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ORIGINAL ARTICLE

Ocular manifestations of Crohn's disease☆

Ressenti des patients lors d'injections intra vitréennes

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Summary Intravitreal anti-vascular epithelial growth factor (anti-VEGF) injections have revolutionised the treatment of macular diseases, but can be stressful for the patient. We surveyed 904 patients receiving injections at 5 centres in France regarding their feelings toward anti-VEGF injections. The mean age was 77.4 years, and the injections were performed mostly for age related macular degeneration (72%). Half of the patients had previously received > 10 injections, 35.6% had received 3—10 injections, and 14.2% had received < 3 injections. The mean (SD) stress score was 4.2 [on a scale from 1—10 (0 = least stressful, 10 = extremely stressful)]. Most patients (70%) reported low to moderate stress (score ≤ 5). The number of previous injections did not influence stress scores. Paradoxically, 61.2% of patients reported finding injections to be less stressful over time. Most patients found injections to be less traumatic than expected (64%) or just as they had anticipated (25%). Most patients (88%) were not bothered by the presence of other patients in the waiting room. Most patients (78.8%) preferred to be injected quickly before they had time to feel stressed about the procedure. Injections were generally well accepted; most patients would prefer to maintain their current schedule of injections and their current vision (55.7%), or would be willing to have more frequent injections for

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better vision (39.5%). Our results suggest that stress appears to be more related to the patient's psychological make-up than to the treatment experience or the number of injections received.

MOTS CLÉS
Injections intra vitréennes ;
Anti-VEGF ;
Patient ;
Stress ;
Anxiété ;
DMLA

Résumé Les injections intra-vitréennes (IVT) ont révolutionné la prise en charge en ophtalmologie, mais peuvent être stressantes. Nous avons interrogé 904 patients bénéficiant d'IVT dans 5 centres pour évaluer leur ressenti. L'âge moyen était de 77,4 ans et le motif déclaré de l'IVT était la dégénérescence maculaire liée à l'âge dans 72% des cas. La moitié des patients avaient déjà reçu plus de 10 IVT, 35,6% avaient reçu 3 à 10 IVT et 14,2% avaient reçu moins de 3 IVT. Le niveau de stress était côté en moyenne à 4,2 sur une échelle de 1 à 10 (0 = le moins stressant, 10 = extrêmement stressant). La plupart des patients (70%) présentaient un stress faible à modéré (score $\leq$ 5). Le nombre d'IVT précédentes n'influençait pas le score de stress. Paradoxalement, 61,2% des patients ont déclaré avoir trouvé des IVT moins stressantes au fil du temps. La plupart des patients ont trouvé les IVT moins traumatisantes (64%) ou comme ils les avaient imaginées (25%). La majorité des patients (88%) n'étaient pas gênés par la présence d'autres patients dans la salle d'attente. Généralement, 78,8% des patients souhaitaient que la procédure d'injection aille vite. Les IVT étaient généralement bien acceptées. Plus de la moitié des patients (55,7%) étaient prêts à conserver leur rythme actuel d'IVT pour maintenir leur vision et près de 40% étaient prêts à recevoir davantage d'IVT pour améliorer leur vision. Les résultats suggèrent que le niveau de stress est davantage lié au profil psychologique du patient qu'à l'expérience acquise du traitement ou au nombre d'IVT reçues.

Introduction

Treatment with anti-vascular epithelial growth factor (anti-VEGF) revolutionised treatment of macular diseases [1—5]. By slowing disease progression, anti-VEGF significantly reduces the risk of severe visual impairment in patients with retinal pathologies such as age-related macular degeneration (AMD), diabetic macular oedema (DME) and retinal vein occlusion (RVO) [6—9].

Anti-VEGF therapy is delivered by intravitreal injection (IVI) and can require frequent and repeated visits to specialised centres to maintain visual results [10—13]. The treatment regimen usually begins with a ''loading phase'' of one injection per month for 3 months, followed by a fix regimen injection [14], a regular Pro Renata (PRN) [15] or Treat and Extend (T&E) [16] schedule.

In the case of an individualised treatment regimen, visual acuity and anatomic outcomes are assessed, then anti-VEGF treatment is administered according to the activity of the disease [15—17].

Adherence to treatment is crucial for maintaining visual acuity as long as possible; however, a 5-year retrospective chart review found that 57% of patients were lost to follow-up. Patients discontinued treatment mostly due to the long distance from home (51.7%), dissatisfaction with treatment (34.5%) and the burden of regular clinic visits (24.1%) [18].

IVI clinics can be very busy with large numbers of patients in the clinic waiting room. Injections are usually performed in a dedicated treatment room, after instillation of local anaesthesia, peri-orbital skin cleansing, ocular surface sterilisation, orbital draping and insertion of a sterile eyelid speculum [19].

Anti-VEGF injections can be a stressful event for patients, generating anticipatory anxiety, apprehension of pain and discomfort [13,20—27]. The impact of repeated injections on the well-being and mental health of patients should be considered to optimise quality of life and treatment compliance. However, few studies have explored the complexity and diversity of patient experiences with anti-VEGF therapy and their perception of the IVI procedure. Optimising the patient experience during injections is important for adherence [20] and maintaining quality of life for patients. It is therefore crucial to better understand how patients experience these treatments and how they manage the anxieties associated with treatment.

This survey aimed to evaluate patient stress and perceptions of IVI and its organisation to describe the factors that explain patients' feelings and to identify ways to improve IVI delivery.

Methodology

This non-interventional study surveyed patients with macular disease regarding their feelings and perspectives about anti-VEGF injections. We performed this survey on anonymous data. According to French legislation in 2016, anonymous surveys, such as the present survey, do not need to be approved by an ethic committee, and analysis of these anonymous data for research purpose is allowed [French Law

on Privacy: National commission of information technology and liberty (CNIL) Decision No. 89—117].

Patients gave their non-opposition, and the study was carried out according to the declaration of Helsinki.

Questionnaire

An anonymous questionnaire comprising of 11 questions was constructed by the authors (see Supplementary information). Preliminary questions concerned demographics and medical history. Patients were then asked how stressful they found IVI treatments on a scale from 0 to 10 (with 10 being extremely stressful) and how the level of stress changed with number of injections. Other questions concerned the logistics of the clinic visit and treatment, and patient preferences for treatment.

Participating centres and patients

Five centres distributed around France participated in the study (Paris, Bordeaux, Nice, Strasbourg, Montauban). Questionnaires were distributed in the waiting room to all patients waiting for an anti-VEGF IVI for macular disease.

Each ophthalmologist had a 3-week window to consecutively recruit an unlimited number of eligible patients during routine clinic visits for IVI. Since patients are generally not treated with anti-VEGF more frequently than once monthly, the 3-week recruitment window captured most of the eligible population per clinic. It was checked that participating patients were not due to re-attend the clinic within 3 weeks for contralateral IVI. Patients who agreed to participate were provided with the questionnaire and a prepaid addressed envelope before the injection. Patients could either complete the questionnaire before the injections in the clinic and return the questionnaire directly to the team, or they could complete the questionnaire at their leisure and return the questionnaire by post using the prepaid envelope.

Data analysis

Data were analysed using SAS 9.4. Descriptive statistics were provided for quantitative and qualitative variables.

Results

Participants

Altogether, 5 centres and 15 ophthalmologists participated in the study between November 2016 and November 2017; 904 patients completed questionnaires. Most questionnaires (830) were returned directly to the care team and 74 were returned by post.

The mean age of respondents was 77.4 years and ranged from 30 to 98 years. Just over half of respondents (57%) were female. The most common indication for IVI treatment was AMD (72%), followed by RVO (9%) and DME (8.5%). Of note, 8.8% of patients did not know why they were receiving an IVI treatment.

Table 1 Demographics and medical history.

	Total $n = 904$
Age	822
n (available data)	77.4 (10.0)
Mean (SD)	30/98
Min/Max	
Sex	894
n	384 (43.0%)
Male	510 (57.0%)
Female	
Reason for injection	878
n (available data)	632 (72.0%)
AMD	75 (8.5%)
Diabetes	79 (9.0%)
Retinal vein occlusion	77 (8.8%)
I don't know or I'm not sure	10 (1.1%)
AMD and diabetes	2 (0.2%)
Retinal vein occlusion and diabetes	3 (0.3%)
AMD and Retinal vein occlusion	
Total number of injections (approx.)	892
n (available data)	50 (5.6%)
1	77 (8.6%)
< 3	199 (22.3%)
3 to 6	119 (13.3%)
6 to 10	166 (18.6%)
10 to 20	
> 20	281 (31.5%)

AMD = age related macular degeneration.

At the time of the questionnaire, 50.1% of patients had received over 10 injections, 35.6% had received 3—10 injections and 14.2% had received fewer than 3 injections (Table 1).

Travel to clinic

Just over half of the patients reported living in an urban setting (54.9%), compared to a rural setting. Travel time between home and injection clinic was less than 30 minutes for 37.2% of patients, 30 minutes to 1 hour for 42.5% of patients and more than one hour for 29.8% of the patients. Patients most commonly travelled to the clinic with family or friends (50.6%), followed by public transport (21.6%), taxis and ambulance (19.5%), and least frequently by driving themselves (7.7%).

As treatment continues over time, a trend emerged with patients travelling to the clinic more frequently via public transport, taxi or ambulance, and without a companion.

Stress

The mean (SD) level of stress indicated by patients was 4.2 (3.2) on the scale ranging from 0 (least stressful) to 10 (extremely stressful) (Table 2). A stress score of 5 or lower was reported by 69.8% of patients. The top score of 10 (extreme stress) was reported by 8% of the patients. Overall, most patients found the IVI treatments less traumatic

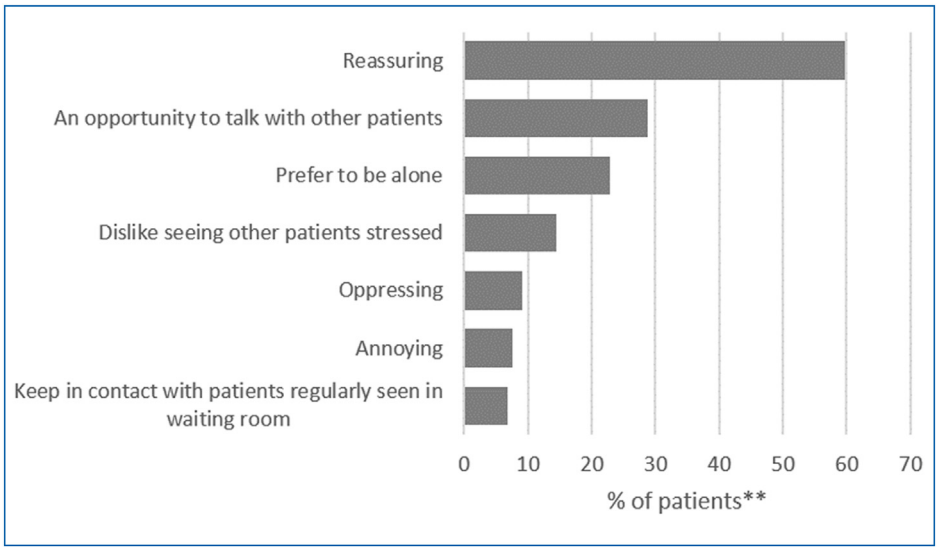

Figure 1. Patient perceptions of sharing waiting room with other patients waiting for anti-VEGF injections*. *Question in survey = On the day of the injections, there are often many other patients also waiting for injections in the waiting room. You find this: (more than one response can be selected). **Note: 41.0% of patients selected more than one response.

Table 2 Stress.

	Total $n = 904$
Stress score regarding anti-VEGF injections	821
n (available data)	4.2 (3.2)
Mean (SD)	5.0
Median	2.0/6.0
Q1/Q3	0/10
Min/Max	821
Stress score regarding anti-VEGF injections	
0	167 (20.3%)
1—4	236 (28.7%)
5	171 (20.8%)
6—9	176 (21.4%)
10	71 (8.6%)

(64%) or just as (25%) they had anticipated. Only 11% found the IVI worse than they had imagined. Ophthalmology clinic waiting rooms are often busy, and we wanted to know if the presence of other patients waiting for IVI added to stress levels. The majority of patients found it reassuring to see other patients in the waiting room (60%) and 28% found it a good opportunity to ask questions of other patients. However, nearly a quarter of the patients would prefer to be alone in the waiting room (22%), find the presence of other patients oppressing (9%) or annoying (7%), or dislike seeing the stress of other patients (14.5%) (Fig. 1). Patient attitudes towards the presence of others in the waiting room did not vary notably, based on the number of injections received.

The mean stress score did not vary notably based on the number of previous injections (Fig. 2). Paradoxically, when asked if stress levels changed as treatment continued, 61.2% of patients indicated that they found the procedures less stressful as time went by as they were less surprised (by the unknown), and 32.3% of patients reported no change in their stress levels. Only 6.5% of the patients reported that stress increased along with number of injections.

Treatment preference and acceptability

As an indicator of acceptability of anti-VEGF injections, we asked patients if they would recommend the treatment to a close friend of relative with the same ocular disease. Most patients (87%) agreed that they would recommend starting injections quickly, and 13% had no opinion.

Most patients would prefer to keep their current schedule of injections and their current vision (55.7%), or even more injections for better vision (39.5%). Only 5% of patients would prefer fewer injections, with a corresponding drop in vision.

Most patients (78.8%) prefer that IVI is performed quickly, before they have time to be stressed about the procedure. The remaining 21.2% prefer that the procedure is slower, giving them time to relax. Patient preferences for the rapidity of the injection procedure did not vary notably according to the number of previous injections.

Discussion

The beneficial effects of anti-VEGF IVI in the management of macular pathologies are widely documented. These can only be obtained if patients are willing to accept regular and repeated visits and injections. The fear of injection is described as a common reason for interrupting treatment [20,28]. To our knowledge, this is the largest study to date to assess patient perceptions of IVI.

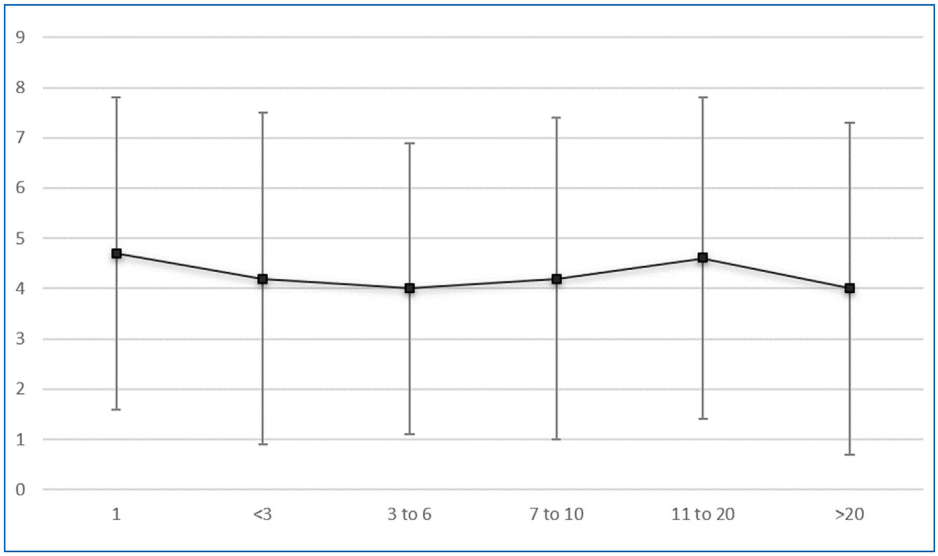

Figure 2. Stress according to number of injections received.

Acceptability

Our data reveal good acceptability for IVI: over 50% of patients were willing to maintain their injection rate to maintain vision and nearly 40% were willing to receive more injections to improve their vision. In addition, most patients (87%) said they would recommend anti-VEGF therapy to their loved ones if it were indicated. These results support previous studies showing that 68% of AMD patients would continue injections even if their vision deteriorated [26] and 93.7% of AMD patients would undergo treatment again if they had to choose again [28].

Stress

Previous studies showed that IVI treatment can be a frightening prospect [20,28]. In our study, nearly 70% of the patients reported relatively low stress with scores between 0 and 5. A stress score between 6 and 10 was reported by 30% of the patients, supporting a recent observational study conducted in Israel [25], where 25% of the participants reported high levels of anxiety (score $\geq$ 6 on a visual analogue scale from 0 to 10). We found strong variation between the levels of stress experienced by patients. Twenty percent of the patients reported feeling ''not stressed at all'' while 8% reported ''extreme'' stress levels.

The majority of the patients in our study describe the injections as a less stressful or unpleasant experience than they had imagined (64%) and only 11% of patients found the injections more unpleasant than anticipated. These results are consistent with the study by Chua et al., who found that 51% of the patients reported that IVI was more comfortable than they had expected, and 34% found it just as uncomfortable as anticipated [22].

Fear or anxiety about injections can be based in fear of the unknown [27], and some studies have shown a marked decrease in fear up to 93% after the first injection [22]. Indeed, 61.2% of patients in our study said that stress decreased over time. However, we paradoxically did not observe a change in stress according to the number of IVIs received (Fig. 2), in line with observations from Senra [29] and Droege [28], who found no correlation between number of IVIs and anxiety. Of note, our assessment of the influence of number of injections on stress relies on retrospective self-evaluation by patients, which may be subjective and prone to recall bias. The influence of the number of injections on the stress score would be better evaluated by an objective longitudinal follow-up of the patient during treatment. This could also be because most patients were already used to IVI treatment (only 5% were receiving IVI for the first time). It has previously been reported that stress and anxiety are elevated from the earliest injections [28]. The fact that we did not observe increased stress with more injections may be because there were few patients at the beginning of their treatment regimen, and most patients were used to the injections.

Factors influencing stress

The IVI patient experience could be improved by taking into account patients' expectations and preferences regarding the injection procedure. For example, most patients preferred an injection to be administered quickly. This supports the findings of previous studies by a qualitative interview-based study by Thetford et al. who reported that improving ''service delivery'' could improve the patient experience [27].

Given that most IVI clinics are busy with numerous other patients present in the waiting room, we asked how patients felt about this. Most patients had positive or neutral opinions. A minority found the presence of other patients oppressing (9%) or annoying (7%), or disliked seeing the stress of other patients (14.5%). Tailor et al. also reported that waiting for injection is a significantly uncomfortable step in the treatment procedure [30]. Reducing waiting times could reduce anxiety for some patients, especially for the first few injections [27].

Our results suggested that the level of stress is more related to the patient's psychological profile than to the

experience of the treatment. A stressed patient will likely remain stressed throughout his treatment, despite the best efforts of the care team. Ophthalmologists should consider taking into account the psychological profile of patients when organising clinic visits for IVI. Stress can be minimised by fully understanding the reasons for the patient's anxiety and by personalising their care according to their worries and expectations, by limiting the waiting time for injections, for example.

Logistics

We included two questions about travelling to the IVI clinic. Previous studies have shown that transport can be a barrier to attending clinic [28], compliance increased with shorter distance between patients' home and the IVI clinic [20], and a long distance from home was significantly correlated with treatment discontinuation ($P < 0.001$) [18]. In our study, 72.3% of patients had to travel more than 30 minutes to attend clinic and most commonly travelled to the clinic with family or friends, public transport, taxi or ambulance.

Limitations

Our study had several limitations. Although it was a large study, the questionnaire has not been validated as a tool to measure stress. A validated tool, such as the Hospital Anxiety and Depression scale [31], could yield more robust results. A follow-up study with the collaboration of psychologists and patient organisations would allow us to gather more robust data, based on these preliminary findings. It would also be interesting to assess whether stress levels change during treatment, on an individual by-patient basis.

Conclusion

These data are reassuring, given the importance of compliance with a regular injection schedule to maintain visual acuity. The mean (SD) level of stress indicated by patients was 4.2 (3.2) on the scale ranging from 0 (least stressful) to 10 (extremely stressful). IVIs appear, in the majority of cases, to be less traumatic than what the patients expected. Our results suggest that stress is more related to the patient's psychological profile than to the treatment experience, and that a stressed patient appears to remain stressed. Compliance and quality of life can be improved for these patients by personalising the injection procedure to the patient, taking into account their preferences regarding speed of procedure and the presence of other patients in the waiting room.

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Disclosure of interest

Dr Vincent Gualino has interests with Alcon, Allergan, Bayer, and Novartis; Dr Eric Fourmaux, with Allergan, Bayer, and Novartis; Dr BenjaminWolff, with Allergan, Bayer, and Novartis; Dr Typhaine Grenet, with Novartis; and Dr Jennyfer Zerbib with Novartis and Bayer.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jfo.2020.02.006.

References

[1] Rosenfeld PJ, Brown DM, Heier JS, et al. Ranibizumab for neovascular age-related macular degeneration. N Engl J Med 2006;355:1419—31, http://dx.doi.org/10.1056/NEJMoa054481 [First published online: 2006/10/06].

[2] Nguyen QD, Brown DM, Marcus DM, et al. Ranibizumab for diabetic macular edema: results from 2 phase III randomised trials: RISE and RIDE. Ophthalmology 2012;119:789—801, http://dx.doi.org/10.1016/j.ophtha.2011.12.039 [First published online: 2012/02/15].

[3] Brown DM, Campochiaro PA, Bhisitkul RB, et al. Sustained benefits from ranibizumab for macular edema following branch retinal vein occlusion: 12-month outcomes of a phase III study. Ophthalmology 2011;118:1594—602, http://dx.doi.org/10.1016/j.ophtha.2011.02.022.

[4] Campochiaro PA, Brown DM, Awh CC, et al. Sustained benefits from ranibizumab for macular edema following central retinal vein occlusion: twelve-month outcomes of a phase III study. Ophthalmology 2011;118:2041—9, http://dx.doi.org/10.1016/j.ophtha.2011.02.038 [First published online: 2011/06/29].

[5] Wolf S, Balciuniene VJ, Laganovska G, et al. RADIANCE: a randomised controlled study of ranibizumab in patients with choroidal neovascularisation secondary to pathologic myopia. Ophthalmology 2014;121:682e2—92e2, http://dx.doi.org/10.1016/j.ophtha.2013.10.023 [First published online: 2013/12/12].

[6] Bloch SB, Larsen M, Munch IC. Incidence of legal blindness from age-related macular degeneration in Denmark: years 2000 to 2010. Am J Ophthalmol 2012;153:209e2—13e2, http://dx.doi.org/10.1016/j.ajo.2011.10.016 [First published online: 2012/01/24].

[7] Skaat A, Chetrit A, Belkin M, et al. Time trends in the incidence and causes of blindness in Israel. Am J Ophthalmol 2012;153:214e1—21e1, http://dx.doi.org/10.1016/j.ajo.2011.08.035 [First published online: 2012/01/24].

[8] Bressler NM, Doan QV, Varma R, et al. Estimated cases of legal blindness and visual impairment avoided using ranibizumab for choroidal neovascularisation: non-Hispanic white population in the United States with age-related macular degeneration. Arch Ophthalmol 2011;129:709—17, http://dx.doi.org/10.1001/archophthalmol.2011.140 [First published online: 2011/06/15].

[9] Varma R, Bressler NM, Doan QV, et al. Visual impairment and blindness avoided with ranibizumab in Hispanic and non-Hispanic Whites with diabetic macular edema in the United States. Ophthalmology 2015;122:982—9,

http://dx.doi.org/10.1016/j.ophtha.2014.12.007 [First published online: 2015/02/12].
[10] Kim LN, Mehta H, Barthelmes D, et al. Meta-analysis of real-world outcomes of intravitreal ranibizumab for the treatment of neovascular age-related macular degeneration. Retina 2016;36:1418—31, http://dx.doi.org/10.1097/iae.0000000000001142 [First published online: 2016/07/09].
[11] Qin VL, Young J, Silva FQ, et al. Outcomes of patients with exudative age-related macular degeneration treated with anti-vascular endothelial growth factor therapy for three or more years: a review of current outcomes. Retina 2018;38:1500—8, http://dx.doi.org/10.1097/iae.0000000000001753 [First published online: 2017/07/04].
[12] Holz FG, Tadayoni R, Beatty S, et al. Determinants of visual acuity outcomes in eyes with neovascular AMD treated with anti-VEGF agents: an instrumental variable analysis of the AURA study. Eye 2016;30:1063—71, http://dx.doi.org/10.1038/eye.2016.90 [First published online: 2016/05/21].
[13] Sivaprasad S, Oyetunde S. Impact of injection therapy on retinal patients with diabetic macular edema or retinal vein occlusion. Clin Ophthalmol 2016;10:939—46, http://dx.doi.org/10.2147/opth.S100168 [First published online: 2016/06/17].
[14] Heier JS, Brown DM, Chong V, et al. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology 2012;119:2537—48, http://dx.doi.org/10.1016/j.ophtha.2012.09.006 [First published online: 2012/10/23].
[15] Ho AC, Busbee BG, Regillo CD, et al. Twenty-four-month efficacy and safety of 0.5 mg or 2.0 mg ranibizumab in patients with subfoveal neovascular age-related macular degeneration. Ophthalmology 2014;121:2181—92, http://dx.doi.org/10.1016/j.ophtha.2014.05.009 [First published online: 2014/07/13].
[16] Silva R, Berta A, Larsen M, et al. Treat-and-extend versus monthly regimen in neovascular age-related macular degeneration: results with ranibizumab from the TREND study. Ophthalmology 2018;125:57—65, http://dx.doi.org/10.1016/j.ophtha.2017.07.014 [First published online: 2017/09/13].
[17] Schmidt-Erfurth U, Chong V, Loewenstein A, et al. Guidelines for the management of neovascular age-related macular degeneration by the European Society of Retina Specialists (EURETINA). Br J Ophthalmol 2014;98:1144—67, http://dx.doi.org/10.1136/bjophthalmol-2014-305702 [First published online: 2014/08/20].
[18] Boulanger-Scemama E, Querques G, About F, et al. Ranibizumab for exudative age-related macular degeneration: a five-year study of adherence to follow-up in a real-life setting. J Fr Ophtalmol 2015;38:620—7, http://dx.doi.org/10.1016/j.jfo.2014.11.015.
[19] AFSSAPS. In: AFSSAPS., editor. Good practices for intravitreal injection. 2011 [https://www.ansm.sante.fr/var/ansm_site/storage/original/application/c19b85aee777e3b339c6646723d319d1.pdf].
[20] Polat O, Inan S, Ozcan S, et al. Factors affecting compliance to intravitreal anti-vascular endothelial growth factor therapy in patients with age-related macular degeneration. Turk J Ophthalmol 2017;47:205—10, http://dx.doi.org/10.4274/tjo.28003 [First published online: 2017/08/29].
[21] Boyle J, Vukicevic M, Koklanis K, et al. Experiences of patients undergoing anti-VEGF treatment for neovascular age-related macular degeneration: a systematic review. Psychol Health Med 2015;20:296—310, http://dx.doi.org/10.1080/13548506.2014.936886 [First published online: 2014/07/19].
[22] Chua PY, Mitrut I, Armbrecht AM, et al. Evaluating patient discomfort, anxiety, and fear before and after ranibizumab intravitreous injection for wet age-related macular degeneration. Arch Ophthalmol 2009;127:939—40, http://dx.doi.org/10.1001/archophthalmol.2009.139 [First published online: 2009/07/15].
[23] Senra H, Ali Z, Balaskas K, et al. Psychological impact of anti-VEGF treatments for wet macular degeneration — a review. Graefes Arch Clin Exp Ophthalmol 2016;254:1873—80, http://dx.doi.org/10.1007/s00417-016-3384-0 [First published online: 2016/06/06].
[24] Boyle J, Vukicevic M, Koklanis K, et al. Experiences of patients undergoing repeated intravitreal anti-vascular endothelial growth factor injections for neovascular age-related macular degeneration. Psychol Health Med 2018;23:127—40, http://dx.doi.org/10.1080/13548506.2016.1274040 [First published online: 2017/01/10].
[25] Segal O, Segal-Trivitz Y, Nemet AY, et al. Anxiety levels and perceived pain intensity during intravitreal injections. Acta Ophthalmol 2016;94:203—4, http://dx.doi.org/10.1111/aos.12802 [First published online: 2015/07/29].
[26] Sii S, Aspinall P, Borooah S, et al. Exploring factors predicting changes in patients' expectations and psychosocial issues during the course of treatment with intravitreal injections for wet age-related macular degeneration. Eye 2018;32:673—8, http://dx.doi.org/10.1038/eye.2017.271 [First published online: 2018/12/09].
[27] Thetford C. Living with age-related macular degeneration treatment: patient experiences of being treated with ranibizumab (Lucentis)(R) intravitreal injections. Br J Vis Impair 2013;31:89—101, http://dx.doi.org/10.1177/0264619613481778.
[28] Droege KM, Muether PS, Hermann MM, et al. Adherence to ranibizumab treatment for neovascular age-related macular degeneration in real life. Graefes Arch Clin Exp Ophthalmol 2013;251:1281—4, http://dx.doi.org/10.1007/s00417-012-2177-3 [First published online: 2012/10/23].
[29] Senra H, Balaskas K, Mahmoodi N, et al. Experience of anti-VEGF treatment and clinical levels of depression and anxiety in patients with wet age-related macular degeneration. Am J Ophthalmol 2017;177:213—24, http://dx.doi.org/10.1016/j.ajo.2017.03.005 [First published online: 2017/03/18].
[30] Tailor R, Beasley R, Yang Y, et al. Evaluation of patients' experiences at different stages of the intravitreal injection procedure — what can be improved? Clin Ophthalmol 2011;5:1499—502, http://dx.doi.org/10.2147/opth.S24358 [First published online: 2011/11/10].
[31] Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361—70 [First published online: 1983/06/01].