

Older is better -- Top-10 comparison of diabetes drugs give metformin top grade

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A type 2 diabetes drug taken orally and in widespread use for more than a decade has been found to have distinct advantages over nine other, mostly newer medications used to control the chronic disease, according to a study by researchers at Johns Hopkins.

In their report, published online July 16 in the journal *Annals of Internal Medicine*, the Hopkins team found that metformin, first approved by the U.S. Food and Drug Administration in 1995 (and sold as Glucophage, Riomet and Fortamet), not only controlled blood sugar levels but also was less likely to cause weight gain and more likely than others to lower bad cholesterol levels in the blood.

Researchers say these health benefits are important because they can potentially ward off heart disease and other life-threatening consequence from diabetes. More than 15 million Americans have type 2 diabetes.

“Sometimes newer is not necessarily better,” says lead study author Shari Bolen, M.D., an internist at Hopkins. “Issues like blood sugar levels, weight gain and cost could be significant factors to many patients struggling to stay in good health,” says Bolen, an instructor at The Johns Hopkins University School of Medicine.

In what is believed to be the largest drug comparison of its kind, the scientists showed that all of the commonly used oral medications worked much the same at lowering and controlling blood sugar levels, and were equally safe. But metformin stood out because it offered the same level

of effectiveness without lowering glucose measurements too much, and it did so for a lower price.

Metformin was found to lower LDL or bad cholesterol by about 10 milligrams per deciliter of blood, while newer medications studied, such as pioglitazone (Actos) and rosiglitazone (Avandia), or so-called thiazolidinediones, were found to have the opposite effect, increasing levels of the artery-clogging fat by the same amount.

Researchers say the main drawbacks to metformin are digestive problems and diarrhea. Previous reports have found evidence that the medication leads to the buildup of lactic acid in the blood in people with moderate kidney or heart disease, and they note that it should not be prescribed to anyone with either of these conditions. The main advantages to both newer thiazolidinediones were a small increase in HDL or good cholesterol, and less too-low blood sugar levels than three other older, cheaper drugs studied -- glimepiride (Amaryl), glipizide (Glucotrol), glyburide (Micronase, DiabBeta, Glynase PresTab) -- known as second-generation sulfonylureas.

Annual treatment with metformin or the sulfonylureas, they note, costs on average \$100, roughly one-fourth the cost of oral diabetes medications FDA-approved since then, including the two newer thiazolidinediones, both approved in 1999. (Their price is expected to drop once generic versions become available.)

“When you are dealing with an epidemic like diabetes, it is important for people to weigh their treatment options with their physician and to make informed decisions about which medication best suits their needs,” says Bolen.

In the study, Bolen and her colleagues reviewed the scientific evidence from 216 previous studies and compared each drug for its clinical

effectiveness, risks and costs. In addition to metformin, the thiazolidinediones and sulfonylureas, drugs included in their analysis were repaglinide (Prandin), miglitol (Glyset), acarbose (Precose), and nateglinide (Starlix).

Among the team's other findings were that glimepiride, glipizide, and glyburide led more frequently to too-low blood sugar levels than the other drugs. The sulfonylureas and acarbose appeared to have no effect on bad cholesterol. And except for metformin and acarbose, drug treatment led to an increase in weight from 2 to 11 pounds.

Researchers also noted the increased risk of heart failure, albeit small (less than three people in a hundred), in people taking thiazolidinediones who did not have a history of heart disease. They also caution that despite recent reports about the potential for increased risk of heart attack from rosiglitazone, there is not yet sufficient information to verify the finding.

Researchers say further studies are needed to compare the long-term effectiveness of one treatment to another and to compare drug effects on quality of life and life expectancy. Additional research will also be needed to compare these findings with results for injectible medications for diabetes, most notably insulin, which was not included in the latest report.

Source: Johns Hopkins Medical Institutions

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