MS and bone marrow transplant

Not for most patients

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HOW WAS THIS STUDY DONE? In the article "Autologous hematopoietic stem cell transplantation in multiple sclerosis: A meta-analysis," Sormani et al.[1] found studies that had already been published about autologous hematopoietic stem cell transplantation (aHSCT) for treatment of multiple sclerosis (MS) (see the next page for an introduction to aHSCT in the treatment of MS).

The authors included 15 studies published between 1995 and 2016 and combined the data. This is basically like putting smaller studies together to create one big study. Doing this makes it easier to see if a treatment works and if there are dangerous side effects. However, doing an analysis like this can be tricky. One reason for this is that patients included in the combined studies can be different in important ways. For example, some studies included only people with relapsing-remitting MS, while others also included people with secondary progressive MS. We know that these different forms of MS respond differently to treatment.

Another reason it can be hard to combine patients from different studies is that the treatment they are given can be different. Some of the studies used very strong chemotherapy prior to the aHSCT. Other studies used less strong chemotherapy medications. So, although the treatments can be different, they all get lumped together as aHSCT. Dr. Sormani and her team were aware of these challenges and used statistics to help adjust for these differences. They were also cautious in the conclusions they made from their results, knowing how challenging an analysis like this can be.

WHAT WERE THE MAIN FINDINGS? This study combined data from 764 people with MS who underwent aHSCT. They found that 2 years after getting the treatment, 83% of patients did not have any evidence of MS disease activity. This number dropped to 67% at 5 years. This means that at 5 years, 2 out of 3 people did not have signs of their MS being active, while 1 out of 3 people did.

The authors also looked at the risk of dying from the treatment. This risk was 2.1%, or about 2 out of 100 people. The risk of death was higher in patients with secondary progressive MS and more disabled patients. They also found that the risk of death had declined significantly since 2012, with only 1 death occurring among 232 people with MS undergoing aHSCT. The reduced risk of death since 2012 may be related to improved selection of patients for transplantation. The authors did not look at other risks, like serious infections, that can arise during treatment. The people with MS who appeared to benefit the most were those with very aggressive relapsing-remitting MS who were not dependent on a cane for walking.

WHAT DOES THIS MEAN FOR PATIENTS WITH MS? It is too soon, based on these results, to routinely recommend aHSCT for treatment of MS. There are 15 Food and Drug Administration–approved treatments for relapsing-remitting MS, including the recently approved and highly effective medication ocrelizumab. Given the data and the risks associated with aHSCT, only patients with aggressive relapsing MS who have failed other standard therapies should consider this therapy. Even then, they should consider it only if they are willing to accept the low, but present, risk of death. An important limitation of the current studies is that the treatment is not directly compared with other highly effective treatments for MS. This is an important area that should be studied in the future so that we can determine if aHSCT is more or less effective than other highly effective medications for MS, such as natalizumab or ocrelizumab.

It is very important to consider the risks of treatments like this. The diseases that are typically treated with aHSCT are cancers, such as lymphoma. This is an important difference because untreated lymphoma will lead to death. This is very different from MS, which is not a fatal disease. When treating a disease like lymphoma, a small risk of death from the treatment itself is more acceptable because a person will die without treatment. However, the risks look very different when treating a disease like MS.

REFERENCE

1. Sormani MP, Muraro PA, Schiavetti I, et al. Autologous hematopoietic stem cell transplantation in multiple sclerosis: a meta-analysis. Neurology 2017;88:2115–2122.

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About multiple sclerosis and hematopoietic stem cells in the treatment of multiple sclerosis

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Adapted from Brown MG. Cost of disease-modifying therapies for multiple sclerosis. Neurology 2015;84: e181–e185.

WHAT IS MULTIPLE SCLEROSIS? Multiple sclerosis (MS) is an inflammatory disease that affects the central nervous system (CNS). In MS, the immune system does not function normally and it launches attacks on the brain and spinal cord, which make up the CNS. The immune cells target the fatty insulation that surrounds the wires, or axons, of the nerves. This insulation, or myelin, helps the nerves conduct signals more quickly and efficiently. Without the myelin, the nerves do not fire well and are also more susceptible to damage. Symptoms in MS are related to this dysfunction. Depending on what part of the CNS is attacked, people will experience different symptoms including vision loss, weakness, numbness, and loss of balance, among other possible symptoms.

MS affects women about twice as often as men. It is usually diagnosed around age 30. The cause of MS is unknown. The current clues suggest that it is related to a mix of environmental exposures and genetics. For instance, MS occurs more often in people who live in northern latitudes. Also, a person is more likely to get MS if he or she has a first-degree relative (mother, father, brother, or sister) with MS. Twenty-five percent of identical twins, who have identical genetic makeup, develop MS if their twin has MS. In comparison, only 2% of fraternal twins, whose genetic makeup is like a brother or sister, develop MS if their twin has MS.

The most common form of MS is relapsing-remitting MS. People who experience this type of MS will have neurologic symptoms from attacks, or relapses, of inflammation that then resolve. They may feel completely normal in between relapses. Another form of MS is called progressive. Patients with this form will have a slow decline, for example in balance or walking, over months to years. There are also people who experience both progression and relapses. MS can also change in a person over time. Early in the disease a person with MS may have more relapses, then years later have symptoms of progression. This is called secondary progressive MS.

HEMATOPOIETIC STEM CELLS IN TREATMENT OF MS There has been much interest in stem cells for treatment of MS. However, not all stem cells are the same. In addition, not all experimental treatments target the same disease mechanism in MS. A stem cell is an immature cell that can mature into a specific type of adult cell. The most immature stem cells may become muscle cells, skin cells, red blood cells, immune cells, or any other kind of cell.

As stem cells mature, they start to get restricted in what types of cells they can become. For example, some stem cells can only become cells of the bloodstream. These are called hematopoietic stem cells. These are found in the bone marrow and give rise to all the cells in the blood, including red and white blood cells, and cells of the immune system.

The immune system does not function normally in MS. Instead, it attacks the brain and spinal cord of people with MS. Because of this, some doctors have thought that if we can use chemotherapy medications to wipe out all the abnormal immune cells in a person's body and then give that person his or her own hematopoietic stem cells back that it might reset the immune system and prevent inflammation that causes MS. This is called an autologous hematopoietic stem cell transplantation. We do not expect these stem cells to directly repair any of the damage that MS has already caused. Rather, the goal is to prevent new MS attacks and further damage caused by inflammation. There are other types of stem cell treatments being studied for repair in MS, but these are not hematopoietic stem cells and therefore these studies were not included in the analysis by Dr. Sormani and her team.

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