acidity, treated with omeprazole.
  - His labs are as follows:
    - A1c – 10.1%; TC-180 mg/dL; TG - 392 mg/dL; HDL 30 mg/dL; LDL 72 mg/dL

Laura Shane-McWhorter, PharmD

Case - QE

- What is the best course of action for QE to better control lipids?
  - Continue the current regimen
  - Add gemfibrozil
  - ↑ the atorvastatin dose
  - Control the blood glucose

Laura Shane-McWhorter, PharmD

Case - QE

- What is the best course of action for QE to better control lipids?
  - Continue the current regimen
  - Add gemfibrozil
  - ↑ the atorvastatin dose
  - Control the blood glucose ✓

Laura Shane-McWhorter, PharmD

Case - QE

- What if QE's labs were the following:
  - A1c – 6.1%; TC-150 mg/dL; TG - 352 mg/dL; HDL 30 mg/dL; LDL 90 mg/dL
- Remember, he is on atorvastatin 10 mg
  - Continue the current regimen
  - ↑ the atorvastatin dose
  - Control the blood glucose
  - Evaluate non-HDL

Laura Shane-McWhorter, PharmD

Case - QE

- What if QE's labs were the following:
  - A1c – 6.1%; TC-150 mg/dL; TG - 352 mg/dL; HDL 30 mg/dL; LDL 90 mg/dL
- Remember, he is on atorvastatin 10 mg
  - Continue the current regimen
  - ↑ the atorvastatin dose
  - Control the blood glucose
  - Evaluate non-HDL ✓

Laura Shane-McWhorter, PharmD

Case - QE

- How should non-HDL be calculated?
  - Total cholesterol – HDL = non-HDL
  - Target non-HDL is 30 mg/dL higher than target LDL
  - QE's LDL is 90 mg/dL; goal is < 100 mg/dL
  - So, QE's goal non-HDL is < 130 mg/dL
  - QE's non-HDL is 150 mg/dL – 30 mg/dL or 120 mg/dL
  - QE's non-HDL is at goal ✓

Laura Shane-McWhorter, PharmD

Case - QE

- What if QE's labs were the following:
  - A1c – 6.1%; TC-180 mg/dL; TG - 450 mg/dL; HDL 30 mg/dL; LDL 72 mg/dL
- He is now on atorvastatin 20 mg
  - Continue the current regimen
  - Add fenofibrate
  - ↑ the atorvastatin dose
  - Control the blood glucose

Laura Shane-McWhorter, PharmD

Case - QE

- What if QE's labs were the following:
  - A1c – 6.1%; TC-180 mg/dL; TG - 450 mg/dL; HDL 30 mg/dL; LDL 72 mg/dL
- Remember, he is on atorvastatin 20 mg
  - Continue the current regimen
  - Add fenofibrate ✓
  - ↑ the atorvastatin dose
  - Control the blood glucose

Laura Shane-McWhorter, PharmD

Case - QE

- What if QE's triglycerides decreased after maximizing fenofibrate dose, but he was still not at goal?
- Remember, he is on atorvastatin 20 mg
  - Continue the current regimen
  - Add fish oil
  - ↑ the atorvastatin dose
  - Control the blood glucose

Laura Shane-McWhorter, PharmD

Case - QE

- What if QE's triglycerides decreased after maximizing fenofibrate dose, but he was still not at goal?
- Remember, he is on atorvastatin 20 mg
  - Continue the current regimen
  - Add fish oil ✓
  - ↑ the atorvastatin dose
  - Control the blood glucose

Laura Shane-McWhorter, PharmD

Case - DF

- DF is a 38 y/o female with DM, HTN, and hyperlipidemia. She presents to clinic with diffuse muscle pain in her lower back/extremities. She had been on pravastatin 40 mg for 2 yrs but was changed to simvastatin based on ↑ LDL, 10 days ago.
  - What labs/monitoring should be done?

Laura Shane-McWhorter, PharmD

Case - DF

- What labs/monitoring should be done?
  - Check CK and compare to baseline value
    - If > 10 times the ULN, D/C statin
    - If CK is 3-10 times the ULN, follow symptoms and re-check CK on a weekly basis until:
      - **There is no medical concern…OR**
      - **Sx worsen…OR**
      - **CK ↑ to > 10 ULN**
  - Check TSH (hypothyroidism predisposes to myopathy)
  - R/O strenuous exercise as a cause

Circulation 2002;106:1024-8

Laura Shane-McWhorter, PharmD

Case - DF

- If statin must be D/C, due to CK being > 10 x ULN, what other options are available?
  - Wait 'til CK is normal before reinitiating therapy
  - Consider lipophilicity of the statin that is chosen
- What other drugs may be used but are not as optimal as a statin?

Laura Shane-McWhorter, PharmD

Case - SR

- SR is a 50 y/o female with type 2 DM. She is taking metformin/glyburide 2.5/500 mg – 2 po bid, rosiglitazone 8 mg qd, lisinopril 20 mg qd, pravastatin 40 mg qd, and aspirin 81 mg qd. All labs are WNL at baseline and 6 months.
- After 12 months, AST is 120 U/L and ALT is 140 U/L; Billirubin and alkaline phosphatase are normal. A1c is 9%. So, rosiglitazone and pravastatin are D/C and 3 months later, A1C is 11%
- Glargine is added and titrated up to 30 U hs. A1c is 7.4% after being on glargine for 3 months.
- After 6 months, AST is 28U/L and ALT is 32 U/L, but LDL is 216 mg/dL.

Laura Shane-McWhorter, PharmD

Case - SR

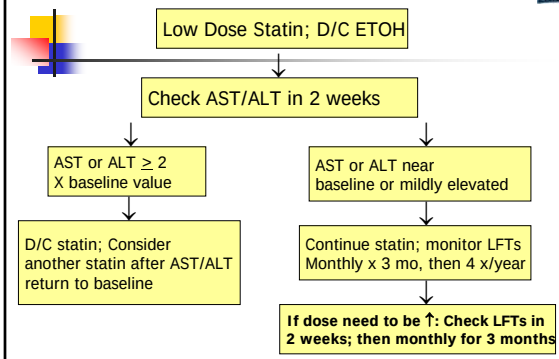
- In a person with a history of LFT elevation with a statin
  - Should a statin be reinstated?
  - If so, how to reinstate?

Laura Shane-McWhorter, PharmD

Case - SR

- In a person with a history of LFT elevation with a statin – how to reinstate?
  - Cleveland Clinic Journal of Medicine 2004;71:58-62 and Nutr Metab Cardiovas Dis 2004;14:215-24
    - Statin-induced hepatotoxicity occurs in 1-3% of patients
    - Characterized by ↑ aminotransferases
    - ↑ aminotransferases revert to normal after dose ↓ or statin is D/C
    - When aminotransferases are normal, a rechallenge with the same or other statins may not result in ↑ aminotransferases

Laura Shane-McWhorter, PharmD



Cleveland Clinic Journal of Medicine 2004;71:58-62

Laura Shane-McWhorter, PharmD

Case - LC

- LC is a 45 y/o Asian male with a h/o of type 2 DM for 5 years. His BMI is 24 kg/m^2. He is on rosiglitazone 4 mg/day and glipizide 10 mg daily, with A1c of 6.9%. His BP is normal on losartan 50 mg/day and LDL is 157 mg/dL. All labs are normal, except for serum creatinine of 2.2 mg/dL.

Laura Shane-McWhorter, PharmD

Case - LC

- What agent should be initiated for elevated LDL and what should be considered?

Case - LC

- What agent should be initiated for elevated LDL and what should be considered?
  - Statin at normal doses?
  - Statin at reduced doses?
  - Gemfibrozil and a statin?
  - Fenofibrate in combination with a statin?

Case - LC

- What should be considered? (K/DOQI Guidelines)
  Adjust for GFR (mL/min/1.73m^2)

	60-90	15-59	<15
Lipitor[1]	No	No	No
Zocor/Lescol[1]	?	?	?
Pravachol[1]	No	No	No
Mevacor[1]	No	↓ 50%	↓ 50%
Crestor[2]	No	5*	5*
Lopid[1]	No	No	No
Tricor[1]	↓ 50%	↓ 75%	Avoid

[1]Am J Kidney Dis 2003;41 (suppl 3):S16 [2](* CrCl < 30 mL/min; www.Crestor.com)

Case - LC

- What should be considered? (NCEP Guidelines)
  Adjust Dose (mg) for GFR (mL/min/1.73m^2)[1]

	≥ 30	<30	+ Cyclosporine
Lipitor	10-80	10-80	10-40
Zocor	20-80	10-40	10-40
Pravachol	20-40	20-40	20-40
Mevacor	20-80	10-40	10-40
Lescol	20-80	10-40	10-40
Crestor[2]	10-40	5	5

[1]NCEP ATP III: JAMA 2001;285:2486-97
[2]Am J Health-Syst Pharm 2005;62:1033-47

Case - LC

- Any other considerations?
  - Dose of statin
    - Why?

Questions?

Thank You for Joining CHAMPS and Laura Shane-McWhorter today!

Your opinions are very important to us.

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