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Review

Multiple sclerosis disease modifying medicine utilisation in Australia

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ABSTRACT

With the introduction of new disease modifying medicines (DMM) for relapsing remitting multiple sclerosis (RRMS) in Australia, we aimed to examine trends in utilisation from 1996 to 2013. We analysed trends in use by administrative area (state/territory). Prescription data from Medicare Australia were converted to defined daily doses (DDD)/1000 population/day using population data. Overall RRMS DMM use increased progressively from 0.024 to 0.68 DDD/1000 population/day between 1996 and 2013. From 1996 to 1999 interferon β1B was the only such agent available. Interferon β1A became the most widely used RRMS DMM in 2001. Glatiramer acetate became available in 2004 and its use thereafter increased slowly. Natalizumab was introduced in 2008 with slow growth and fingolimod use grew substantially once it was subsidised in 2011. Both these medicines have accounted for the growth in total use of RRMS DMM in 2012 and 2013. Overall RRMS DMM use was higher in more southern states than in northern states. Patterns of preferred agent varied between different Australian states and territories. RRMS DMM use in Australia has grown progressively since 1996, probably related to growing medical and patient confidence in the benefits obtained from using such drugs, longer survival in MS patients (partly related to use of drug treatments), and easier recognition of MS with the wider availability of magnetic resonance imaging (MRI). The availability of fingolimod, the first DMM that can be taken by mouth, may have led RRMS patients who rejected parenteral therapy to commence treatment of their disease.

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory, primary demyelinating disease of the central nervous system and is the most common cause of continuing neurological disability in young adults in western societies [1]. In most patients, MS follows a relapsing-remitting course (relapsing remitting multiple sclerosis [RRMS]) at least in its earlier stages. In these stages there is often complete clinical recovery between attacks, but over time recovery between attacks becomes incomplete and most patients ultimately enter a secondary progressive phase [1]. In about 10% of patients, the disease runs a primary progressive course, with continuing deterioration in neurological function from the outset, without relapses and remissions [2,3]. The overall progressive nature of the disorder, the eventual debilitation, and the peak age of onset of 30–49 years, [1] result in high levels of support and medical care being required and significant loss of productivity in the workforce [4]. Half the people living with MS in Australia are unemployed [5]. It is estimated that in 2010, in Australia, MS cost one billion dollars, with lost productivity being the largest cost component [6]. The greatest use of resources was for immunomodulating medicines, consultations and nursing [7].

MS treatment was essentially symptomatic until new disease modifying medicines (DMM) became available in Australia after 1985, including interferon β1B, interferon β1A, glatiramer acetate, natalizumab and fingolimod [8,9]. These medicines are approved for use in the relapsing-remitting phase of the disease and appear capable of favourably altering its natural history [2]. In Australia, they are publically subsidised on the Pharmaceutical Benefits Scheme (PBS) under the 'Authority Required' prescription mechanism [10] for patients who (i) have had at least two attacks in the preceding 2 years with partial or complete recovery and remain ambulant, and (ii) have their diagnosis confirmed by MRI of the brain or spinal cord. Until recently, public rebates were available only on MRI studies ordered by a specialist. As a result, prescriptions of these agents are generally initiated by specialists (specifically neurologists) but may be continued by general practitioners in the community. These drugs are too expensive to be routinely obtained by private prescription (i.e. where the consumer

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pays the total cost) and the PBS has mechanisms to ensure that individuals do not receive more than one such agent simultaneously [11].

We examined the patterns of utilisation of RRMS medicines between 1996 and 2013 in Australia and differences at various times in utilisation among the nation's states and territories.

2. Methods

All the medicines were available under the Australian Government's subsidised medicine formulary, the PBS. The PBS provides a broad range of Australian registered medicines to Australian citizens with two levels of patient co-payments: general (AUD$36.10, 2013) and concessional (AUD$5.90, 2013) [12]. Concessional beneficiaries are those who receive social security benefits because they hold a Pensioner card, a Health Care card, or a Commonwealth Seniors Health card. The medicines considered in this study are listed only for use in patients with diagnosed RRMS that meet the criteria mentioned above and are all priced substantially above the level of co-payment. Patients who have progression of disease despite treatment are not eligible for repeat prescriptions of subsidised medicines [2]. None of these medicines has any other subsidised therapeutic use and they are almost invariably used in the same standard dose without individual variation. A single prescription (initial plus five repeats) supplies one person for 24 weeks. The medicine cost for all the agents (except natalizumab and fingolimod) for one person with RRMS is approximately AUD$1092 per 28 day period – more than AUD$13,100 per annum. There would likely be very little prescription of these agents in public hospitals due to costs and because patients with RRMS are mostly managed on an outpatient basis. Natalizumab, a monoclonal antibody, has been available since July 2008 (under PBS Section 100 Public from August 2010) for use in approved hospitals for monthly intravenous infusion as day procedures for the treatment of RRMS. It costs AUD$2,038 for a month's supply. Fingolimod was subsidised in 2011 and costs AUD$2,313 per month.

The number of dispensed prescriptions for RRMS medicines was obtained from public domain Medicare Australia PBS statistics provided by the Australian Government Department of Health [8]. Data were collected for the period between January 1996 and December 2013 and stratified by administrative areas – state or territory – for each formulation of each medicine. The amount of medicine dispensed (as prescriptions) was standardised to utilisation using the defined daily dose (DDD) per 1000 population per day. The DDD, as established by the World Health Organization Collaborating Centre for Drug Statistics Methodology, is the assumed average maintenance dose per day (expressed in terms of the dose contained in marketed dosage forms) for a medicine used for its main indication in adults [13]. For DDD calculations we used the midyear population for each state or territory and Australia as a whole [14]. Yearly totals of DDD were summed for each administrative region and for the whole nation.

The medicines in alphabetical order by generic name (with the trade name and DDD) are: fingolimod (Gilenya, 0.5 mg [Novartis, Basel, Switzerland]), glatiramer acetate (Copaxone, 20 mg [Teva Pharmaceutical Industries, Petah Tikva, Israel]), interferon β1A (Avonex, 4.3 mcg [Biogen Idec, Weston, MA, USA]), interferon β1A (Rebif, 4.3 mcg [Merck Serono, Darmstadt, Germany]), interferon β1B (Betaferon, 4 mU [Bayer HealthCare AG, Levekusen, Germany]); and natalizumab (Tysabri, 10 mg [Biogen Idec]). Interferon β1B was listed on the PBS in November 1996 followed by interferon β1A-Avonex preparations in February 1999 and interferon β1A-Rebif preparations in May 2000. Glatiramer acetate was listed in May 2004, natalizumab in July 2008 and fingolimod in September 2011.

3. Results

3.1. Utilisation use over time

Overall use of RRMS DMM increased 28-fold between 1996 and 2013 (from 0.024 to 0.680 DDD/1000 population/day; Table 1). The most commonly prescribed medicine from 2001 was interferon β1A with a peak utilisation of 0.359 DDD/1000 population/day in 2010 (Fig. 1). Glatiramer acetate use reached 0.085 DDD/1000 population/day in 2010 and had about 15% share of the market in the last few years (Table 1). Interferon β1A use, as a proportion of all RRMS DMM use, decreased from about two thirds in 2003 to less than half in 2013 (Table 1). Natalizumab use has increased to 12% and fingolimod has increased to 21% of RRMS DMM use in 2013. There was a relative plateau in overall RRMS DMM use between 2005 and 2007, but use increased in 2009 and subsequently – the increase being largely accounted for by growth in use of fingolimod and natalizumab (Fig. 1).

3.2. Utilisation use by state or territory

The total Australian RRMS DMM use was 0.592 DDD/1000 population/day in 2013 (Fig. 2). Tasmania had the highest utilisation with 0.845 DDD/1000 population/day in 2013 and the Northern Territory (NT) the lowest with 0.105 DDD/1000 population/day, about one eighth that of the Australian Capital Territory (ACT). In all jurisdictions, interferon β1A was the most used RRMS DMM. Interferon β1B use was low and fairly consistent across most states and territories, with higher use in Tasmania. Although there was increasing use along a general north– south gradient of states, there was a major exception in that its use in the ACT (0.733 DDD/1000 population/day) was greater than in the geographically surrounding state of New South Wales (NSW; 0.532 DDD/1000 population/day). The population in the ACT is about 5% of NSW. The use of fingolimod, relative to the other medicines, was low in the NT, Queensland and Tasmania.

3.3. Utilisation use with time in different administrative areas

The introduction of each new RRMS DMM to the PBS was associated with changes in the proportion of overall use for which each agent was responsible, both nationally and in the individual states and territories. The proportions for each medicine in each administrative area for the years 2001 (before glatiramer acetate became available), 2007 and 2013 are shown in Table 2. Overall in Australia and in each administrative area, as glatiramer acetate, natalizumab and fingolimod use grew, the use of β-interferons showed a relative decline (especially after 2006). In the areas where interferon β1A initial use was higher, use declined to a fairly consistent figure of around 40–50% of overall use. Interferon β1B use declined progressively in all states and territories as use of the other medicines grew, with the decrease being greatest in the NT (from 74% to 35%). The ratio of interferon β1B to interferon β1A use was below unity in 2007 and 2013 (except for 347% in the NT in 2013, Table 3). The wide variation in ratios in the NT likely reflects the very small number of patients. In 2013 the ratio of use ranged from 49% in Tasmania to 13% in the ACT.

4. Discussion

Over the period between 1996 and 1999, when interferon β1B was the only RRMS DMM available in Australia, its use in the whole country increased more than 4-fold. This growth may have mainly been a result of prescribers becoming increasingly familiar with the idea of a new type of therapy being available, and people with