

A Summary of the JNC 8 Hypertension Guidelines

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ALASKA NATIVE DIABETES TEAM

Diabetes Dispatch

The Eighth Joint National Committee (JNC 8) finally released the 2014 Evidenced-Based Guidelines for the Management of High Blood Pressure in Adults which update and replace the decade old JNC 7 hypertension guidelines. The aim of the update was to provide simplified recommendations for the management of blood pressure based on evidence from randomized controlled trials and the panel's expert opinion.

The JNC8 guidelines differ from the JNC 7 guidelines in two key areas: blood pressure goals and first line medication therapies. While the previous guidelines based blood pressure goals and treatment on comorbidities, the new guidelines take a more generalized approach.

Blood Pressure Goals

Patients with diabetes, chronic kidney disease (CKD), or younger than 60 years, have a blood pressure goal <140/90 mmHg. Patients who are 60 years or older, without comorbidities, have a more conservative blood pressure goal <150/90 mmHg.

Population	BP Goal
General >60 years	<150/90 mmHg
General <60 years	<140/90 mmHg
Diabetes	<140/90 mmHg
Chronic Kidney Disease	<140/90 mmHg

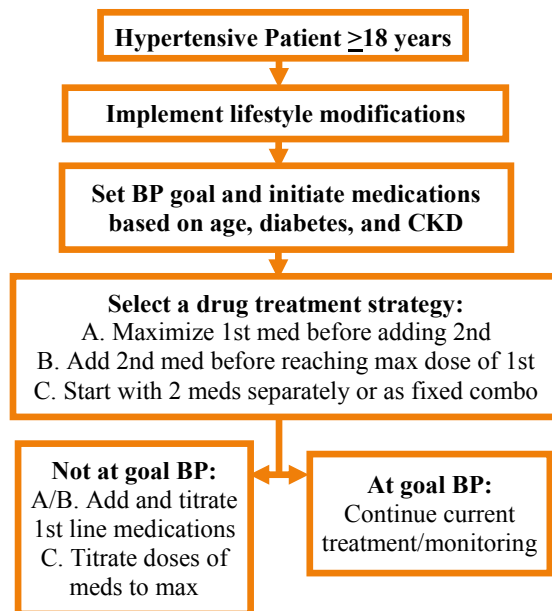
First Line Therapy

In regards to first line medications, JNC 8 stated that thiazide diuretics have the most evidence supporting their use in hypertension; however, the guidelines classify angiotensin converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), and thiazide diuretics all as first line agents in the

general population. Other classes of medications such as beta-blockers and alpha2-adrenergic agonists are considered alternatives when combinations of first line medications are unsuccessful at achieving blood pressure control.

There are two patient populations that have more specific drug recommendations. All patients with CKD, regardless of race, should take either an ACEI or ARB as first line or add-on therapy. The ALLHAT trial demonstrated that ACEIs and ARBs did not significantly reduce cardiovascular risk in black patients; thus, CCBs and thiazide diuretics are preferred first line agents in this population.

Population	Initial Drug Treatment Options
General >60 years	Nonblack: thiazide diuretic, ACEI, ARB, or CCB Black: thiazide diuretic or CCB
General <60 years	
Diabetes	
Chronic Kidney Disease	ACEI or ARB



Objectives:

- Review JNC 8 blood pressure goals and first line medications for specific patient populations
- Identify important considerations for Afrezza® use
- Review the conversion between rapid-acting injectable insulin and Afrezza® doses
- Recognize the correlation between tuberculosis and diabetes

A Summary of the JNC 8 Hypertension Guidelines—Continued

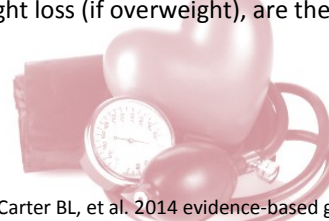
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ADA Standards of Care

The American Diabetes Association (ADA) has slightly different recommendations than JNC 8. While JNC 8 suggests treating patients with both diabetes and hypertension to a blood pressure goal <140/90 mmHg, ADA standards of care advise treating to a goal of <140/80 mmHg. The ADA also states that a lower blood pressure goal of <130/80 mmHg may be reasonable in younger patients if it does not increase treatment burden.

In regards to medication therapy, either an ACEI or ARB should be included in a patient's pharmacological regimen. Additionally, one or more medications should be administered at bedtime to prevent unsafe elevations in blood pressure overnight.

Both organizations agree that lifestyle modifications such as increased physical activity, healthy diet with reduced sodium intake, and weight loss (if overweight), are the baseline of treatment.



References

James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507–520.

American Diabetes Association. Standards of medical care in diabetes—2014. *Diabetes Care*. 2014;37(suppl 1):S14-S80.

Afreeza®: Conventional Insulin Administered in an Unconventional Way

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Afreeza® is rapid-acting recombinant human regular insulin that is formulated as a dry powder for inhalation. Afreeza® is produced by MannKind Corporation, a biopharmaceutical company that focuses on researching treatments for diseases like diabetes mellitus (DM) and cancer. Two recent studies conducted by MannKind found Afreeza® to be non-inferior to insulin aspart in patients with type 1 diabetes (AFFINITY-1) and superior to placebo in patients with type 2 diabetes (AFFINITY-2). On June 27, 2014, the drug was granted an FDA-approved indication to improve glycemic control in adults with both type 1 and type 2 DM.

Place in Therapy

As for its place in therapy, Afreeza® is an alternative to the rapid-acting injectable insulins (lispro, aspart, and glulisine) in patients with type 1 and type 2 DM. It is especially appealing to patients who are afraid of or do not like to use needles. The drug is not a replacement for long-acting insulin, so all patients with type 1 DM as well as some with type 2 DM must still use a longer-acting agent in addition to Afreeza®. If patients are currently taking injectable rapid-acting insulin before meals, they can be easily switched to Afreeza® using the conversion chart shown to the right.

Pharmacokinetics

Afreeza® contains regular human insulin, and therefore lowers blood glucose levels by stimulating peripheral glucose uptake by skeletal muscle and fat, and by inhibiting hepatic glucose production. The inhaled insulin is absorbed faster by the body as peak insulin levels are achieved within 12-15 minutes of administration and decline back down to baseline in about 180 minutes. Even though it has faster absorption, Afreeza® does not have a faster onset of activity compared to insulin lispro. However, its quicker return to baseline insulin levels suggest it could have less risk for hypoglycemia than its rapid-acting counterparts. After it is absorbed through the lungs and into the systemic circulation, the drug's metabolism and elimination are comparable to those of regular human insulin.

Injected Mealtime Insulin Dose	AFREZZA® Dose	# of 4 unit (blue) cartridges needed	# of 8 unit (green) cartridges needed
up to 4 units	4 units	1	0
5-8 units	8 units	0	1
9-12 units	12 units	1 +	1
13-16 units	16 units	0	2
17-20 units	20 units	1 +	2
21-24 units	24 units	0	3

Afrezza®: Conventional Insulin Administered in an Unconventional Way

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How is Afrezza® Supplied?

Afrezza® will be supplied in single-use cartridges consisting of 4 and 8 units of insulin that will be given at the beginning of a meal. Dosing should be individualized to each patient's needs. The inhaler itself is small, whistle-like, easily fits into a pocket, and can be discreetly used.

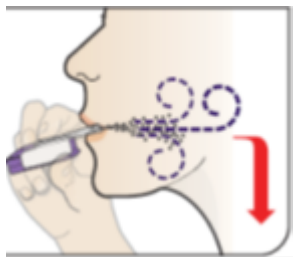


Storage

Using the inhaler itself and handling the associated cartridges are fairly simple. The inhaler, which can be stored in or out of the refrigerator, is only meant to be used for 15 days before being discarded and replaced with a new one. The single-use cartridges are supplied in sealed foil packages (each containing two 3 X 5 blister cards of cartridges). Unused foil packages should be refrigerated. Once a foil package has been opened, it can be stored at room temperature, as long as unopened strips of the blister cards are used within 10 days, and the remaining cartridges in an opened strip are used within 3 days. It is important to know that the cartridges and inhaler should be at left at room temperature for 10 minutes before use.

Directions for Use

To use Afrezza®, patients should simply remove a cartridge from a strip and place it flat inside the opened inhaler with the cup facing down and the pointed ends of the inhaler and cartridge lined up. After loading and closing the inhaler, they should be sure to keep it level to avoid loss of drug powder (otherwise they must get a new cartridge and begin again). To inhale, patients should remove the purple mouthpiece cover, exhale fully, and then place the inhaler in their mouth while keeping their head level. The inhaler should then be tilted downward (with the head remaining level), and patients should inhale deeply through the inhaler, holding their breath for as long as comfortable and at the same time removing the inhaler from their mouth. After holding their breath, patients can exhale to resume normal breathing, put the mouthpiece back on the inhaler, and remove and discard the used cartridge.



Warnings and Precautions

Afrezza® has a black box warning for patients with chronic pulmonary disease (such as asthma or chronic obstructive pulmonary disease [COPD]) due to the risk of acute bronchospasm. It must be used with caution in patients who are also on anti-adrenergic drugs (beta-blockers, clonidine, reserpine, etc.), as these medications could reduce or eliminate signs of hypoglycemia resulting from Afrezza®.

There are a few limitations of the drug. It is not recommended for the treatment of diabetic ketoacidosis or in patients who smoke or have recently quit smoking. FDA post-marketing studies for Afrezza® will examine the drug's effects on pediatric patients and assess the risk for cardiovascular diseases associated with its use.

Adverse Effects

The most common adverse reactions occurring with the use of Afrezza® include cough, throat pain or irritation, and hypoglycemia. Additionally, the drug has also been associated with incidences of pulmonary function decline, lung cancer, diabetic ketoacidosis, hypokalemia, life-threatening hypoglycemia, and fluid retention and heart failure with concomitant use of thiazolidinediones.

Monitoring

In addition to usual diabetes-related monitoring (HbA1c, fasting blood glucose, etc.), patients on Afrezza® must monitor pulmonary function (FEV1) at baseline, 6 months, and yearly thereafter. Potassium levels as well as heart, kidney, and liver function should also be monitored over the course of therapy.

Market Availability

In August, MannKind announced a worldwide exclusive licensing agreement with Sanofi to help with development, commercialization, and distribution of Afrezza®. Plans are in place for the drug to become available on the market within the first quarter of 2015. MannKind's executives claim that Afrezza® will be priced competitively with insulin pens. After many years of delay and several setbacks, it appears that with its recent FDA approval, Afrezza® is on its way to becoming an option for the treatment of both type 1 and type 2 DM.

References

- Afrezza® [Full Prescribing Information]. Valencia, CA: MannKind Corp; 2014.
- Afrezza® [Medication Guide]. Valencia, CA: MannKind Corp; 2014.

Tuberculosis and Diabetes: an Epidemic in the Making?

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Alaska Native People and American Indians have the highest rate of diabetes in people >20 years at 15.9% when compared to other races and ethnicities. People with diabetes can have a suppressed immune system which puts them at an increased risk of contracting infectious diseases such as tuberculosis (TB). Additionally, type 1 diabetes is an autoimmune disease that can be triggered by viral infections and new evidence suggests that type 2 diabetes can also be activated by inflammation and immune response. According to the Centers for Disease Control and Prevention (CDC), Alaska has the highest rate of TB in the country at 9.7% (71 cases). Worldwide, a “dual epidemic” of diabetes and TB is slowly developing in low- and middle- income countries threatening global TB control.

CDC 2013 Tuberculosis Statistics per 100,000 People

Reporting Area	Cases	Case Rate	Rank According to Rate	Population Estimates
United States	9,582	3.0	—	316,128,839
Alaska	71	9.7	1	735,132
Hawaii	115	8.2	2	1,404,054
California	2,171	5.7	3	38,332,521

Treatment of TB in patients with diabetes is more complicated than in the general population. With a compromised immune system from diabetes, latent TB is 3 times more likely to become active TB. The disease manifests itself differently in diabetes as it primarily concentrates in the lower lobes of the lung and weakens pulmonary capillaries causing blood and protein to leak into the lung tissue. As a result, treatment

takes about 3 months longer than usual. Inflammation that accompanies TB also makes achieving glycemic control more difficult which can adversely affect the kidneys and heart. Overall, the risk of dying from TB is 4 to 5 times higher in patients with diabetes.

To reduce the incidence of negative outcomes in patients with both diabetes and TB, regular screening is important. According to the World Health Organization, patients with diabetes should be asked about the presence of a wet, productive cough and low-grade fever lasting longer than 2 weeks at initial diagnosis and each regular checkup. If a patient is positive for these symptoms, he should obtain a Tuberculin skin test (TST) and/or chest x-ray for further evaluation. All patients with tuberculosis should be screened for diabetes using either hemoglobin A1c, oral glucose tolerance, or fasting blood glucose tests.

The Indian Health Service also recommends that a TST or T-cell interferon- γ release assay (IGRA) should be performed in patients with diabetes at least once after diagnosis and more often as indicated. If a test is positive, a medical history, review of symptoms, targeted physical exam, and chest x-ray should be obtained. For every 8 to 10 patients with tuberculosis tested for diabetes, approximately 1 to 2 patients will have underlying disease. With regular screening, early treatment of tuberculosis with diabetes could potentially lead to less morbidity and mortality.

References

- World Health Organization and International Union against Tuberculosis. Collaborative framework for care and control of tuberculosis and diabetes. 2011.
- Nainggolan L. Double trouble: diabetes and TB are 2 converging pandemics. Medscape Medical News. Reporting from the World Diabetes Congress 2013; 2-6 Dec. 2013; Melbourne, Australia.

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Goal-The goal of the Diabetes Dispatch is to increase the reader's knowledge of diabetes treatments and technologies and to provide the most current information on new drugs, therapies, and devices.

- UAN# 0139-9999-14-029-H01-P/T
- Release date: 11/14/2014
- ANMC HED Activity # 13-30010
- Expiration Date : 11/14/2017

The speakers/authors disclose that they do not have significant financial interests in any product or class of products discussed directly or indirectly in this activity, including research support.

Continuing Education Quiz

Diabetes Dispatch: Fall 2014

1. According to JNC 8 guidelines, what is the blood pressure goal of a 64 year old male with diabetes?
 - a. BP goal <150/90 mmHg
 - b. BP goal <140/90 mmHg
 - c. BP goal <140/80 mmHg
 - d. BP goal <130/80 mmHg
2. What is the recommended first line treatment of hypertension in a patient with both CKD and diabetes per JNC 8?
 - a. Thiazide diuretic
 - b. Calcium channel blocker
 - c. ACE inhibitor
 - d. Any of the above
3. Which of the following is not an ADA recommendation for the management of high blood pressure in patients with diabetes?
 - a. Administer one or more medications at night
 - b. Medication regimen should include an ACEI or ARB
 - c. Lifestyle modifications are the baseline of treatment
 - d. Treat to BP goal <140/90 mmHg
4. A patient's blood pressure is not at goal even though she is appropriately taking both a thiazide diuretic and an ACEI at the maximum doses. What medication should be initiated next?
 - a. Calcium channel blocker
 - b. Angiotensin II receptor blocker
 - c. Beta blocker
 - d. Aldosterone antagonist
5. Which of the following is true regarding Afrezza?
 - a. Afrezza can replace long-acting insulin injections
 - b. Even though Afrezza is absorbed faster than injected insulin, it does not have a faster onset of activity
 - c. Afrezza will be supplied in multiple-use cartridges consisting of 8 and 4 units of regular insulin
 - d. Afrezza can be used in patients with COPD
6. All of the following are potential adverse effects of Afrezza except:
 - a. Cough
 - b. Hypoglycemia
 - c. Throat pain
 - d. Hyperkalemia
7. A patient is currently using 17 units of meal-time injectable insulin. What is the equivalent dose of Afrezza?
 - a. 20 units
 - b. 1 blue cartridge plus 2 green cartridges
 - c. 17 units
 - d. Both a and b
 - e. None of the above
8. How many Afrezza cartridges does a patient need to inhale to obtain a dose of 24 units?
 - a. 3 green cartridges
 - b. 2 green cartridges
 - c. 3 blue cartridges
 - d. None of the above
9. According to CDC statistics, which state has the highest rate of tuberculosis in the United States?
 - a. Alaska
 - b. California
 - c. Texas
 - d. Hawaii
10. To reduce morbidity and mortality associated with tuberculosis in patients with diabetes, regular screening is important. What are the recommendations for screening?
 - a. Screen TB patients for diabetes upon diagnosis
 - b. Regularly ask patients with diabetes about symptoms of cough and low-grade fever lasting >2 weeks
 - c. All of the above



Pharmacists and Technicians:

The Alaska Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

To obtain CPE credit for this lesson you must answer the questions on the quiz (70% correct required) return the quiz and evaluation tool. Should you score less than 70%, you will be asked to repeat the quiz. This activity is accredited for 1.0 hour CPE (0.1CEU). Upon satisfactory completion, AKPhA will report participant CPE to CPE Monitor within 60 days of completion.

Pharmacist and technicians may receive credit for completing this course if returned by November 14, 2017.

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Disagree Agree

Disagree Agree

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|---|-----------|---|-----------|
| 1) The activity met my educational needs | 1 2 3 4 5 | 6) The activity learning assessment was appropriate | 1 2 3 4 5 |
| 2) The activity met every learning objective* | 1 2 3 4 5 | 7) The activity was presented in a fair and unbiased manner | Yes No |
| 3) The author was knowledgeable in the topic | 1 2 3 4 5 | If not, please describe _____ | |
| 4) The educational materials were useful | 1 2 3 4 5 | 8) Overall, I was satisfied with the activity. | Yes No |
| 5) Teaching and learning methods were effective | 1 2 3 4 5 | | |

*If a particular objective was not met, please explain: _____

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