FLOPPY-IRIS SYNDROME ASSOCIATED WITH TAMPSULOSIN. A PROSPECTIVE CASE-CONTROL STUDY

SÍNDROME DE IRIS FLÁCCIDO POR TAMSULOSINA. ESTUDIO PROSPECTIVO FRENTE A GRUPO CONTROL

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ABSTRACT

Objective: The main objectives of this study were: To assess the incidence of the intraoperative floppy-iris syndrome associated with tamsulosin and to analyse the incidence of intraoperative and postoperative complications as compared to a control group. Secondary objectives were: to describe the pupillary modifications associated with tamsulosin and to quantify the endothelial cell loss.

Methods: A prospective review of 38 eyes of 38 patients was performed. Patients were assigned to two different groups. Group 1 (cases) included 19 eyes of 19 male patients taking tamsulosin, and group 2 (controls) included 19 eyes of 19 male patients not taking tamsulosin.

Results: Only two patients (10\%) of our study had the complete triad seen in floppy-iris syndrome; 9 patients (47\%) showed 2 of the 3 main features of the syndrome and only 2 patients showed iris billowing during phacoemulsification. None of the patients in group 2 showed any of the characteristic intraoperative features. The complication rate was similar in both groups.

Conclusions: Intraoperative floppy-iris syndrome occurred in 67\% of the patients treated with tamsu-

RESUMEN

Objetivos: Los objetivos de este estudio son: determinar la incidencia real del síndrome del iris flácido intraoperatorio asociado al tratamiento con tamsulosina y analizar las diferentes tasas de complicaciones tanto intra como postoperatorias frente a un grupo control. Los objetivos secundarios son: describir las alteraciones pupilares asociadas a la toma de tamsulosina y cuantificar la pérdida endotelial de la cirugía de catarata.

Método: Estudio prospectivo que incluye 38 ojos de 38 pacientes divididos en dos grupos. El grupo 1 (casos) compuesto por 19 ojos de 19 pacientes varones en tratamiento con tamsulosina y el grupo 2 (controles) compuesto por 19 ojos de 19 varones sin tratamiento con tamsulosina. En todos los casos, se trata de pacientes consecutivos que acuden a nuestro hospital para ser intervenidos de catarata.

Resultados: La incidencia de iris flácido en nuestra serie se limita a dos pacientes (10\%) que presentaron la tríada completa, 9 pacientes (47\%) presentaron 2 de los 3 signos, y solo dos pacientes (10\%) presentaron bamboleo del iris aislado. Ninguno de los pacientes del grupo control presentó...
losin. The only postoperative secondary effect was a lower pupil reactivity in patients taking tamsulosin (Arch Soc Esp Oftalmol 2007; 82: 349-354).

**Key words:** Floppy-iris syndrome, tamsulosin, cataract, alpha blockers, iris billowing.

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**INTRODUCTION**

Inadequate pupil dilation or intraoperative pupil changes observed may compromise cataract surgery and increase the risk of complications (1). Intraoperative floppy iris syndrome (IFIS) is an intraoperative situation that has been recently described in connection with pupillary modifications observed in patients taking tamsulosin (2).

IFIS is characterized by the presence of three intraoperative signs: floppy iris stroma which billows under regular fluidic conditions, a tendency for the iris to prolapse due to phacoemulsification incisions and duly built paracentesis, and progressive intraoperative pupil contraction, regardless of the usual drug guidelines to achieve mydriasis (2).

It has been found that one of the causestriggering this syndrome is patients taking tamsulosin (2-7), an alpha 2 selection blocker (8) used in the treatment of benign prostate hyperplasia (9-12).

The above mentioned syndrome has been described recently and therefore there is not enough information on its actual prevalence. Chang and Campbell (2) report that prevalence among patients being treated with tamsulosin is 3% for their population of patients who have undergone cataract surgery. These same authors (2) report that the syndrome appears in over 60% of patients being treated with this medication. We still needed to define the length of treatment with tamsulosin necessary to develop the syndrome, as well as the impact of developing IFIS on cataract surgery outcomes.

With this end, we initiated the study with the following objectives: to determine the actual incidence of floppy iris syndrome in patients being treated with tamsulosin and to analyze the incidence of both intraoperative and postoperative complications in two groups of patients with similar characteristics, only different in that one took tamsulosin and the other did not. The secondary objectives were: to describe pupillary modifications associated to taking tamsulosin and to quantify endothelial cell loss due to cataract surgery in these two groups of patients.

**SUBJECTS, MATERIAL AND METHOD**

A prospective study was conducted including 38 eyes of 38 different patients divided into two groups. Group 1 (cases) comprised 19 eyes of 19 male patients being treated with tamsulosin and group 2 (controls) comprised 19 eyes of 19 males not being treated with tamsulosin. In all cases, the patients had come to our hospital for cataract surgery and were assigned to either one of the two groups following these criteria: patients under treatment with tamsulosin who came for cataract surgery were included consecutively in group 1, while every male patient showing up immediately after a case was included in group 2 (control). Excluded from both groups were all those patients presenting an ophthalmological pathology which could compromise the surgery such as incidents of prior traumatisms or the presence of zonular detachment. All patients were operated by the same surgeon during the period from November 2005 to May 2006.

Prior to surgery, and for all patients, anamnesis was conducted on any ophthalmological or general conditions that could alter the outcome of our study.
as well as a detailed ophthalmological examination that included: preoperative visual acuity, determination of cataract degree, color of iris, biometry and measurement of the depth of the anterior chamber with IOL Master (Zeiss, Jena, Germany) pupillometry (CSO Eye TOP 6.4, CSO, Italy) under photopic, mesopic, scotopic conditions and after dilation with tropicamide and endothelial cell count. Intraoperatively we studied the mydriasis process, the type of anesthesia used, the time of ultrasound during phacoemulsification, the presence of the three signs comprising the floppy iris syndrome as well as surgery complications and the need for additional procedures during surgery.

There were visits the following day, week and month, in which we assessed final visual acuity, endothelial cell count and a new pupillometry was conducted under photopic, mesopic, scotopic conditions and after dilation with tropicamide.

## RESULTS

Both groups of patients were comparable with regard to age (p=0.42) with an average age of 76.7 SD 5.81 years (average and standard deviation) in group 1 and SD 75.3 SD 4.77 years in group 2. Likewise, the two groups were comparable in biometry and anterior chamber depth, with an average axial length of 23.5 SD 0.4 mm in group 1 and 23.41 SD 0.53 mm in group 2, differences which were not statistically significant (p=0.7). Preoperative visual acuity was 0.37 in group 1 and 0.37 in group 2 respectively. The difference between the preoperative size of pupils conducted with pupilometer (CSO Eye TOP 6.4) (CSO Ophthalmic. Florence. Italy) showed a comparable pupil diameter in both groups with the following measurements (table I): 1) Photopic conditions: 3.11 SD 0.58 and 3.43 SD 0.57 mm respectively (p=0.15); 2) Mesopic: 3.71 SD 0.79 and 3.9 SD 0.52 mm (p=0.39); 3) Scotopic: 3.95 SD 0.8 and 4.10 SD 0.59 mm (p=0.53); and 4) After 20-minute dilation with tropicamide: 6.42 SD 0.74 and 6.18 SD 0.86 mm (p=0.38) respectively. Neither were there any preoperative differences (p=0.82) between endothelial cell count conducted prior to surgery in both groups, with 2267 SD 285 cells/mm 2 in group 1 and 2418 SD 417 cells/mm 2 in group 2.

The mydriasis process was routinely conducted, in all cases, with homatropine (Colircusí Homatropina®. Alcon Cusí, SA. El Masnou. Barcelona. Spain) and phenylephrine (Colircusí Fenilefrina®. Alcon Cusí, SA. El Masnou. Barcelona. Spain), with no need to conduct any additional procedures due to insufficient intraoperative mydriasis. All patients were operated under topical anesthesia. With regard to the presence of intraoperative complications, these were limited to one patient with intumescent cataract in the control group (Group 2) who presented a tear in anterior rhexis conducted under Trypan Blue 0.1% (Vision Blue) (sign of the Argentinean flag) and which was favorably resolved with the implantation of the intraocular lens in sulcus, with no need for vitrectomy due to lack of vitreorrhagia and one patient of group 1 (tamsulosin) who presented zonular detachment and vitreous humor invasion and required anterior vitrectomy. The time for ultrasound used during phacoemulsification was 66 SD 5 and 58 SD 6 seconds on average (p=0.34) for groups 1 and 2 respectively. No additional intraoperative procedure was conducted to achieve adequate mydriasis in any of the patients.

With relation to the incidence of floppy iris syndrome defined by the triad: floppy iris that billows under regular fluidic conditions, tendency of iris to prolapse through correctly tunneled incisions and tendency towards progressive intraoperative myosis with conventional mydriasis processes, it is worth noting the following: only two patients (10%) presented the full triad, while nine patients (47%) presented two of the 3 signs and only 2 patients (10%) presented isolated iris billowing with no presence of the other signs. Thus, the presence of a distinctive sign of floppy iris syndrome was limited to 67% of the patients under treatment with tamsulosin while none of the patients in the control group showed any characteristics of this syndrome.
After phacoemulsification, patients followed a similar regime of check-ups in both groups, reporting similar average intraocular pressure measurements (IOP) both immediately after surgery and a week later. IOP on the first day following surgery was 16.37 SD 3.95 and 17.37 SD 4.5 mmHg respectively and a week after surgery, average IOP was 13.42 SD 2.55 and 14.05 SD 3.34 mmHg respectively, without any case of postoperative hypertension.

With regard to postoperative modification of pupil diameter (table II), in group 1 there was evidence of a tendency towards a diminished postoperative pupil diameter under photopic, mesopic, scotopic conditions and after dilation with tropicamide with the following average pupil sizes: 2.77 SD 0.52; 3.33 SD 0.77; 3.55 SD 0.83 and 5.0 SD 0.94 mm and a percentage reduction compared to preoperative pupil of 11%, 10%, 10% and 22% respectively. On the contrary, pupillometry of patients in group 2 showed a lower tendency towards a diminished postoperative pupil diameter under photopic, mesopic, scotopic conditions and after dilation with tropicamide with the following measurements: 3.17 SD 0.4; 3.72 SD 0.57; 4.03 SD 0.75 and 5.54 SD 0.8 mm and a percentage pupil decrease of 8.9%, 5%, 0.02% and 10% respectively. Comparison of average differences between pre and postoperative pupils in both groups using a T-test for independent samples was lower in the group of patients under treatment with tamsulosin, these differences being statistically significant for mesopic and scotopic pupils and after 20-minute dilation with tropicamide with two-tailed p-values of 0.05; 0.07 and <0.001 respectively.

As usual after phacoemulsification, in both groups of patients we found a loss of endothelial cells of 13% and 24% respectively, with no statistically significant differences between the two groups.

### DISCUSSION

Since the description of intraoperative floppy iris syndrome (IFIS) due to the use of tamsulosin by Chang and Campbell in 2005 (2), and given the greater risk of intraoperative complications, this situation has sparked the interest of cataract surgeons. This is why, properly and preoperatively recording patients with benign prostate hyperplasia (BPH) under treatment with tamsulosin, will allow better planning of cataract surgery, avoiding complications derived from unexpected technical difficulties (2,13).

In the initial series of the abovementioned authors (2) they found that 3% of their patients who underwent cataract surgery were being treated with tamsulosin and that IFIS appeared in 67-100% of these patients. Likewise, a high percentage (31%-48%) of them required some type of pupil intervention to achieve adequate mydriasis during phacoemulsification. However, other authors (15) in the United Kingdom have found a lower incidence associated to treatment with tamsulosin in their study population (0.71%), and neither appearance of IFIS was as frequent nor the need to conduct pupil interventions as high as in the original series. In our series, the incidence of IFIS in patients taking tamsulosin was 67%, although only 10% of patients presented all the symptoms. On the other hand, when we analyzed each one of the intraoperative signs defining IFIS, it should be noted that iris billowing was the most frequent sign in our series (47% of the cases). Likewise, we were able to verify that severity of IFIS is variable and does not necessarily appear with the full clinical triad.

Treatment with tamsulosin or the presence of IFIS are not, in principle, contraindications against phacoemulsification. However, the possibility of a greater number of complications derived from the technical difficulty presented by

<table>
<thead>
<tr>
<th>Preop.</th>
<th>Group 1</th>
<th>Group 2</th>
<th>P value</th>
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<tbody>
<tr>
<td>average</td>
<td>average</td>
<td>average</td>
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</tr>
<tr>
<td>Photopic</td>
<td>3.11 SD 0.58</td>
<td>2.77 SD 0.52</td>
<td>0.44 SD 0.1</td>
</tr>
<tr>
<td>Mesopic</td>
<td>3.71 SD 0.79</td>
<td>3.33 SD 0.77</td>
<td>0.48 SD 0.1</td>
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<tr>
<td>Scotopic</td>
<td>3.95 SD 0.8</td>
<td>3.55 SD 0.83</td>
<td>0.48 SD 0.17</td>
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<tr>
<td>Tropicamide</td>
<td>6.42 SD 0.74</td>
<td>5 SD 0.94</td>
<td>1.52 SD 0.2</td>
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Average in millimeters SD standard deviation, statistically significant p-value to compare pre-and postoperative averages in both groups through T-test for independent samples.
Corneal surgery in these patients (1) requires a series of preventive measures prior to the operation. Thus, as well as proper anamnesis and in the event the patient is taking tamsulosin, there should be available iris retractors and supercohesive viscoelastics for those cases in which regular mydriatic intervention does not prevent the appearance of intraoperative myosis that makes it impossible to continue phacoemulsification. Thus, and although we did not find a higher incidence of complications in the group of patients being treated with tamsulosin, we understand that the presence of IFIS considerably hinders phacoemulsification in these eyes. The longer time of ultrasound used in the group of patients under treatment with tamsulosin, and in particular in those cases presenting some of the distinctive characteristics of IFIS, evidences the greater technical difficulties and although in this series we did not observe a greater loss of endothelial cells in the group with tamsulosin, a larger sample might show this loss of endothelial cells generated by a higher energy consumption (14). On the other hand, as already mentioned above, the syndrome severity is not always the same since both the surgery difficulty and the risk of complications is greater in cases presenting the full clinical triad. In any case, it is our understanding that phacoemulsification in patients with IFIS is safe provided it is conducted by expert surgeons who have taken all necessary precautions.

Given the recent description of this syndrome, the relationship between length of treatment with tamsulosin and appearance of IFIS is yet to be determined. However, the pathogenic hypothesis that maintains that the syndrome is due to atrophy for lack of use of the iris dilating muscle (2) suggests that a longer treatment period would increase the risk of developing IFIS and its severity. Also, the usefulness or not of interrupting medication prior to surgery is yet to be determined. Given that the half-life of tamsulosin in plasma is 48-72 hours, it would seem that interrupting medication between 4 to 7 days prior to surgery could be helpful even if it does not prevent appearance of IFIS (2). Thus, most authors recommend interrupting medication 1 to 2 weeks prior to surgery, although the usefulness of this is still to be proven (2,7).

Lower preoperative mydriasis is common in all patients taking some type of alpha-blocker (2). We have observed this trend in our patients in the tamsulosin group although the differences with the control group were not statistically significant. However, we have detected a higher tendency towards postoperative myosis in patients under treatment with tamsulosin than in the patients in the control group. These differences have turned out to be statistically significant except under photopic conditions and they could be due to a greater instrument manipulation of the iris than necessary in these cases.

In conclusion, in this study the IFIS syndrome appeared in 67% of the patients under treatment with tamsulosin although only 10% presented the full triad. In general, these cases can be operated on without complications by highly skilled expert surgeons.

On the other hand, as a new finding we can note the observation of lower postoperative pupil reactivity in patients treated with tamsulosin versus patients in the control group, something which had not been described hitherto in literature.

REFERENCES


