

Indication of antibiotic prophylaxis during intravitreal injections

Written by Catherine Creuzot-Garcher with the assistance of Alain Bron, Isabelle Cochereau, Marc Labetoulle, Bahram Bodaghi.

Introduction

Intravitreal (IVT) injections are among the most commonly performed medical procedures in industrialized countries. This procedure has become a routine practice, but the major fear is still the occurrence of an infectious complication. The recent HAS guidelines define the conditions for performing these injections. The asepsis rules, including the use of povidone iodine, are the cornerstone of infection prevention. The place of antibiotic prophylaxis is being discussed.

Literature review

Prevalence of endophthalmitis

Endophthalmitis is the most feared complication after IVT injection. The results of the first comparative studies on the use of anti-VEGF IVT injections in the treatment of AMD report variable values (VISION study (0.16%, 12 cases for 7,545 injections), MARINA study (0.05%, 5 cases for 10,443 injections), ANCHOR study (0.05%, 3 cases for 5,921 injections)) depending on the conditions for performing IVT injections. Subsequently, several studies have reported overall rates of endophthalmitis ranging between 0 and 0.092%. After meta-analysis of more than 100,000 injections, McCannel has found an incidence of endophthalmitis post-IVT injections of 0.049%.⁽¹⁾ These rates are very close to that of another meta-analysis by Fileta including 350,000 injections with a prevalence of 0.056% ⁽²⁾. The values mainly vary depending on the conditions of injection (dedicated room or not, operating room), the use of speculum or not, the instillation of povidone iodine and antibiotic prophylaxis.

Place of antibiotic prophylaxis

Antibiotic prophylaxis is widely used in routine practice, but this is only justified by the systematic use of antibiotic therapy in the pivotal studies that are mentioned in the SPC (Summary of Product Characteristics) of antiangiogenic agents. Currently, only 3 studies have assessed the potential role of antibiotics in the occurrence of endophthalmitis post-IVT

injection: Bhavsar (sole prospective study, 8,027 injections), Bhatt in 2011 (4,767 injections) and Cheung in 2012 (15,895 injections) (3-5). These 3 studies have found no significant difference in the rate of endophthalmitis occurring post-IVT injection with or without antibiotics. A recent multicentric study conducted by the FRCR-net grouping the register of endophthalmitis over 3 years from 316,576 IVT injections administered in 25 French centers found a prevalence of 0.021% (article submitted).

Since the prevalence of endophthalmitis is very low, it is very difficult to demonstrate the superiority of a practice with the necessary power. The European recommendations no longer include the obligation of systematic antibiotic prophylaxis.

Discussion and arguments

Complying with the HAS guidelines on the asepsis rules is the most important element

The HAS guidelines have precisely defined the conditions of injection (6):

- Control of the eye condition before injection to rule out any palpebral or conjunctival infection, a prerequisite for the injection,
- Administration of the IVT injection in a dedicated injection room meeting standards of good practice recommendations. There is no need to perform these IVT injections in the operating room,
- Recommended equipment for the practitioner: surgical mask and sterile gown, charlotte, wear of sterile gloves after surgical hand wash and use of hydroalcoholic solution,
- Assistance in meeting the aseptic conditions. It is recommended for the assistant to wear a mask and a charlotte and to use a hydroalcoholic solution between each patient,
- Installation: sterile table field, sterile compresses, sterile operating field, sterile speculum and scleral marker,
- Aseptic conditions by application of povidone iodine (Betadine® scrub) in the periocular area, on the eyelids and eyelashes, rinsing with sterile water then new application of povidone iodine 10% (dermal Betadine®) and instillation of ophthalmic povidone iodine 5% (ophthalmic Betadine®) with 2 minutes of contact.

Asepsis with povidone iodine is the key undisputable element in infection prophylaxis

The preoperative bactericidal qualities of povidone iodine have been shown for many years in cataract surgery. It should be remembered that no cases of angioedema have been reported to date post Betadine® application and that there is no cross sensitivity to iodized products. During IVT injections, the interest of asepsis with povidone iodine is also indisputable (3).

Antibiotics are probably unnecessary

Preoperative antibiotic prophylaxis could prolong the action observed with povidone iodine but does not influence the rate of surviving conjunctival micro-organisms. The intravitreal penetration is also far below the minimum inhibitory concentrations (MIC) required to achieve a therapeutic effect. Finally, the rationale for prescribing a prolonged instillation of antibiotics to protect a conjunctival injection point made by a 30-32G needle, which is probably closed in a few hours, should be questioned.

Repeated instillations of antibiotics may lead to adverse effects

Long-term antibiotic therapy has demonstrated effects on the selection of resistant micro-organisms. The IVT injection issue is related to both the cumulative number of days of antibiotics in a patient receiving on average 5 injections per year and the passage of these antibiotics into the nasopharyngeal flora. Indeed, systematic antibiotic prophylaxis results in the emergence of resistant strains in the nasopharynx. There is an increasing rate of resistance to fluoroquinolones or azithromycin within the conjunctival flora in the United States. This selection of multiresistant micro-organisms may be problematic in patients with infection if they receive an injection or undergo cataract surgery because it would be more difficult to treat, but also more generally at the bacterial ecology of a whole country. These results should, however, be qualified because *in vitro* and *in vivo* resistances are not always equivalent and should also take into account the pharmacokinetics, pharmacodynamics or concentrations of antibiotics.

If antibiotic prophylaxis is to be used, it should be short and generate little resistance

Since compliance with asepsis rules is applied in IVT injection practice, the legitimacy of an antibiotic prophylaxis is questioned. Several studies point out the lack of interest of antibiotic prophylaxis or even its detrimental effect. The practices of antibiotic prophylaxis in combination with IVT injection widely differ depending on the habits of injecting ophthalmologists (before and/or after injection, single treatment, prolonged treatment of 1, 3 or 5 days, eye drops or ointment). The French study conducted by the FRCR-net has found an increased risk of infections in patients treated with antibiotics or under antiseptic conditions after IVT injection. Due to the retrospective nature of all these studies, any decision should be considered with caution and should not definitively exclude combining antibiotic prophylaxis with IVT injections. However, a prolonged treatment of 3-5 days would lead to the loss of the preventive properties of this antibiotic therapy, thus making it curative which is questionable given the rapid closure of the punctiform incision of IVT injection. However, if it is used by

the injecting ophthalmologist, the choice should certainly move towards prophylaxis only AFTER injection and as a single administration (eye drops or ointment). Instilling an antiseptic immediately after the injection is also a practice that may be recommended.

Conclusions

The changes in European recommendations on antibiotic prophylaxis during IVT injections enable the development of our practices since it is no longer legally required. Systematic antibiotic prophylaxis as part of IVT injections is not necessary and should be reserved for high-risk patients (immunosuppression, fragile conjunctiva). If it is proposed, it should only be prescribed after injection and for a very short time (ideally a single instillation after injection).

References

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