J Anesth (2012) 26:779–782
DOI 10.1007/s00540-012-1406-6

CLINICAL REPORT

Peribulbar block in patients scheduled for eye procedures and treated with clopidogrel

Emile Calenda · Laure Lamothe · Olivier Genevois · Annie Cardon · Marc Muraine

Received: 22 February 2012 / Accepted: 20 April 2012 / Published online: 12 May 2012

Abstract Our hypothesis was that the continuation of clopidogrel does not increase the risk of eye hemorrhage, compared to patients not treated with clopidogrel, when a peribulbar anesthesia is required. Our prospective case-control study enrolled two groups of 1,000 patients scheduled for intraocular eye surgery requiring a peribulbar block. Patients treated with clopidogrel were included in group A (1,000 patients). Patients who had never been treated with clopidogrel constituted the control group (group B, 1,000 patients). Hemorrhages were graded as follows: 1 = spot ecchymosis of eyelid and or subconjunctival hemorrhage; 2 = eyelid ecchymosis involving half the lid surface area; 3 = eyelid ecchymosis all around the eye, no increase in intraocular pressure; 4 = retrobulbar hemorrhage with increased intraocular pressure. Grade 1 hemorrhages were observed in 30 patients (3.0 %) in group A and in 20 patients (2.0 %) in group B. No grade 2, 3, or 4 hemorrhage was encountered. There was no significant difference in the grading of hemorrhage between the groups ($p = 0.017$). Clopidogrel was not associated with a significant increase in potentially sight-threatening local anesthetic complications.

E. Calenda (✉) · L. Lamothe · A. Cardon
Département d'Anesthésie Réanimation, Rouen University Hospital, Centre Hospitalier Universitaire de Rouen, 1 rue de Germont, 76031 Rouen cedex, France
e-mail: emile.calenda@chu-rouen.fr

O. Genevois · M. Muraine
Department of Ophthalmology, Rouen University Hospital, Centre Hospitalier Universitaire de Rouen, 1 rue de Germont, 76031 Rouen cedex, France

Keywords Clopidogrel · Eye procedure · Hemorrhage · Peribulbar block

Introduction

Because of the central role of platelets in cardiovascular atherothrombosis, there is a well-established therapeutic role for antiplatelet therapy [1]. Drugs involved in antiplatelet therapy are commonly classified by the target in platelet activation. Because of its proven benefits and low cost, aspirin, which is a cyclooxygenase 1 (COX1) inhibitor, remains the most prescribed. However, aspirin is a weak antiplatelet agent. Clopidogrel is metabolized through cytochrome P450 in the liver. Its active metabolite irreversibly antagonizes the P2Y12 receptor. The clinical benefit of adding clopidogrel to aspirin has been demonstrated in patients with acute coronary syndrome, instable angina, or myocardial infarction [2]. However, in patients with stable cardiovascular disease or in asymptomatic patients with multiple cardiovascular risk factors, the combination of clopidogrel plus aspirin was not significantly more effective than aspirin alone in reducing the rate of myocardial infarction, stroke, or death from cardiovascular causes. Furthermore, the risk of moderate to severe bleeding was increased [3]. Monitoring of clopidogrel by platelet function assays revealed interpatient response variability [4]. That response variability and the relatively slow onset of clopidogrel have led to development of new P2Y12 antagonists such as prasugrel. Patients scheduled for intraocular surgery are often elderly and may have concurrent diseases. Clopidogrel is used to prevent myocardial infarction and cerebrovascular ischemic events. Continuation or discontinuation of clopidogrel in these patients is always a concern. Phacoemulsification of the

lens with topical anesthesia is recognized as safe in patients treated with clopidogrel but always discussed for posterior segment surgery. The length of withdrawal of clopidogrel therapy perioperatively was associated with a significantly increased incidence of acute coronary syndrome [5].

Ophthalmic surgeons should pay close attention to the indications for clopidogrel therapy in their patients and should enlist appropriate collaboration with their colleagues in cardiology to minimize risks to their patients [6]. Pre- and intraoperative risk factors for thrombosis have to be balanced against the risk factors for surgical bleeding. The perioperative management must be an interdisciplinary decision resulting from a collaboration between cardiologists, surgeons, and anesthetists [7].

Our hypothesis was that the continuation of clopidogrel does not increase the risk of hemorrhage, compared to patients not treated with clopidogrel, when a peribulbar anesthesia is required.

Thus, we undertook a prospective case-control study to ascertain the relationship between the continuation of clopidogrel and bleeding associated with a peribulbar block.

Case report

Approval of our hospital ethics committee was obtained for that prospective case-control study. Patients who underwent elective ophthalmic surgery under peribulbar block from January 2005 to December 2010 were recruited. Patients were allocated to two groups on the basis of their antiplatelet therapy. A consecutive 1,000 patients who continued to receive clopidogrel, at a maintenance dose of 75 mg daily, and consented to the oral explanation for the risk of hemorrhage, were allocated to group A. We did not assess the platelet function by a laboratory assay in these patients, even in cases of hemorrhage, because hemorrhagic side effects were not severe. Patients treated with omeprazole were excluded because strong evidence of interaction between clopidogrel and omeprazole has been reported [8]. Patients taking other proton pump inhibitors were maintained in the protocol. Group B was represented by 1,000 patients who had never received clopidogrel and were scheduled for the same surgery and the same anesthesia procedure. Patients treated with another hemorrhagic drug, such as warfarin, were excluded. Patients with preexisting factors such as congenital coagulopathy, deficit in blood factors of coagulation, renal dysfunction, and unstable high blood pressure with treatment were likewise excluded in both groups.

All patients received oral hydroxyzine (UCB Pharma SA) (0.5–1 mg/kg), or alprazolam (Pharmacia–Upjohn) (0.01 mg/kg) 1 h before surgery. A short-acting drug (midazolam) 0.5 or 1 mg was intravenously administered 5 min before peribulbar anesthesia in patients who seemed very anxious.

Two anesthesiologists were present in the surgery room. The first anesthesiologist checked the anesthesia file and the second performed the peribulbar block (blinded for the continuation of clopidogrel). The first anesthesiologist was in charge of the collection of data. The surgeon was blinded for the continuation of clopidogrel and assessed bleeding according to the defined protocol. Bleeding was assessed until 24 h after the peribulbar anesthesia. Hemorrhages were graded in each group as follows: 1 = spot ecchymosis of eyelid and or subconjunctival hemorrhage; 2 = eyelid ecchymosis involving half the lid surface area; 3 = eyelid ecchymosis all around the eye, no increase in intraocular pressure; 4 = retrobulbar hemorrhage with increased intraocular pressure.

Peribulbar blocks were performed by three anesthesiologists experienced in that technique according to Hamilton's technique [9] and as described in our previous studies [10, 11]. The first percutaneous insertion of the needle (25 gauge, 32 mm long) was parallel to the orbital floor at the lateral aspect of the inferior orbital rim (maximal depth 25 mm), and the second (maximal depth 25 mm) at the level of the supraorbital notch. The injection was immediately stopped when the globe seemed tense. As soon as the globe became soft, the second injection was started until another sensation of tension of the globe. A Tono-Pen XL (Reichert Technologies, USA), which provides intraocular pressure (IOP) readings that correlate closely with Goldmann tonometry, is commonly used in cases of suspected high IOP. We used a mixed anesthetic solution of equal quantity of lidocaine 2 % (20 mg/ml) and bupivacaine 0.50 % (5 mg/ml). We did not apply pressure by an ocular cuff after the peribulbar block. We have never administered more than 10 ml lidocaine 2 % and 10 ml bupivacaine 0.50 %.

A Fisher exact test was chosen to compare the two groups, and $p < 0.05$ was considered as significant.

Discussion

The volume of local anesthetic was 15 ± 5 ml (mean ± standard deviation) in group A and 14 ± 6 ml in group B. Because the p value of the analysis of variance (ANOVA) test was 0.061 (risk chosen, $\alpha = 0.05$), we can accept the hypothesis stipulating that the mean of volumes injected by each anesthesiologist is equal; consequently, no differences were found among the three anesthesiologists. No patient expressed cardiac or neurological mild or severe complications or any other general side effect. The physical characteristics and ophthalmic procedures of both groups

are collected in Table 1. Grades 1 hemorrhages were observed in 30 patients (3.0 %) in group A and in 20 patients (2.0 %) in group B. Grade 2, 3, or 4 hemorrhage was not encountered. There was no significant difference in the grading of hemorrhage between the groups ($p = 0.017$).

Dick and Jacobi [12] reported in a multicentric retrospective study (172,880 surgeries in 1995) that 63 % of surgeons advise their patients to continue acetyl salicylic acid. They concluded that anti-platelet therapy influenced the anesthetic technique and the surgical approach. Kallio et al. [13] observed hemorrhage in 3.7 % of 482 patients taking acetyl salicylic acid and concluded that the continuation of acetyl salicylic acid does not predispose to hemorrhage when a retrobulbar/peribulbar block has been performed, but they did not investigate clopidogrel at all. Although a consensual approach seems to emanate regarding aspirin, that is not the case with clopidogrel. Benzimra et al. [14] reported, in a multicentric audit of 55,567 operations, 524 patients treated with clopidogrel only. They found 8 % of hemorrhagic complications such as subconjunctival hemorrhage (4.39 %) and eyelid hemorrhage (0.19 %). No retrobulbar hemorrhage was noticed. They concluded that clopidogrel is associated with an increase in minor complications of the sharp needle. Their study was retrospective but reported the largest number of patients ever treated with clopidogrel. Mason et al. [15] reported, in a retrospective study, no incidents of retrobulbar or orbital hemorrhage in the 133 retrobulbar or peribulbar blocks performed in the clopidogrel group. We have not found prospective studies describing complications after peribulbar blocks in patients treated with clopidogrel, so we have chosen to carry out a prospective, case-control, monocentric study with a control group over a long period of time. This is the first prospective study with a large number of patients. The overall incidence of hemorrhage in our study was 3 % (30/1,000) in the group of patients treated with clopidogrel and 2 % (20/1,000) in the group of patients not treated with clopidogrel. This prospective, comparative study included an important cohort of patients and led to the conclusion that clopidogrel was not associated with a significant increase in potentially sight-threatening local anesthetic complications.

The discontinuation of clopidogrel in ophthalmic procedures requiring a peribulbar anesthesia is no longer justified. This attitude will avoid acute heart syndrome or arterial thrombosis and will simplify the perioperative ophthalmic procedure.

Table 1 Demographic variables

	Group A	Group B	*p* value
Number of patients	1,000	1,000	
Age (years) (mean and range)	72 (38–94)	71 (36–86)	
Weight (kg) (mean and range)	74 (45–125)	72 (54–94)	
Clopidogrel	Yes	No	
Operations			
Cataract	540	500	0.39
	54 %	50 %	
Pterygium	8	6	0.97
	0.8 %	0.6 %	
Vitrectomy	230	240	0.44
	23 %	24.6 %	
Buckling and/or circling	150	160	0.25
	15 %	16 %	
Keratoplasty	60	55	0.60
	6 %	5.5 %	
Amniotic membrane	12	39	0.43
	1.2 %	3.9 %	

Conflict of interest None of the authors has conflict of interest with the submission.

Informed consent Approval of our hospital ethics committee was obtained for the prospective case-control study.

References

1. Michelson AD. Antiplatelet therapies for the treatment of cardiovascular disease. Nat Rev Drug Discov. 2010;9(2):154–69.
2. Michelson AD. P2Y12 antagonism: promises and challenges. Arterioscler Thromb Vasc Biol. 2008;28(3):s33–8.
3. Bhatt DL, Fox KA, Hacke WA, Berger PB, Black HR, Boden WE, Cacoub P, Cohen EA, Creager MA, Easton JD, Flather MD, Haffner SM, Hamm CW, Hankey GJ, Johnston SC, Mak KH, Mas JL, Montalescot G, Pearson TA, Steg PG, Steinhubl SR, Weber MA, Brennan DM, Fabry-Ribaudo L, Booth J, Topol EJ, CHARISMA Investigators. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. N Engl J Med. 2006;354(16):1706–17.
4. Michelson AD, Frelinger AL, Furman MI. Resistance to antiplatelet drugs. Eur Heart J. 2006;8:G53–8.
5. Collyer TC, Reynolds HC, Truyens E, Kilshaw L, Corcoran T. Perioperative management of clopidogrel therapy: the effects on in-hospital cardiac morbidity in older patients with hip fractures. Br J Anaesth. 2011;107:911–5.
6. Hess TM, Liu ES. Clopidogrel therapy in ophthalmic procedures: a survey of subspecialty ophthalmologists and review of current guidelines. Can J Ophthalmol. 2011;46:528–30.
7. Metzler H, Huber K, Kozek-Langenecker S, Vicenzi MN, Münch A. Coronary stents, dual antiplatelet therapy and peri-operative problems. Anaesthesist. 2007;56:401–10.
8. Abraham NS, Hlatky MA, Antman EM, Bhatt DL, Bjorkman DJ, Clark CB, Furberg CD, Johnson DA, Kahi CJ, Laine L, Mahaffey KW, Quigley EM, Scheiman J, Sperling LS, ACCF/ACG/AHA. ACCF/ACG/AHA 2010 expert consensus document on the concomitant use of proton pump inhibitors and thienopyridines: a focused update of the ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use. A Report of the American College of

Cardiology Foundation Task Force on Expert Consensus Documents. J Am Coll Cardiol. 2010;56:2051–66.
9. Hamilton RC. Techniques of orbital regional anaesthesia. Br J Anaesth. 1995;75:88–92.
10. Muraine M, Calenda E, Watt L, Proust N, Cardon A, Eupherte L, Brasseur G. Peribulbar anaesthesia during keratoplasty: a prospective study of 100 cases. Br J Ophthalmol. 1999;83:104–9.
11. Calenda E, Olle P, Muraine M, Brasseur G. Peribulbar anesthesia and sub-Tenon injection for vitreoretinal surgery: 300 cases. Acta Ophthalmol Scand. 2000;78:196–9.
12. Dick B, Jacobi FK. Cataract surgery and anticoagulation—current status. Klin Monatsbl Augenheilkd. 1996;209:340–6.
13. Kallio H, Paloheimo M, Maunuksela EL. Haemorrhage and risk factors associated with retrobulbar/peribulbar block: a prospective study in 1383 patients. Br J Anaesth. 2000;85:708–11.
14. Benzimra JD, Johnston RL, Jaycock P, Galloway PH, Lambert G, Chung AK, Eke T, Sparrow JM, EPR User Group. The Cataract National Dataset electronic multicentre audit of 55,567 operations: antiplatelet and anticoagulant medications. Eye. 2009;23:6–10.
15. Mason JO 3rd, Gupta SR, Compton CJ, Frederick PA, Neimkin MG, Hill ML, Heersink MJ, Vail RS, White MF Jr, Feist RM, Thomley ML, Albert MA Jr. Comparison of hemorrhagic complications of warfarin and clopidogrel bisulfate in 25-gauge vitrectomy versus a control group. Ophthalmology. 2011;118:543–7.