This Week's Question:

An obese 20-year-old male patient with Pre-diabetes who you have counseled on life style changes to no avail and despite your strong advice and attempts to enlist his family for support, he is still gaining weight. He now has a fasting plasma glucose of 122 mg/dL, dangerously close to meeting the definition for diabetes.

According to the available information what medication might you recommend?

1. Orlistat
2. Acarbose
3. Metformin
4. A Glitazone
5. None of the above, continue with lifestyle counseling.

In summary, there are now 3 published randomized trials that have examined the use of medications in the prevention of diabetes. It is difficult to compare and extrapolate the results because the trials were significantly dissimilar and involved different populations. Some observations about the profile of the patients can be made, however. In the DPP, significant efficacy from **metformin** in preventing diabetes was seen in subjects who were **younger, heavier men with a higher baseline fasting glucose**. In the STOP-NIDDM, significant efficacy from **acarbose** in preventing diabetes was seen **in older, leaner, normotensive women with a lower baseline fasting insulin level.** In the TRIPOD study, significant efficacy from **troglitazone** in preventing diabetes was seen in **women who had significant insulin resistance and hyperinsulinemia at baseline**.

To return to the question, the best choice of action for this patient remains the same. Intensive lifestyle efforts including diet, exercise, behavior modification, weight loss, and cardiac risk reduction are still the recommended methods for preventing diabetes. A referral to a comprehensive, multidisciplinary weight management center may provide assistance beyond what can be offered in a private practice setting. From the studies described above, however, a clinician may wish to consider including a medication for selected patients who seem to be losing the battle. In this case, the patient may already have converted to type 2 diabetes, and a medication in addition to lifestyle changes would then be considered. From the patient profiles noted, a medication such as metformin would seem to be a reasonable choice.

More Data:

There have been several additional articles published over the last year. The Diabetes Prevention Program (DPP) was a landmark study involving 3234 patients with IGT followed for an average of 2.8 years.[1] Some patients in the DPP were randomized to lifestyle interventions. The lifestyle intervention consisted of a minimum of 150 minutes of physical activity per week, and resulted in a 7% reduction in weight. The risk reduction

in conversion of IGT to diabetes from lifestyle was 58%. The DPP also included a group that was assigned to metformin 850 mg twice daily. The risk reduction in progression to diabetes was significant -- 31% -- but not as dramatic as the lifestyle-intervention group. This led the ADA to issue a Position Statement, stating that lifestyle intervention is both significantly more effective and better studied than are medications. With the lack of available data to support using drugs, the ADA has concluded that "there is insufficient evidence to support the use of drug therapy as a substitute for, or in addition to, lifestyle modification to prevent diabetes."[2]

Two additional studies have looked at diabetes prevention using medication. The Study to Prevent Noninsulin-Dependent Diabetes Mellitus, or STOP-NIDDM, was a multinational, randomized, controlled trial. A total of 1429 patients with IGT were randomized to either 100 mg of acarbose thrice daily or to placebo, and were followed for a mean of 3.3 years. Forty-two percent of placebo-treated patients developed diabetes, compared with 32% of patients treated with acarbose, representing a 25% reduction. When patients who discontinued treatment early were dropped from the analysis, acarbose-treated patients experienced a 91% reduction in acute myocardial infarction, and were 49% less likely to develop any cardiovascular event. [3]

References

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3. Chiasson JL, Josse RG, Gomis R, et al. STOP-NIDDM Trail Research Group. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. Lancet. 2002;359:2072-2077.

4. Buchanan TA, Xiang AH, Peters RK et al. Preservation of pancreatic beta-cell function and prevention of type 2 diabetes by pharmacological treatment of insulin resistance in high-risk Hispanic women. Diabetes. 2002;51:2796-2803.