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Original Article

Peripheral iridectomy for glaucoma is more effective than compound trabeculectomy and significantly reduces Hcy and hs-CRP levels

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Abstract: Objective: To investigate the efficacy of peripheral iridectomy and compound trabeculectomy for glaucoma and the changes in homocysteine (Hcy) and hypersensitivity C-reactive protein (hs-CRP) levels before and after treatment. Methods: Altogether 104 patients with primary angle-closure glaucoma who were admitted from February 2020 to January 2022 were enrolled in this study for a retrospective analysis. Among them, 49 cases treated by peripheral iridectomy were considered as the research group, and 55 treated by compound trabeculectomy were seen as the control group. The intraocular pressure (IOP), vision, anterior chamber depth (ACD), surgical efficiency and complications before and after surgery was compared between the two groups of patients. Patients' venous blood was collected before and after treatment to test the Hcy and hs-CRP levels, and the relationship between the levels and treatments was analyzed. The ROC curves of Hcy and hs-CRP diagnostic efficacy after treatment were also plotted, and the relationship between Hcy and hs-CRP and patient outcomes was tested by Pearson correlation coefficient. Results: There were no marked differences in IOP, vision and ACD between the two groups before surgery (P>0.05). After surgery, the IOP was dramatically lower, and ACD and vision were dramatically higher in the research group than those in the control group (P<0.01). Compared to the control group, the treatment success rate in the research group was markedly higher, and the incidence of adverse reactions was lower. There was no difference in Hcy and hs-CRP levels before surgery between the two groups (P>0.05). After surgery both Hcy and hs-CRP levels decreased (P<0.05), and levels in the research group were lower than in the control group (P<0.05). Patients with better outcomes had lower postoperative Hcy and hs-CRP levels (P<0.05). ROC curves of the diagnostic efficacy of Hcy and hs-CRP after treatment manifested that the areas under the curve were >0.7. Both Hcy and hs-CRP levels were found to be negatively correlated with patient outcomes by Pearson correlation coefficient (P<0.001). Conclusion: The efficacy of peripheral iridotomy for glaucoma is better than that of compound trabeculectomy. Monitoring Hcy and hs-CRP levels in patients before and after surgery can effectively assess clinical outcomes as well as the safety of the procedure.

Keywords: Peripheral iridectomy, compound trabeculectomy, glaucoma, Hcy, hs-CRP

Introduction

Glaucoma is a blinding eye disease that seriously endangers the function of the optic nerve, characterized by progressive visual loss and visual field defects. It is the second most prevalent blindness worldwide after cataracts, with more than 60 million cases in 2010 and more than 80 million in 2020 [1, 2]. One of the main risk factors for glaucoma is elevation of pathological intraocular pressure (IOP), which exceeds the tolerance of the individual's intraocular tissue and thus poses a risk to the optic nerve [3, 4]. High IOP can cause a decrease in the thickness of the optic nerve fiber layer, a progressive increase in the cup-to-disc ratio, and progressive visual field defects, which are risks to human health because the damages are irreversible [5]. Lowering IOP has become the main treatment modality, commonly with long-term medication, laser and surgical treatments [6].

Trabeculectomy is a common clinical procedure for lowering IOP. After continuous improvement, it has gradually become the standard treatment

for glaucoma [7]. This procedure allows the outward drainage of atrial fluid under the lamellar scleral flap in glaucoma patients. By creating a new waterproof channel, the fluid can be drained into the subconjunctival space and then absorbed by the lymphatic vessels of the conjunctival tissue as well as capillaries, thereby reducing the IOP [8]. However, in the past with trabeculectomy, it has been difficult to control the tightness of the flap suture, which increases the risk of postoperative complications and can have a marked impact on the quality of the procedure as well as the outcome [9]. Compound trabeculectomy, however, is performed with improved materials and techniques, using adjustable sutures with mitomycin, which effectively reduces complications and improves outcomes [10]. Peripheral iridotomy has also been shown to be effective in patients with glaucoma by eliminating pupillary block, restoring the physiological atrial drainage circulatory system of the eye, and balancing anterior and posterior chamber pressures [11]. This procedure also causes less damage to patients' ocular tissues. It is simple to perform, and has fewer postoperative complications, which can promote faster recovery [12]. An association between homocysteine (Hcy) and retinal diseases including glaucoma and cataracts has also been shown [13]. Nevertheless, there are few studies on the effects of different treatments on Hcy levels in glaucoma patients.

This research compared the treatment efficacy of peripheral iridectomy with compound trabeculectomy in patients with primary angle-closure glaucoma, in the hope of providing some clinical evidence for future treatment.

Materials and methods

Patient data

We retrospectively assessed the clinical data of 104 patients with primary angle-closure glaucoma who were admitted from February 2020 to January 2022. Forty-nine of these patients treated by peripheral iridectomy were considered a research group, including 30 males and 19 females, with a mean age of (56.78±4.68) years and a disease duration of (4.49±2.08) months. The other 55 patients treated with compound trabeculectomy were used as a control group, including 28 men and 29 women, with a mean age of (56.00±4.25) years and a disease duration of (4.31±1.87) months. This study was approved by the Medical Ethics Committee (2019030), and all patients were informed and signed an informed consent form for the surgery.

Inclusion and exclusion criteria

Inclusion criteria: Patients met the diagnostic criteria of primary angle-closure glaucoma [14]; patients were 18 years old or older; patients used 1 to 3 IOP-lowering drugs with IOP >21 mmHg after medication; patients met the surgical indications; patients were monocular surgery cases; patients had a complete clinical profile.

Exclusion criteria: Patients suffered from other eye diseases such as keratoconus or uveitis; patients had a history of ocular trauma, internal ocular pathology or ocular surgery; patients had severe immune system disorders or coagulation disorders; patients had poor postoperative IOP control after receiving IOP-lowering drugs or even needed a second surgery; patients had systemic diseases requiring long-term application of glucocorticoids or other drugs that may affect the eye; patients had coexisting serious infectious or inflammatory diseases; patients were unable to tolerate or cooperate with the treatment.

Treatment options

The control group underwent compound trabeculectomy. Surface anesthesia was performed with oxybuprocaine hydrochloride eye drops (Santen Pharmaceutical Co., Ltd., lot number B2045), 1 time/5 min for 3 times. The eye was fixed with the aid of the superior rectus muscle, then tractioned, and a conjunctival flap was created at the appropriate corneal location to expose the sclera. A cotton pad soaked with mitomycin C dilution (Zhejiang Hisun Pharmaceutical Co., Ltd., lot number 2016062507) (concentration 0.2 mg/mL) was placed under the conjunctival flap and scleral flap for about 2 min, and then saline was injected into the cornea for cleaning. The trabecular meshwork tissue of approximately 3 mm×1 mm or 2 mm×1 mm in size was then excised, and the scleral flap was closed with 2 stitches at the top using 10-0 sutures, with 8-0 absorbable sutures on both sides of the sclera using an adjustable

suture technique, and finally the conjunctival flap was closed with 4 interrupted sutures.

The research group underwent peripheral iridectomy. Altogether 1% pilocarpine eye drops (Bausch & Lomb, lot number 20130803) were used in the eyes 10 min before surgery to narrow the pupils. The anesthesia was the same as the control group. A small L-shaped fornix-based conjunctival flap was made at 1:00 (right eye) or 11:00 (left eye) above the corneosclera, and the sclera was cauterized to stop the bleeding. At 1.5 mm from the corneal margin, 1/2 to 2/3 of the sclera was incised parallel to the corneal margin, and the incision was 3 mm long. The iris was dissected into the anterior chamber with a tunnel knife parallel to the scleral incision, and the posterior lip of the incision was compressed to release the iris. A balancing salt solution was used to wash out the pigment, reset the iris and restore the pupil to a round shape. The L-shaped conjunctival flap incision was aligned and fixed by cautery. Patients in both groups were treated promptly with antibiotics and Tobramycin and Dexamethasone Eye Ointment (Qilu Pharmaceutical, lot number 20190213). IOP was measured regularly.

Efficacy criteria

Patients were evaluated for treatment efficacy at 1 month postoperatively. Full control: IOP dropped to less than 21 mmHg with widened atrial angle, and there were no progressive changes in visual acuity, fundus or visual field. Partial control: IOP decreased to 21 mmHg-30 mmHg, with partial widening of atrial angle, and no progressive changes in visual acuity, fundus and visual field. Poor control: IOP was above 30 mmHg, with no significant change in atrial angle, or progressive impairment of visual acuity, fundus and visual field. Success rate = full control rate + partial control rate.

Outcome measures

Main outcome measures: (1) The efficacy of treatment was evaluated and compared between both groups at 1 month postoperatively. (2) Patients in both groups were counted for adverse reactions within one month after surgery, and the total incidence was calculated. (3) The preoperative and one-month postoperative vision, IOP and anterior chamber depth (ACD) were measured using an international standard vision chart, a Topcon CT-80 non-contact tonometer and a Nidec RS-3000 optical interference tomography scanner, respectively.

Secondary outcome measures: (1) To measure the Hcy and hypersensitivity C-Reactive Protein (hs-CRP) in patients before and 1 month after surgery, 3 mL of fasting venous blood was drawn from patients, and the serum was separated after centrifugation at 3 000 r/min for 10 min. Hcy was measured by luciferase assay (Abcam, USA, lot number ab228559), and hs-CRP was measured by enzyme-linked immunoassay (Sangon biological engineering, D711-314). The kits were purchased from Abcam, USA. (2) All patients were divided into an effective group and an ineffective group according to the treatment efficacy, and the Hcy and hs-CRP levels after treatment were compared between these two groups. The value of diagnostic efficacy of Hcy and hs-CRP after treatment was examined by plotting ROC curves. (3) The relationship between Hcy and hs-CRP and efficacy was analyzed by Pearson correlation coefficient.

Statistical methods

SPSS 19.0 statistical software was applied for data analysis. The measured data all conformed to a normal distribution and were expressed as mean ± standard deviation; t-test was used for comparison between groups, and paired t-test was for that within groups. The counted data were compared by X^2 test, and all statistical analyses were two-sided with a significance level set at 5%. The value of diagnostic efficacy of Hcy and hs-CRP after treatment was examined by plotting ROC curves. The relationship between Hcy and hs-CRP and efficacy was analyzed by Pearson correlation coefficient. Results were statistically significant if the *p*-value was less than 0.05.

Results

Patient baseline data

There was no statistical difference between both groups in terms of sex, age, course of disease, site, complicated cataract, atrial angle structure, crystalline thickness, educational background or place of residence (P>0.05), which showed that the two groups were comparable (**Table 1**).

Table 1. Baseline data

	Research group (n=49)	Control group (n=55)	X^2/t	P
Sex			1.118	0.290
Male	30 (61.22)	28 (50.91)		
Female	19 (38.78)	27 (49.09)		
Age (year)	56.8±4.7	56.0±4.3	0.891	0.375
Course of disease (month)	4.49±2.08	4.31±1.87	0.465	0.643
Site			0.965	0.326
Left eye	22 (44.90)	30 (54.55)		
Right eye	27 (55.10)	25 (45.45)		
Complicated cataract			0.618	0.432
Yes	12 (24.49)	10 (18.18)		
No	37 (75.51)	45 (81.82)		
Atrial angle structure			0.598	0.439
Fully closed	19 (38.00)	25 (45.45)		
Incompletely closed	31 (62.00)	30 (54.55)		
Crystalline thickness (mm)			0.199	0.656
<4.5	39 (79.59)	41 (75.93)		
≥4.5	10 (20.41)	13 (24.07)		
Educational background			1.553	0.460
Primary school and below	8 (16.33)	13 (23.64)		
Junior high school	28 (57.14)	25 (45.45)		
High school and above	13 (26.53)	17 (30.91)		
Place of residence			1.252	0.263
Cities and downs	37 (75.51)	36 (65.45)		
Countryside	12 (24.49)	19 (34.55)		

Comparison of efficacy in patients

The treatment success rate of the research group was 95.92%, which was higher 81.82% in the control group, and the difference was significant (P<0.05) (**Table 2**).

Comparison of adverse reactions in patients undergoing operation

Patients in both groups suffered adverse reactions such as anterior chamber hemorrhage, corneal edema, elevated IOP and iris damage after treatment, but did not experience serious adverse reactions. The overall incidence of adverse reactions was 8.16% in the research group and 23.64% in the control group. The overall adverse reaction rate in the research group was statistically lower than that in the control group (P<0.05) (**Table 3**).

Comparison of clinical indexes of patients before and after treatment

The vision, IOP and ACD of patients were observed before treatment and one month after surgery, and no marked difference was found between the two groups before treatment (P>0.05). One month after surgery, vision and ACD were dramatically higher (P<0.05) and IOP was lower (P<0.05) in both groups. The first two values were markedly higher (P<0.05) and IOP was lower (P<0.05) in the research group than those in the control group after surgery (**Figure 1**).

Changes in Hcy and hs-CRP levels before and after treatment

Hcy and hs-CRP levels before and 24 h after treatment were observed, with no obvious difference between groups before treatment (P>0.05). Both levels were dramatically lower after surgery (P<0.05), and the levels in the research group were lower than those in the control group (P<0.05) (**Figure 2**).

Relationship between efficacy and Hcy and hs-CRP levels

All patients were divided into effective and ineffective groups according to whether the treat-

Table 2. Comparison of efficacy

	Research group (n=49)	Control group (n=55)	X^2	P
Full control	26 (53.06)	26 (47.27)	0.347	0.556
Partial control	21 (42.86)	19 (34.55)	0.756	0.385
Poor control	2 (4.08)	10 (18.18)	5.047	0.025
Successful	47 (95.92)	45 (81.82)	5.047	0.025

Table 3. List of adverse reactions

	Research group (n=49)	Control group (n=55)	X^2	P
Anterior chamber hemorrhage	1 (2.04)	6 (10.91)		
Corneal edema	2 (4.08)	4 (7.27)		
Elevated IOP	0 (0.00)	1 (1.82)		
Iris damage	1 (2.04)	2 (3.64)		
Overall incidence of adverse reactions	4 (8.16)	13 (23.64)	4.537	0.033

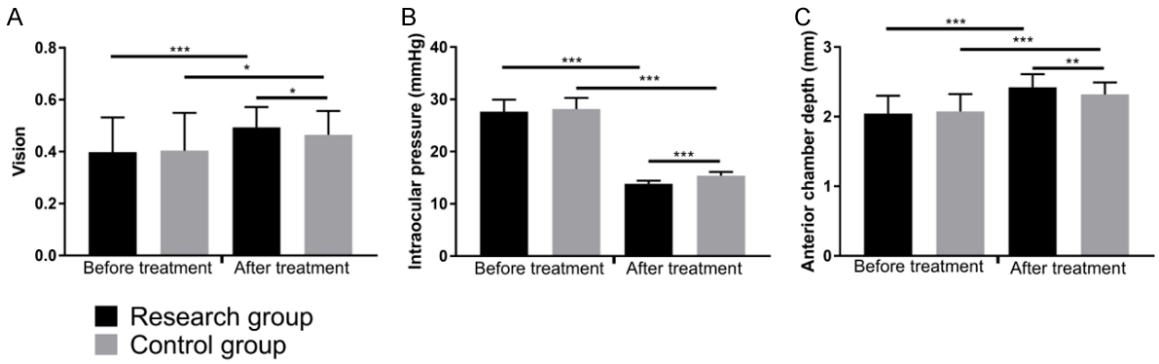

Figure 1. Comparison of clinical indicators before and after treatment. A. The vision of patients in both groups improved dramatically after treatment, and the improvement was better in the research group than in the control group (P<0.05). B. IOP was dramatically lower in both groups after treatment, and the IOP was lower in the research group than that in the control group (P<0.001). C. The ACD was dramatically higher in both groups after treatment, and the ACD was higher in the research group than that in the control group (P<0.01). *P<0.05, **P<0.01, ***P<0.001. IOP: intraocular pressure; ACD: anterior chamber depth.

ment was successful or not, and the Hcy and hs-CRP levels after treatment were compared. Both levels were much lowerin the effective group than those in the ineffective group (P<0.05). The ROC curves of the diagnostic efficacy of Hcy and hs-CRP after treatment manifested that the areas under the curve (AUC) were >0.7, indicating that both had good diagnostic value (**Figure 3**).

Correlation of Hcy and hs-CRP levels with patient outcomes

We detected the relationship between Hcy and hs-CRP and patient outcomes after treatment by Pearson correlation coefficient and found that both Hcy and hs-CRP levels were negatively correlated with patient outcomes (P<0.001), as shown in **Figure 4**.

Discussion

Closed-angle glaucoma is a type of glaucoma in which the peripheral iris blocks the trabecular meshwork or creates permanent adhesions to the meshwork, blocking the outflow of atrial fluid and causing an increase in intra-ocular pressure, IOP, which is a common irreversible blinding disease in ophthalmology [15, 16]. Patients with primary acute angle-closure glaucoma in a high IOP state are most likely to choose conservative treatment, i.e., the use of drugs to lower IOP. But the specific effect is not obvious, and there is also a large proportion of

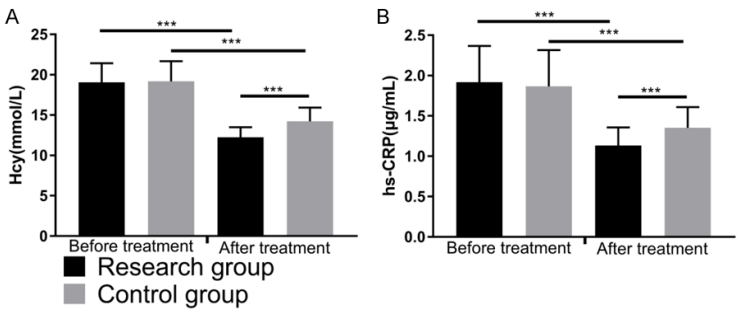

Figure 2. Changes in Hcy and hs-CRP levels before and after treatment in patients. A. Hcy was dramatically lower in both groups after treatment, and the Hcy was lower in the research group than that in the control group (P<0.001). B. hs-CRP was dramatically lower in both groups after treatment, and the hs-CRP was lower in the research group than that in the control group (P<0.001). ***P<0.001. Hcy: homocysteine; hs-CRP: hypersensitivity C-reactive protein.

patients whose IOP cannot be lowered and may also miss the optimal timing for Surgery [17, 18]. Trabeculectomy is a highly invasive surgical procedure that may affect patients' healthy ocular structures, with a high risk of injury and a high probability of postoperative complications [19]. Peripheral iridotomy combines the physiological structure and hydrodynamic properties of the eye with a deep scleral vertical excision of the trabecular strips along with an excisional treatment at the root of the peripheral iris, and the iris is excised to form a drainage port in the scleral flap to drain the anterior and posterior atrial fluid in the eye, thus effectively improving central ACD and atrial angle [20]. In this research, we compared the efficacy of peripheral iridectomy with compound trabeculectomy in the treatment of patients with primary angle-closure glaucoma.

First, our study revealed that the success rate of treatment was dramatically higher, while the incidence of postoperative adverse effects was lower in the research group than those in the control group. We also found that postoperative vision and ACD were dramatically higher and IOP was lower in the research group than those in the control group, which suggests that our peripheral iridectomy can better control IOP and improve vision compared with compound trabeculectomy. Accelerated subconjunctival fibrosis, abnormal endothelial cell proliferation and opening closure were mentioned as common causes of trabeculectomy failure in a study by D'cruz et al. [21], and iridotomy helps to control IOP and maintains corneal transparency. Kalala et al. [22] investigated the efficacy of deep sclerectomy and confirmed that this treatment had better local efficacy and safety, as well as lower costs when comparing with trabeculectomy, which is like our results.

We discovered that the Hcy and hs-CRP levels were dramatically lower in both groups after treatment, while the postoperative levels in the research group were lower than those in the control group. This suggests that our peripheral iridectomy has better anti-inflammatory effects when comparing with compound trabeculectomy. Optic nerve damage is the ultimate outcome of all types of glaucoma, whether it is mechanical damage directly brought about by elevated IOP or secondary to vascular damage and oxidative stress (OS), or even direct damage to ganglion cells by inflammatory factors, with increased OS and loss of retinal ganglion cells being the main features [23]. Inflammatory cytokines such as Hcy and hs-CRP, as participants in the inflammation of the body, have also been found to be relevant to the pathologic process of ocular diseases [24, 25]. OS is induced and elevated when patients are exposed to high concentrations of Hcy, while the proliferation of human trabecular meshwork cells is inhibited [26]. We compared the Hcy and hs-CRP levels of patients with different outcomes and found that those with successful outcomes had lower post-treatment levels, suggesting that patients with lower levels of inflammation tend to have better outcomes. The ROC curve plotted manifested that the AUC for diagnostic efficacy of Hcy after treatment was 0.742, and the AUC for diagnostic efficacy of hs-CRP was 0.830, both showing high diagnostic value.

Nevertheless, there are still some limitations in this study. We compared the efficacy of peripheral iridectomy with compound trabeculectomy for primary angle-closure glaucoma, and explored the role of Hcy and hs-CRP in patients, which may be involved in the mechanism for improving visual function in both treatments.

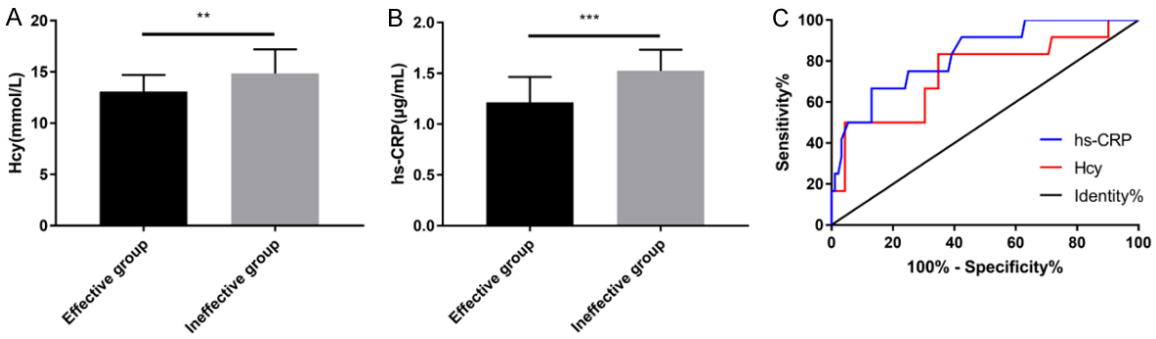

Figure 3. Relationship between efficacy and Hcy and hs-CRP levels. A. Patients in the effective group had dramatically lower Hcy level than those in the ineffective group (P<0.01). B. Patients in the effective group had dramatically lower hs-CRP level than those in the ineffective group (P<0.001). C. The area under the curve for the diagnostic efficacy of Hcy after treatment was 0.742, with a sensitivity and specificity of 83.88% and 65.22%, respectively. The area under the curve for the diagnostic efficacy of hs-CRP after treatment was 0.830, with a sensitivity and specificity of 66.67% and 86.96%, respectively. **P<0.01, ***P<0.001. Hcy: homocysteine; hs-CRP: hypersensitivity C-reactive protein.

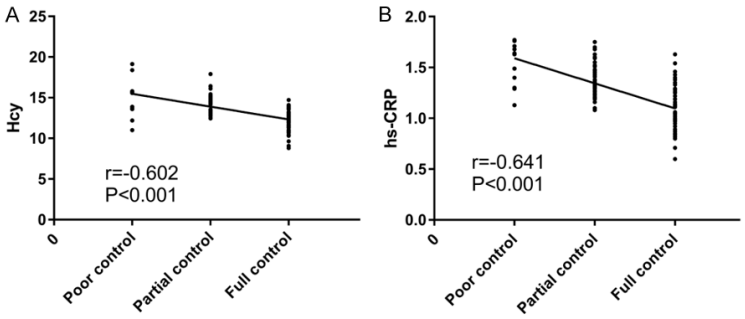

Figure 4. Correlation of Hcy and hs-CRP levels with patient outcome. A. Hcy was negatively correlated with patients' outcome (r=-0602, P<0.001). B. The hs-CRP was negatively correlated with efficacy (r=-0641, P<0.001). Hcy: homocysteine; hs-CRP: hypersensitivity C-reactive protein.

This research only looked at primary angle-closure glaucoma and has not yet observed other types of glaucoma, pending our further study. Besides, the combination of multiple procedures is also applied to treat patients with refractory or surgically unsuccessful glaucoma, and it is hoped that similar cases will be compared later.

To sum up, the efficacy and safety of peripheral iridectomy for the treatment of glaucoma is better than that of compound trabeculectomy. Monitoring the levels of Hcy and hs-CRP before and after operation can effectively evaluate the clinical efficacy.

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Disclosure of conflict of interest

None.

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