Management of Diabetic Macular Edema in the UK National Health Service

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In recent years, diabetes mellitus has become a global health problem. In the United Kingdom the number of patients diagnosed with diabetes exceeded 3 million for the first time in 2014; this is equivalent to 4.6% of the UK population, mainly due to the increase in prevalence of type 2 diabetes.[1] In the United Kingdom, only a small proportion of patients have private health care insurance, and about 90% of the population relies on the National Health Service (NHS).[2] The NHS is funded by general taxation, so the increase in the number of diabetic persons will inevitably cause a huge financial burden not only on the health system but also on the public sector as a whole, including social services. It is estimated that 10% of the entire NHS budget is spent on the care of people with diabetes, and of this 80% is spent on consequences and complications of the disease.[1] This has grave consequences not only for patients themselves but for their families and livelihoods, as diabetic retinopathy is the main cause of blindness in the United Kingdom in people of working age.[3]

In the past decade in the United Kingdom, there has been a significant leap forward in the prevention of severe vision loss in diabetic retinopathy and maculopathy through the implementation of a national diabetic retinopathy screening program, which has resulted in early detection of disease complications.[4] Although devolved separately to the 4 constituent parts of the United Kingdom, namely England, Wales, Scotland, and Northern Ireland, the screening program largely functions as a United Kingdom-wide scheme.

The UK National Ophthalmology Database Study[5] has estimated that clinically significant macular edema (CSME) is present in 13.9% of patients having structured assessments who have been referred to eye departments, with 7.4% having center-involved diabetic macular edema (DME). The proportion of patients with diabetes who had structured assessment recorded increased from 50.7% in 2007 to 86.8% in 2010.

Laser photocoagulation was the cornerstone of treatment in DME for decades; however, center-involved DME was difficult to treat with this modality, and analysis of UK national audit data[6] shows that poorer visual outcome is related to worse visual acuity at baseline, diffuse (vs focal) maculopathy, and grid treatment. As a result, there is a significant number of patients losing their vision.

INTRAVITREAL INJECTIONS FOR DIABETIC MACULAR EDEMA

The first intravitreal drug widely used for center-involved DME in the United Kingdom was triamcinolone acetonide (IVTA; Kenalog, Bristol-Myers Squibb). Triamcinolone acetonide improves vision through drying up central macula. Due to a high incidence of complications[7] including cataract, glaucoma, and uveitis, it is difficult to justify as a treatment in the era of anti-VEGF therapies. Nevertheless, in the absence of alternative options, it has remained in use in a number of ophthalmology departments.

Intravitreal bevacizumab (Avastin, Genentech) has also been in widespread use for DME, and its use has increased following the publication of the BOLT study, which provided good evidence to support the use of bevacizumab in patients with center-involved DME.[8] In the United Kingdom, however, the use of bevacizumab in the NHS has been inconsistent, with many hospital commissioning groups concerned about using this drug in an off-label capacity for the treatment of age-related macular degeneration (AMD) and DME. This was further accentuated in 2012 when a cluster of primary care trusts discontinued the policy of funding for bevacizumab as an alternative treatment to ranibizumab

(Lucentis, Genentech) for wet AMD after Novartis, (which markets ranibizumab in the United Kingdom and Europe) successfully sought a judicial review of the policy.[9]

The National Institute of Health and Clinical Excellence (NICE) approved the use of ranibizumab for the treatment of DME on February 2013 for patients in England and Wales.[10] Prior to this approval, there was great regional variation in the availability of anti-VEGF therapy for patients with DME, a familiar problem for ophthalmologists striving to deliver the best care for their patients in the UK NHS, and described by many as a lottery.[11]

The NICE appraisal concluded that ranibizumab is most cost-effective in patients with central macular edema of 400-µm thickness or more when there are signs of vision loss. As a result, clinical commissioning groups and the local health authorities are required to comply with the recommendation in the final guidance within 3 months of its publication, and all NHS patients will be able to access this treatment free at the point of delivery.[10] Clinical commissioning groups have legal obligations to fund NICE-approved technology through secondary health care in hospitals and eye departments, and, although NICE takes into consideration the cost-effectiveness of health technology before approving it, controversy remains as to how NICE-approved treatments can be funded in an era of fiscal constraint.[12]

Guidance issued by the Royal College of Ophthalmologists for the treatment of DME[13] advises consideration of anti-VEGF therapy including ranibizumab and bevacizumab if there is center-involved macular edema (central macular thickness [CMT] ≥250 µm and visual acuity in the region of 6/10 to 6/90.) However, with this major advance in treatment options for NHS patients with DME, there is a major capacity issue looming for the NHS as to how it tackles the increasing burden of delivering these intravitreal therapies for DME and AMD, and this remains a concern.

SUSTAINED DELIVERY OPTION FOR DIABETIC MACULAR EDEMA

In November 2013, NICE approved the use of the fluocinolone acetonide intravitreal implant (Iluvien, Alimera Sciences) in pseudophakic eyes of patients with chronic DME for more than 36 months who have not benefited from other treatment modalities. This clears the pathway for patients to access this technology and gives more hope to those who did not respond to other treatments, including anti-VEGF injections. Although the implant provides a substantial benefit in chronic DME for at least 2 years, eye departments will still need to follow these patients for side effects including high intraocular pressure and glaucoma. Up to 3.7% of these patients will need incisional glaucoma surgery.[14] NICE will also in the future appraise aflibercept for use in DME.

SUMMARY

The NICE approvals of ranibizumab and the fluocinolone implant are significant milestones for NHS patients with DME, both acute and chronic. Although in the case of DME therapy the NICE approval process has been protracted and frustrating for patients and ophthalmologists alike, it remains an admirable means of introducing new, cost-effective therapies to the population of England and Wales, which are free to patients at the point of delivery but paid for by general taxation. How the NHS copes with the increasing demands to fund new therapies in ophthalmology and other specialties, however, remains to be seen. ■

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