Influence of bromopride in the prophylaxis of nausea associated with fluorescein angiography

INTRODUCTION

Fluorescein angiography is a technique used for the interpretation of ocular diseases. It allows sequential visualization of the blood flow simultaneously in the retina, choroid and iris, and it gives diagnostic support to clinical impressions based on alterations in fluid dynamics resulting from ocular disease processes(1-2).

This procedure is considered relatively safe and although numerous adverse reactions have been reported in literature, the most frequent are mild, such as nausea and vomiting(3-5). The incidence of these adverse reactions has varied among the authors (2%-14%) (6-8).

Nausea and vomiting can occur independently, but they are so strictly associated that it is possible to presume that they are mediated by the same neural path and can be considered a set(9-10). The efficient treatment of nausea depends on the correlation with the basic cause. Most pharmacologic therapies are reactive instead of preventive. The benefit of antiemetic agents varies according to the etiology of the symptoms, of the response of the patient to the medication and the occurrence of side effects (9-10).

The dopamine receptors in the stomach seem to mediate the inhibition of the gastric motility that occurs during nausea and vomiting, and these receptors can indicate an action site for the antiemetics antagonists of the dopamine receptor. They also participate in the consequences that result in...
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To Valsalva maneuver (1,13). Angiography, there being cases of subretinal hemorrhage due to capture of images difficult in the initial phase of fluorescein angiography, there being cases of subretinal hemorrhage due to Valsalva maneuver (1,13).

Nausea results in discomfort for the patient and makes the capture of images difficult in the initial phase of fluorescein angiography, there being cases of subretinal hemorrhage due to Valsalva maneuver (1,13)

The objective of this study was to determine the efficacy of bromopride in the prophylaxis of nausea during fluorescein angiography, when compared with a placebo.

METHODS

Patient and medical procedures

This study was a double-masked random clinical trial carried out at the Federal University of Pernambuco. The medical center’s Human Subjects Committee approved the study protocol (protocol 229/2005).

Patients scheduled to undergo fluorescein angiography were recruited between December 2004 and April 2005. Patients were excluded from the study if they were pregnant, or made use of dopaminergic, antihistaminic antagonists, antiemetics, corticosteroids or immunosuppressants. All patients provided a written informed consent before enrollment in the study.

For the examination 20% fluorescein sodium dye (Ophthalmos®) was used at a single 2.5 ml dose, injected into the cubital vein, with a manual infusion rate of approximately 1 ml per second.

For the patients who agreed to participate in the study, the scheduled fluorescein angiography was randomly assigned to one of two groups: 1) to be preceded by a 2 ml intravenous dose of 5 mg/ml bromopride or 2) to be preceded by a 2 ml intravenous dose of 0.9% sodium chloride (placebo), both 20 minutes before the dye injection. Randomization was performed in blocks of four. Patients were randomly assigned to one of the two groups until two patients had been assigned to each one of the two groups, completing the block of four. Randomization was performed by computer at the time of enrollment.

The syringes with bromopride or saline solution were prepared by a nursing technician, before the procedure, and identified by a record number for posterior evaluation of the results. It was not possible to visually distinguish the content from the syringe; thus, the doctors and the patients did not know which substance was being applied. Mean age, sex, prevalence of diabetes and arterial hypertension of both groups were compared with the purpose to know if the groups were well balanced. Diabetes and arterial hypertension were selected because they are the most prevalent coexisting illnesses in fluorescein angiography patients (14-15).

Data collection

The data had been collected through a specific file, which contained history and physical examination of the patient, filled in by the anesthetist at the moment of clinical evaluation. The definition of nausea used in the study was a vague, intensely disagreeable sensation of sickness or queasiness that may or may not be followed by vomiting. Nausea occurring during the angiography had been registered in a file of protocol by the ophthalmologist. Nausea occurring subsequently was collected by a standardized telephone interview of the patient conducted by the study coordinator twelve hours after the examination.

Sample size and statistical analysis

A minimum sample of 340 patients (170 per group) was planned. Assuming a 7% incidence of nausea in the placebo group, this sample would allow 80% power of being able to detect a difference as small as 6.5% in the bromopride group. As a parameter of central trend and dispersion for the data, means and standard deviation (SD) had been determined. Tests were made to detect differences between variables, using chi-square test and relative risk (RR) for categorical variables, and t test for quantitative variables. The results of this analysis were considered significant if p value was less than 0.05.

RESULTS

We enrolled 352 patients scheduled to undergo fluorescein angiography between December 2003 and April 2004. The sample consisted of 176 patients assigned to each group. The two groups were well balanced in terms of age, with a mean age of 57.2 years (SD=11.7 years) in the bromopride group and 58.6 years (SD=14.4 years) in the placebo group (p=0.398). The groups were also well balanced with respect to sex and prevalence of diabetes and arterial hypertension (Table 1).

Nausea was observed in 12 (6.8%) patients of the bromopride group and in 11 (6.3%) patients of the placebo group (p=0.660). All cases of nausea occurred during the angiography.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Bromopride (n=176)</th>
<th>Placebo (n=176)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.2±11.7</td>
<td>58.6±14.4</td>
<td>0.398</td>
</tr>
<tr>
<td>Number of patients (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>99 (56.2)</td>
<td>93 (52.8)</td>
<td>0.520†</td>
</tr>
<tr>
<td>Arterial hypertenssion</td>
<td>77 (43.7)</td>
<td>73 (41.5)</td>
<td>0.666†</td>
</tr>
<tr>
<td>Diabetes</td>
<td>65 (36.9)</td>
<td>69 (39.2)</td>
<td>0.660†</td>
</tr>
</tbody>
</table>

* t test; † chi-square test

Table 1. Characteristics of the patients and coexisting illness, according to the group assignment, fluorescein angiography study, Recife, 2005

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The frequency of nausea in the present study was 6.53%, which is in accordance with the literature(6-8). The pathophysiology involves the activation of chemoreceptor of the vomiting nervous center, located in the postrema area, posterior region of the fourth ventricle, alternatively as well as through other stronger influences of the central nervous system (for example, limbic system) that function as primary detectors of the emetic stimulation and induce vomiting through integration with the postrema area, vagal nerve or vestibular system(9-10,12,16).

Only two random clinical trials exist to discuss the use of medicines for nausea and vomiting prophylaxis in fluorescein angiography, where granisetron and metoclopramide have respectively been used(19-20).

Some authors carried out a study with 120 patients comparing oral granisetron and a placebo and they observed 3 (5%) cases of vomiting in the placebo group and none with this medication. Despite the small sample, these authors suggested granisetron would be indicated for vomiting prophylaxis in fluorescein angiography(19). Granisetron is a selective antagonist of the 5-HT receptor of 5-hydroxytryptamine and is usually indicated for nausea prophylaxis associated with a cytostatic therapy. However its use is associated with a larger incidence of digestive intolerance caused by medicines demonstrated that bromopride was efficient in the prophylaxis of these symptoms(25).

In this study, the use of the bromopride before the fluorescein angiography did not decrease the incidence of nausea. A possible explanation for the inefficacy of the bromopride in the prophylaxis of nausea would be the insufficient time for the drug to start acting, however, after intravenous administration, drug bioavailability is immediate and a phase of initial distribution occurs during a short period of time (5-10 minutes) and the half-life is 3 hours(11).

The results suggested that the use of bromopride as prophylaxis for nausea in fluorescein angiography is not a procedure that should be stimulated. However, it is not possible to discard its utility in the treatment of already symptomatic patients. Further studies will be necessary to confirm these findings.

In conclusion, bromopride did not prevent the occurrence of nausea in fluorescein angiography, when compared with a placebo.

Resumo

Objetivos: Determinar a eficiência da bromoprida na profilaxia de náuseas na angiofluoresceinografia, quando comparada a um placebo. Métodos: O estudo foi um ensaio clínico aleatório duplo-mascarado, entre dezembro de 2004 e abril de 2005. Os exames foram realizados com fluoresceína sódica a 20% intravenosa em dose única de 2,5 mL. Os pacientes foram divididos em dois grupos: grupo 1, pacientes que receberam 10 mg/2 mL de bromoprida via intravenosa e o grupo 2, pacientes que receberam uma dose 2 mL de cloreto de sódio a 0,9% (placebo), ambos 20 minutos antes da injeção do contraste. Foram registrados os casos de náusea durante e após o exame. Resultados: Foram selecionados 352 pacientes, 176 em cada grupo. Foram registrados casos de náusea em 12 (6,8%) pacientes do grupo da bromoprida e 11 (6,3%) pacientes do grupo placebo (p=0,829 - risco relativo=1,09). Conclusão: Neste estudo a bromoprida não preveniu a ocorrência de náuseas na angiofluoresceinografia, quando comparada a um placebo.
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**References**


