Who tends to gain weight with HIV treatment?

There has been a signal from two studies that suggest the possibility of weight gain among people who have used the integrase inhibitor dolutegravir (Tivicay and in Triumeq). However, those studies were done by looking back on data captured for another purpose. Such retrospective studies are useful for exploring an idea but firm conclusions cannot be drawn from them. That is why their results are only suggestive. Results from retrospective studies can be used to develop studies of a more robust statistical design.

To better explore the issue of weight gain among people using combination HIV therapy (ART), researchers at clinics in Milan and elsewhere in Italy conducted a large observational study, assessing health-related data drawn from more than 1,000 HIV-positive people. Participants in this study used different regimens, anchored by integrase inhibitors, protease inhibitors or non-nukes. The researchers found that participants taking common combinations of HIV drugs (not limited to integrase inhibitors) had increases in weight and body mass index (BMI, a relative measure of fatness or thinness). People who were most likely to gain weight were those who were relatively thin or older prior to starting therapy.

The Italian researchers attempted to adjust for factors that could have inadvertently biased their results and their findings are an important step up from retrospective studies. Still, observational studies, no matter how large, can never be used to draw firm conclusions, as they cannot prove cause and effect. There are several randomized, controlled studies of dolutegravir-based combinations underway. Once these studies are complete, the data can be analysed to assess trends in BMI and likely provide robust conclusions about the issue of weight gain and specific combinations of drugs.

Study details

The Italian researchers used data from a project called SCOLTA and focused on the following groups of people on certain regimens:

755 ART-experienced participants who were taking regimens with the following integrase inhibitors:

- dolutegravir – 225 people
- raltegravir (Isentress) – 382 people
- elvitegravir (in Genvoya and Stribild) – 148 people

For purposes of comparison, the researchers collected and analysed data from 145 additional participants who were taking a regimen based on the protease inhibitor darunavir (Prezista and in Prezobix) and 218 others who were on a rilpivirine-based (Edurant and in Complera and Odefsey) regimen. Thus, there were a total of 1,118 participants in this study.

The average profile of all participants upon entering the study was as follows:

- age – 46 years
- 71% men, 29% women
- 19% had a CD4+ count below the 200 cell/mm³ mark
- 40% had a detectable viral load
- BMI is an imperfect assessment but it is relatively simple to calculate as it is based on a person’s weight and height. Participants fell into the following BMI categories: 6% were underweight, as they had a BMI less than 18.5; 61% were normal weight, as they had a BMI between 18.5 and 24.9; 27% were overweight, as they had a BMI between 25 and 29.9; and, 7% were obese, as their BMI was greater than 30.

Participants were monitored for at least one year.
Results

Among all participants, BMI increased slightly by 0.19 six months after starting their current regimen and then by a total of 0.25 one year after starting their regimen. This suggests a modest increase in weight.

To account for factors that could have had an impact on weight gain, researchers performed further analyses. Again, all regimens were associated with modest weight gain (an increase in BMI). Furthermore, there were no differences in BMI changes between participants taking a regimen anchored by an integrase inhibitor and participants who took regimens based on the protease inhibitors darunavir or rilpivirine.

Instead, researchers found an association between having the following factors at the start of the study and subsequent increase in weight:

- older age
- low BMI

Why might weight gain increase with ART?

Prior to the widespread release of ART in high-income countries in 1996, some people with HIV experienced inadvertent weight loss that in some cases could become severe. This was commonly called the wasting syndrome. When analyses were done, researchers found that affected people tended to lose muscle mass.

The causes of weight loss in untreated HIV infection are complex and may be related to intestinal inflammation and injury from infections, altered metabolism, decreased levels of hormones such as testosterone, and loss of appetite.

Once ART became available in 1996, researchers reported increased weight in patients, particularly those who had been suffering from the wasting syndrome, though this increased weight was mostly due to fat rather than muscle. Given the improved health that accompanies the use of ART, it is natural to expect some degree of weight gain over time.

Different studies

The researchers who designed the two retrospective studies that captured a signal of weight gain with dolutegravir were attempting to explore an idea to see if there was a possible trend. The next step has been done by the Italian researchers in SCOLTA, a study of an observational design. Such studies are good at finding associations but cannot prove "cause and effect"—that is, observational studies cannot prove that the use of integrase inhibitor–based regimens caused an increase in BMI.

More robust conclusions about weight gain can come from randomized, controlled studies, and several of these have been done and are underway or planned with dolutegravir-containing regimens. However, there is a possible issue with these studies. These randomized, controlled studies are meant to collect data for the licensure of dolutegravir-containing combinations. As such, participants will be young, relatively healthy people with HIV. Their findings may not be applicable to people in the community who are older and/or who have other health conditions.

Bear in mind

There are many issues that can play a role in weight gain. Some of them are listed below:

- psychological and emotional – sometimes anxiety and even depression can cause people to eat more food and not have the energy to exercise; eating disorders
- physical – injuries; osteo-arthritis affecting the joints; low back pain; not enough exercise
- poor dietary habits
- sleeping problems
- biomedical – some cases of pre-diabetes and diabetes; abnormal levels of thyroid hormones; some medicines
- aging – a general trend is that as people age they tend to gain weight

These and other factors need to be taken into account when trying to assess the impact of medicines on weight and BMI. There is much work that lies ahead to be certain about the impact of dolutegravir on weight. But, for now, the
results from the Italian study suggest that a modest increase in weight can occur in people taking commonly used regimens, whether or not these regimens include integrase inhibitors.

—Sean R. Hosein

REFERENCES:

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