Patient satisfaction following a switch from treat-and-extend to observe-and-plan regimen in age-related macular degeneration

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ABSTRACT

Objective Standard treatment of neovascular age-related macular degeneration (nAMD) is intravitreal injections (IVI) of antivascular endothelial growth factor (anti-VEGF) according to treat-and-extend (TnE). Observe-and-plan (OnP), a new regimen based on each individual’s relapse interval lead to fewer clinical visits and has so far shown to be safe in treatment-naïve patients. In this study, we explore patient satisfaction and safety in nAMD when switching from TnE to OnP.

Methods and analysis 38 participants treated according to TnE for ≥12 months were included and switched from TnE to OnP with their last stable interval. Main outcome was patient satisfaction (Leeds Satisfaction Questionnaire). Secondary outcomes were best-corrected visual acuity (BCVA), central retinal thickness (CRT) before and 12 months after switch and number of monitoring visits and injections of anti-VEGF 12 months prior to and following switch.

Results Mean patient satisfaction was higher (3.7±0.5 SD) at 12 months after switch from TnE to OnP than before (3.6±0.5 SD, p=0.009, response rate 76%). BCVA and CRT were unchanged. Number of monitoring visits and injections were lower in the 12 months following switch (p<0.001).

Conclusion A switch to OnP leads to fewer clinical visits and injections of anti-VEGF up to 12 months following switch. Patient satisfaction, while maintaining stable BCVA. This indicates that OnP may be applicable on the large group of nAMD patients who have received IVI for several years. OnP may alleviate the treatment burden on both individual and society of frequent clinical visits while increasing patient satisfaction.

INTRODUCTION

Current standard treatment of neovascular age-related macular degeneration (nAMD) is intravitreal injections (IVIs) of antivascular endothelial growth factor (anti-VEGF) according to treat-and-extend (TnE) protocol. Following 3 monthly doses of anti-VEGF TnE elongates treatment interval as the patient remains in a stable phase of the disease. The interval is subsequently augmented in 2-week increments up to 12 weeks interval. This protocol requires one clinical visit to an eye doctor per injection, leading to approximately eight visits/year in the first year of treatment. Observe-and-plan (OnP) is a protocol where the 3 monthly IVIs are followed by an observation phase where patients are controlled every month until disease relapse. The regimen is based on findings that propose the individual need for retreatment is stable over time. Treatment interval is determined by the number of weeks from loading dose until relapse minus 2 weeks and the patient then receives treatment three times prior to a new clinical visit. It is conceivable that such a treatment plan represent an improvement for the patient because of less demand for clinical visits and a treatment plan that is predictable beyond their next appointment. However, patient-related outcome measures such as satisfaction in patients switching from TnE to OnP has not earlier been described. In treatment-naïve patients OnP protocol reduces clinical visits and injections and may alleviate the treatment burden on both individual and society from frequent clinical visits while increasing patient satisfaction.

Key messages

What is already known about this subject?

► Observe-and-plan (OnP) leads to fewer clinical visits than treat-and-extend (TnE) regimen in antivascular endothelial growth factor treatment of neovascular age-related macular degeneration (AMD) in treatment-naïve patients.

What are the new findings?

► This study adds that switching from TnE to OnP in a non-treatment-naïve population result in higher patient satisfaction, while maintaining stable best-corrected visual acuity.

How might these results change the focus of research or clinical practice?

► These results indicate that switching to OnP in the large population of patients that are in treatment for neovascular AMD is feasible and safe for patients.
visits in the first 2 years following treatment by a half while number of IVI and best-corrected visual acuity (BCVA) is unchanged compared with TnE.\textsuperscript{3,6} OnP, therefore, may reduce the clinical burden while maintaining patient safety in treatment-naïve nAMD patients. Furthermore, the application of OnP in a Nordic healthcare setting has not earlier been described. We hypothesised that OnP would lead to increased patient satisfaction, fewer clinical visits and comparable clinical outcomes in a population of nAMD patients that have been receiving IVI ≥12 months.

**MATERIALS AND METHODS**

To investigate this, we recruited participants with nAMD from the Department of Ophthalmology, St.Olav hospital, Trondheim University Hospital, Norway to perform a switch in treatment protocol from TnE to OnP. The study took place between 2 January 2017 and 31 May 2018. The participants were consecutively included from January to May 2017 and followed for a year in a prospective study. Data from previous years were collected retrospectively from patient medical records. The Norwegian national health insurance scheme has near-universal coverage of the population, and this tertiary clinic covers the population in Sør-Trøndelag County in Central Norway; about 300 000 inhabitants. The inclusion criteria were having received IVI of anti-VEGF for ≥12 months (±4 weeks) prior to switch. Exclusion criteria were non-ability to give an informed consent. At time point 1, patients switched TnE to OnP protocol and were followed prospectively with their last stable interval between IVI (figure 1). According to the OnP strategy, treatment was given with three injections with the same interval they had before the switch. If their interval was 10, 12 or 16 weeks, they received two injections before new evaluations to avoid a too long period between clinical visits. They were then evaluated by a physician to determine if their macula was dry or wet on a clinical visit. The patients who presented with a relapse of intraretinal or subretinal fluid had their interval shortened by 2 weeks.

Patient-related outcome measures was measured with the Leeds Satisfaction Questionnaire (LSQ).\textsuperscript{7} The LSQ was sent to participants via regular mail to fill out in their home and return in an enclosed prepaid envelope prior to time points 1 and 2. Mean overall patient satisfaction score (from 1 to 5) averaged from six subgroups (A–F); (A) general satisfaction, (B) Provision of information, (C) empathy towards the patient, (D) technical quality and competence, (E) attitude towards the patient and (F) access and continuity. Scores >3 represent satisfaction, while <3 represent dissatisfaction. The LSQ has been translated and validated for a Norwegian population.\textsuperscript{8} Some of the questions were rephrased to fit an ophthalmological setting. Number of visits and IVI during 12 months (±4 weeks) prior to and following switch were obtained from patient medical records. BCVA was measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart\textsuperscript{9} at inclusion (time point 1) and at 12 months (time point 2) using an ETDRS-chart at 2 m distance by the same examiner. The central retinal thickness (CRT) was automatically generated by a Cirrus HD-OCT (High definition - Optical Coherence Tomography; Carl Zeiss Meditec AG, Jena, Germany).

**Patient involvement**

Patients were involved in the design and conduct of our research. A group of 10 patients with nAMD were asked to evaluate the questionnaire (online supplemental attachment 1). In general, they thought that the questions were relevant for their situation and did not have much to add.

**Statistical analyses**

Data are presented as mean±SD. Statistical analyses were performed using student’s paired t-test for normally distributed datasets. A p<0.05 was chosen as level of significance. With an estimated SD of 0.67 and a minimal clinical important difference of LSQ of 0.5, a minimum of 28 patients in each group would be needed to detect an improvement of 0.5 on LSQ with 80% power (type II error) at the 5% significance level (type I error).\textsuperscript{8}

**RESULTS**

The study enrolled 38 participants and 38 eyes (all caucasian, 23 women and 15 men). The mean age was 81.2±7.4 years. Prior to protocol switch participants had been treated according to TnE for a mean amount of 3.5±2.0 years. The average treatment interval on study inclusion was 7.34 weeks±3.95. The average treatment interval after 1-year follow-up was 7.34±4.23. We had two patients on 16-week interval, six patients on 12-week interval, one patient on 10-week interval, eight patients on 8-week interval, eight patients on 6-week interval, one patient on 5-week interval and 12 patients on 4-week interval.

Twenty-nine participants (76%) answered the LSQ at both time point 1 and 2. The CRT and BCVA were obtained from all participants at both time points. Number of clinical visits and IVI in both year 1 and year 2 were obtained from 35 participants because 3 participants terminated treatment with anti-VEGF during year 2. Participants received either bevacizumab (n=12), ranibizumab (n=1) or aflibercept (n=25). In our study, only one of the patients switched drug during the follow-up time of 1 year. Overall patient satisfaction improved following switch from TnE to OnP protocol (p=0.009, table 1). There was no change in CRT or BCVA between time points 1 and 2 (table 2). The number of IVI was lower in year 2 (7.8±3.2) than in year 1 (9.1±2.8),
A concern in OnP is the possibility of late recurrence following the long initial observation period. Giannious et al reported two such late recurrence during a 2-year observation period of 112 eyes, while Parvin et al reported no study-regimen related complications during their 2-year observation of 112 eyes following an OnP regimen. In this study design, an initial observation period is not applied since the switch was performed using the participants last stable interval. A randomised controlled trial is needed to answer whether there is an increased risk of late recurrence in OnP compared with TnE.

**CONCLUSION**

This study shows that a switch from TnE to OnP regimen results in higher patient satisfaction, with stable functional results. This implies that OnP is applicable not only in treatment-naïve patients, but also in the large group of patients that have received IVI for years. OnP may alleviate the burden on both individual and society of frequent clinical visits while increasing patient satisfaction.
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