

Is Glycemic Control Necessary During Cataract Surgery in Diabetic Patients?

Merits and demerits of rapid preoperative glycemic correction.

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Cataract surgery is performed in diabetic patients when their blood glucose levels are well controlled. If blood glucose is not well controlled, however, medical treatment is performed and surgery is delayed.

Diabetic patients with poor glycemic control cannot obtain permission to undergo surgery from their physicians due to the risk of postoperative complications including delaying wound healing^{1,2} and increased infections.³⁻⁶

Traditionally, hospital admission is recommended for correction of blood glucose control. However, same-day surgery has become common due to the popularity of small-incision phacoemulsification cataract surgery; this is the method that many diabetic patients are treated with. Small-incision surgery causes less inflammation than conventional extracapsular cataract extraction,⁷ and postoperative progression of retinopathy or maculopathy after small-incision surgery is minimal, although it can occur.⁸⁻¹¹

It is widely known that good blood glucose control is important to prevent the progression of diabetic retinopathy, but there are no clear standards about the range of HbA1c levels over which cataract surgery is safe and postoperative complications or progression of retinopathy and maculopathy can be avoided.

This article discusses perioperative blood glucose control for diabetic patients undergoing small-incision phacoemulsification cataract surgery and the best strategy of controlling blood glucose before and after surgery.

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SURGICAL PROBLEMS: PATIENTS WITH POOR GLYCEMIC CONTROL

The therapeutic policy in Japan has been to control blood glucose and maintain HbA1c at <10% before cataract surgery. Medical treatment is continued and surgery is delayed when HbA1c is not at this level. Is this policy still acceptable with same-day surgery? If the blood glucose level is well controlled, there is less risk of postoperative surgical complications including hyperglycemia,¹² delayed wound healing^{1,2} and infection³⁻⁶ as well as less risk of severe postoperative ocular inflammation¹³ and the occurrence/progression of retinopathy.⁸⁻¹¹

Postoperative hyperglycemia is caused by stress and surgical invasion.¹² According to one study,¹⁴ changes in blood glucose and cortisone levels were minimal during and after minor surgery under local anesthesia. Changes of blood glucose levels will be also minimal during and after phacoemulsification cataract surgery. These changes appeared to be related to alterations of the regimen for oral hypoglycemic agent and insulin due to fasting before surgery. We do not think that preoperative fasting is necessary, and we have not experienced any problems while conducting surgery in diabetic patients without changing

HYPERGLYCEMIA AND RETINOPATHY: DISCOVERING THE MOLECULAR LINK

Researchers have recently uncovered the association between methylglyoxal and angiotensin-2.

Recent research has indicated that the concentration of methylglyoxal (MG) — a reactive alpha-oxoaldehyde — may be involved in pathobiologies of such diseases as diabetic vascular disease, cancer, renal failure and malaria. Now, researchers have uncovered its link with retinopathy.¹

According to a study published in *Cell*, when hyperglycemia occurs, damaged cells produce an abundance of the MG molecule. This molecule is glucose-derived, and activates angiotensin-2 (ANG-2) inside the cell. The presence of ANG-2, in return, may contribute to the loss of small blood vessels in the retina.

As small blood vessels are broken down, oxygen delivery to any part of the retina may be lower than normal. The retina compensates for this slow delivery by stimulating new blood vessel growth, which causes intraretinal bleeding. Patients with diabetes may experience this damage associated with hyperglycemia in cells that do not have the capacity to prevent high blood glucose levels. As glucose levels rise, researchers discovered that each cell produces additional superoxide; this triggers increased MG production. As a result, blood vessel damage results as ANG-2 is activated.

Researchers have concluded that there is a molecular link between hyperglycemia and diabetic retinopathy. If drugs could be manufactured that suppress MG, then retinopathy may be treatable.

“Based on our findings, we now believe that by reducing MG levels through yet-to-be discovered new drugs, we would normalize damaging patterns of gene expression in complication-prone diabetic cells,” said Michael Brownlee, MD, lead investigator and director of the Juvenile Diabetes Research Foundation International Center for Diabetic Complication Research, in a news release.²

1. Yao D, Taguchi T, Matsumura T, et al. Methylglyoxal modification of mSin3A links glycolysis to angiotensin-2 transcription. *Cell*. 2006; 124:275-286. Epub 2006 Jan 12.

2. JDRF-funded researchers discover molecular link between hyperglycemia and retinopathy. Available at http://www.jdrf.org/index.cfm?page_id=104468. Accessed January 13, 2006.

their meals and medications, as is the case for nondiabetic patients. Regarding change to blood glucose level¹⁵ after subconjunctival steroid injection at the end of surgery, blood glucose tends to be slightly high on the day of surgery. When problem-free cataract surgery is completed, the aqueous flare intensity is comparable between patients with and without subconjunctival steroids. The need for subconjunctival steroid injection is questionable.

Decreased collagen formation was observed in hyperglycemic rats during wound healing, and collagen formation is normalized by controlling hyperglycemia with insulin.^{1,2} Our 3.5-mm incision, however, does not require much collagen formation for healing. In contrast, postoperative infection is potentially a major problem.

The postoperative infection rate was higher in diabetic patients than in nondiabetic patients (10.7% vs 1.8%),³ and a correlation between acute postoperative infection and blood glucose level was found.⁴ Postoperative endophthalmitis is the most severe type of infection after ophthalmic surgery. There is no consensus about the relationship of postoperative endophthalmitis to diabetes: Incidence of postoperative endophthalmitis was signifi-

cantly higher in diabetic patients,⁵ but diabetes is not a known risk factor for postoperative infection.^{16,17} Since diabetic patients account for approximately 24% of those developing postoperative endophthalmitis,⁶ this association cannot be ignored. The relationship between blood glucose control and postoperative endophthalmitis has not been studied and remains unclear.

POSTOPERATIVE OPHTHALMIC COMPLICATIONS

Postoperative inflammation is a major problem after ophthalmic surgery. Severity is worse in diabetic patients versus nondiabetic patients.¹⁸ When retinopathy is mild, there is no difference in the severity of inflammation after small-incision phacoemulsification cataract surgery between diabetic patients and nondiabetic patients.¹⁹

Postoperative progression of retinopathy and maculopathy is a common problem, however, there have been no reports about the influence of blood glucose control during the perioperative period. Although progression of maculopathy has a strong influence on the postoperative visual prognosis, detailed investigations of this problem have not been conducted and no clear conclusions have been obtained.

We have experienced some patients who underwent

rapid correction of poor glycemic control before surgery and had a poor postoperative visual prognosis.²⁰ We conducted a study of these patients²¹ and obtained the following findings.

The patients in our study were divided into three groups: a group that achieved rapid correction of poor glycemic control before surgery and maintained good control afterward (group 1); a group with poor glycemic control before and after surgery (group 2); and a group with good blood glucose control before and after surgery (group 3).

We performed small-incision phacoemulsification cataract surgery in one eye and prospectively investigated the progression of retinopathy and maculopathy at 1-year postoperation, using the nonoperated eye as the control. All of the patients had type 2 diabetes and small-incision phacoemulsification cataract surgery was conducted with an acrylic intraocular lens in all cases. Changes of retinopathy and maculopathy were assessed according to the ETDRS (Early Treatment Diabetic Retinopathy Study) scale from findings obtained by ophthalmoscopy and fluorescence fundus angiography.

We found no significant differences in the postoperative progression of retinopathy between the groups ($P=.27$). However, postop progression of maculopathy was significantly more common in the group that underwent rapid correction of poor glycemic control before surgery compared with the other two groups ($P=.02$).

Additionally, retinopathy and maculopathy showed significant progression in patients from group 1 who had moderate to severe nonproliferative diabetic retinopathy before surgery ($P=.002$ and $P=.008$, respectively). When surgery was conducted in patients with poor glycemic control after glucose levels were normalized by rapid correction, no difference in the progression of retinopathy compared with the other groups at 1 year postop was seen, but worsening of maculopathy was more common.

These findings indicate that rapid correction of blood glucose levels before surgery is not useful for preventing postop complications, and, in fact, it may cause postop progression of both retinopathy and maculopathy in patients who already have moderate to severe nonproliferative diabetic retinopathy.

MERIT, DEMERITS OF RAPID CORRECTION

Why does rapid correction of blood glucose cause problem? To prevent the progression of diabetic retinopathy, long-term maintenance of good blood glucose control is necessary.²²⁻²⁵ It was also demonstrated

that retinopathy deteriorated in some patients after blood glucose levels were improved rapidly and controlled strictly.^{26,27} We encounter similar problems in Japan. This phenomenon is called early worsening and often occurs as transient progression of retinopathy after introduction of insulin therapy. Although temporary, it may progress to irreversible proliferative retinopathy and causes visual disturbance.²⁶ If strict blood glucose control — which physicians and ophthalmologists generally believe is good — can cause the progression of retinopathy, this is a serious issue. Progression of retinopathy after rapid correction of blood glucose is often observed in patients who have not been treated for long; patients in whom treatment was suspended; and patients with poor glycemic control. Factors include the rate of decreasing the blood glucose level, HbA1c value before initial treatment, severity of retinopathy and diabetes duration. The details of the mechanism remain unknown.

After intensive insulin therapy, progression of retinopathy was uncommon in patients who had no retinopathy before treatment or patients with simple retinopathy, however progression was observed in patients with advanced retinopathy.²⁵ The severity of retinopathy appears to be a good index of the long-term glycemic load, and the severity of retinopathy before correction of blood glucose control also appears to be a key factor with regard to the final prognosis after rapid correction. Progression of retinopathy after rapid correction of blood glucose control appear to be related to changes of retinal blood flow,²⁸ decreased oxygen-release capacity of red cells due to the lower blood glucose level²⁹ and production of hypoxia-inducible factor-1 alpha after insulin therapy damages the blood retinal barrier.³⁰ The latter was recently confirmed.

There are various definitions of rapid correction. Kumamoto et al²⁵ showed that a decrease of HbA1c by $\geq 3.0\%$ within 6 months postoperation should be avoided. Retinal edema, retinal hemorrhage and soft exudates are often observed in the central fundus of patients whose HbA1c is reduced by $\geq 3.0\%$ within 3 months. If HbA1c decreases by $>0.5\%$ to 1.0% within 1 month, there is an increased risk of worsening retinopathy. It may be extremely difficult to keep the decrease of HbA1c at around 0.5% per month. Patients with poor glycemic control and an HbA1c $\geq 10\%$ often show rapid correction with dietary advice and educational hospitalization alone. Therefore, ophthalmologists should conduct frequent fundus examinations and perform fluorescence fundus angiography in patients with moderate to severe retinopathy.

We do not advise delaying small-incision phacoemulsification surgery for rapid correction of blood glucose in patients whose HbA1c is <15%.

ADVICE FOR PHYSICIANS

If diabetes duration is estimated at ≥ 10 years and HbA1c has been $\geq 9\%$ for at least 3 years, patients with moderate to severe nonproliferative diabetic retinopathy should not receive rapid correction. When an experienced surgeon performs a small-incision phacoemulsification cataract surgery, the influence of preoperative blood glucose control seems to be small. Rapid correction of blood glucose may cause progression of maculopathy and thus influence the postoperative visual prognosis; therefore better education of physicians and family doctors is necessary.

Blood glucose control is still necessary in diabetic patients. Ophthalmic surgeons should help patients to understand the importance of correctly managing diabetes when cataract surgery is conducted. Patients with improved vision after cataract surgery may stop visiting hospital and treatments. Ophthalmologists should emphasize the importance of regular follow-up and medical treatment after surgery. Accordingly, the cooperation of physicians and family doctors is essential.

CONCLUSION

The optimal preoperative glycemic control strategy for diabetic patients undergoing cataract surgery is yet to be determined. Our present study²¹ indicated that rapid preoperative glycemic correction should be avoided in patients with moderate to severe nonproliferative diabetic retinopathy because it may increase the risk of postoperative progression of retinopathy and maculopathy. In addition, it is possible to perform surgery in patients with moderate to severe nonproliferative diabetic retinopathy, regardless of glycemic control. To achieve good visual outcome, surgery may need to be performed in patients with moderate to severe nonproliferative diabetic retinopathy or maculopathy. ■

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