In Resource-Constrained Situations, Low-Dose Rituximab Should Be Utilised To Treat Ms: No

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Opinion

Patients with Multiple Sclerosis (MS) in wealthier areas have access to more than 20 disease-modifying treatments (DMTs), whereas patients in resource-constrained situations frequently have none. When compared to the many diseases-both neurological and non-neurological for which viable, scientifically confirmed treatments exist, the difference in MS treatment access is considerable. The World Health Organization's Model List of Essential Medicines is used by many governments across the world to buy pharmaceuticals. Due to the lack of MS DMTs on the market, immunosuppressive drugs such as rituximab and its quality-assured biosimilars, which are approved for other indications, should be investigated for MS treatment. Interferon beta and glatiramer acetate are the most prevalent MS DMTs in low-income nations with a limited availability of "off-label" MS DMTs. Patients with MS who only have these two alternatives may alternate between low-efficacy medications each time their condition flares up. This regrettable scenario necessitates new thinking on how to best treat MS patients in resource-constrained settings. Rituximab has a number of advantages in resource-constrained settings, including its suitability for several mimicking Central Nervous System (CNS) demyelinating illnesses such neuromyelitis optical. For highly mobile resource-limited populations, such as refugees, semi-annual DMT dosing is practical. While these practical considerations support B-cell therapies as a treatment option in general, they do not support low-dose therapy. Intravenous rituximab treatment, on the other hand, is hindered by a lack of infusion centres, which are typically concentrated in large cities; a scarcity of competent MS professionals; and a higher need for laboratory screening and monitoring compared to other DMTs. Persons with MS in resource-constrained situations, like all people with MS, deserve treatments that are highly effective, safe, tolerant, and economical. For persons with MS, the question of whether low-dose rituximab is equally effective, safer, and cheaper should be investigated.

People with MS do not have enough information about the efficacy of low-dose rituximab to propose it as a standard of therapy. Importantly, there is no conventional definition of low-dose, and there is no consensus dosing strategy for rituximab in neuro-inflammatory illness. Low dosage is initially defined as a dose or cycle of 100 mg to 1000 mg. Patients treated with a median dose of 500 mg Intravenous (IV) every 6 months were found to be extremely beneficial in a Swedish observational cohort in some MS patients. However, there are few long-term rituximab follow-up studies that include disability outcomes. In all cases, sensible rituximab dosing is required, with a focus on the therapeutic goal, which is the degree of B-cell depletion rather than the total dose. It's unclear whether rituximab dose studies in high-income countries can be extrapolated to patients in low-income countries, who are likely to be younger, have a lower BMI, and have different disease risk factors. While real-world data from low-income areas is emerging, and low-dose rituximab appears to be promising, the picture is still incomplete. The authors observed that taking 500 mg IV rituximab every 9-12 months in 34 patients proved to be helpful when a tiered dosage strategy of rituximab was attempted in 118 adults with MS in India. Patients with reduced illness activity received low-dosing via pre-treatment disease management. Patients were assessed using Magnetic Resonance Imaging (MRI) and clinical follow-up, as well as serial flow cytometry for serum B-cell subsets. In contrast, a pre-print research of 85 Iranian MS patients treated with rituximab (500 mg twice a week for six months) found that 18 individuals developed a relapse over the four-year study period. Notably, in these individuals, rituximab was started after a poor clinical response to a first-line DMT. Flow cytometry could not be used in all of the patients due to financial constraints. Patients who would benefit from low-dose rituximab versus higher-dosed rituximab are still undecided. In resource-constrained situations, such as in children, prospective, randomised studies comparing dosages are essential. While low-dose rituximab is expected to be more effective than interferons or glatiramer acetate for many people with MS, higher-dosed B-cell treatments are likely to be even more effective. Selecting the subset of MS patients who could be adequately treated with the lowest doses could necessitate additional expenditures in laboratory tests, neuroimaging, and manpower, which could offset the expenses of lower dosing. Aside from efficacy, there are two key considerations for using low-dose rituximab instead of high-dose rituximab in resource-constrained settings: (1) a decreased risk of major infections and hypogammaglobulinemia, and (2) a reduced cost. For a variety of reasons, including the large diversity of pathogens found in tropical zones and the impact of poverty on infectious diseases, infection risks during immunosuppression may be increased in resource-limited situations. However, minimal evidence supports the concept that low-dose rituximab reduces the risk of serious infection in MS patients when compared to greater dosages. Among resource-limited areas, serious infections have not been observed disproportionately in MS patients treated with rituximab. The cost of lowering the dose is the second key rationale for doing so. If a 10 mL vial of rituximab (10 mg/mL) costs 23 USD in resource-limited settings, a dose of 1000 mg would cost 2,300 USD per cycle or 4,600 USD annually if dosed every 6 months. Only ultra-low-dose rituximab (500 mg every 6 months) could be afforded without further financial assistance because many patients in resource-limited settings pay for drugs out of pocket. According to the World Bank, 40 nations have a GNI per capita of around $1500 USD per year. These prices do not include laboratory testing, administration by competent health care staff, additional medications to increase tolerability, or transportation costs for patients. Furthermore, because MS disproportionately affects young women, a demographic already at a disadvantage, Cost very probably remains a major determinant in treatment choice for most persons living with MS in the poorest settings in terms of education, work opportunities, personal income, and social safety nets in various resource-limited situations. When the cost of an effective treatment is the most important factor in determining dosing for a debilitating and life-threatening condition, the global community must do more than simply recommend a lower dose. In MS, one has to wonder if lower doses of any effective treatment can be ethically suggested only on the basis of cost. Re-negotiation of drug pricing and assuring adequate supply chains of life-sustaining therapies have occurred in various conditions, such as HIV/AIDS, insulin-dependent diabetes, and chronic myeloid leukaemia. Despite the difficulties, political will, activism, and research have all worked together to reduce costs. People with MS in resource-constrained situations should not be denied treatment, receive insufficient treatment, or have fewer treatment options owing to cost concerns.

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