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CLINICAL INVESTIGATION

Efficacy and safety of intravenous injection of lidocaine in the treatment of acute primary angle-closure glaucoma: a pilot study

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Abstract
Aims To study the safety and effectiveness of a combination of both intravenous injection of lidocaine and intraocular pressure-lowering medications, in the intraocular pressure control and relief of symptoms of refractory acute primary angle-closure glaucoma (PACG).
Methods Five consecutive patients with their first attack of acute PACG, with intraocular pressure ≥45 mmHg and a failure to release from the attack under antiglaucomatous medications for 4 hours, were recruited into the study. On presentation, each patient received topical pilocarpine and timolol, and systemic acetazolamide and mannitol as primary treatment. Then the patients accepted 2% lidocaine by intravenous injection at dose of 0.8 mg/kg in concert with antiglaucomatous medications. The intraocular pressures after intravenous injection at 30 minutes, and then at 1, 2, 4, 12, and 24 hours, were documented by applanation tonometry. Symptoms, visual acuity, intraocular pressure, corneal edema, angle status on gonioscopy, pupillary size, and reaction were also measured.
Results Six eyes of five patients seen with acute PACG were recruited. The mean intraocular pressure was reduced from 50.83±5.34 mmHg to 39.5±3.45 mmHg at 30 minutes after intravenous injection, and then to 33.3±3.56 mmHg at 1 hour, and 24.55±5.09 mmHg at 2 hours after intravenous injection. The mean intraocular pressure was less than 21 mmHg at 4 hours and beyond. There was instant symptomatic relief for all patients. No complications were encountered.
Conclusions From this preliminary study, intravenous injection of lidocaine seems to be safe and effective in controlling intraocular pressure and eliminating symptoms in acute PACG. But the exact efficacy and safety need further investigation in large case studies.

Keywords Primary angle-closure glaucoma · Lidocaine · Intraocular pressure

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Acute primary angle-closure glaucoma (PACG) is a potentially blinding-led ocular disorder that is commonly regarded as an ocular emergency. Traditionally, treatment involves lowering the intraocular pressure with medications and then subsequently relieving the papillary by laser peripheral iridotomy [1]. Medical treatment may include the use of intravenous carbonic anhydrase inhibitor, hyperosmotic agent, topical pilocarpine, and β-blockers [2]. Prompt lowering of intraocular pressure is important, because on the one hand the symptoms are very unpleasant, and on the other, the persistently high intraocular pressure can also result in permanent closure of the chamber angle and irreversible optic nerve and endothelial cell damage [3–6].

From our experience, in approximately one third of the patients the combination of topical and systemic medications may fail to lower the intraocular pressure even after 1 to 3 days, requiring additional therapy such as argon laser peripheral iridoplasty, laser peripheral iridotomy, anterior chamber paracentesis or even filtering surgery for control [7, 8]. This may lead to many complications when intraocular pressure stays high.

Lidocaine is a widely used anesthetic agent frequently employed to attenuate the increase in intracranial pressure and intraocular pressure of patients receiving succinylcholine prior to intubation [9, 10].

We propose a method to rapidly reduce the intraocular pressure and to relieve symptoms in patients with acute PACG by performing intravenous injection of small-dosage lidocaine. The effect is not only instantaneous but lasting, unlike immediate argon laser peripheral iridoplasty and anterior chamber paracentesis [8, 11–13], and can be performed on those refractory cases under careful monitoring.

This study is designed to investigate whether intravenous injection lidocaine does create relief and cause a lowering of IOP in acute PACG.

Materials and methods

Prior approval of the study protocol by the Ethics Committee of the Wenzhou Medical College of China was obtained. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Inclusion criteria were: (1) patients with first attack of acute PACG presenting to the Eye Hospital of Wenzhou Medical, (2) intraocular pressure of ≥45 mmHg (by applanation tonometry), (3) duration of attack, as determined by the onset of symptoms, of 72 hours or less, (4) failure over 4 hours of a combination of topical and systemic medications fails to decrease the intraocular pressure, and (5) no other previous ophthalmic disorders that might have a persistent effect on the structure or function of the drainage angle.

Exclusion criteria included: (1) patients unable to cooperate for intravenous injection, (2) patients unable to give an informed consent, (3) patients who had received antiglaucomatous treatment before being seen by the authors, (4) the eye with acute PACG was the patient's only eye, (5) the cornea was clear enough for immediate laser peripheral iridotomy, (6) medical contraindication to systemic lidocaine, and (7) severe cardiovascular disease.

The study period was from October 2005 to April 2006. Informed consent was obtained from all participating patients. Ocular examination, including documentation of visual acuity, intraocular pressure, corneal edema, papillary size and reaction, and gonioscopic findings, was performed. The following topical medications were given to the involved eye: one drop of 2% pilocarpine every 5 minutes, followed by four times every hour; 1 drop of 0.5% timolol maleate gellan twice daily. In addition to topical medications, each patient also received slow-release oral acetazolamide, 500 mg twice daily and intravenous 20% mannitol (250 ml) over 1 hour. The intravenous injection of lidocaine was performed by one of the authors (An-quan Xue) with aseptic techniques. 2% lidocaine at a dose of 0.8 mg/kg (40 mg total) was administered over 3 minutes. After intravenous injection, the following topical and systemic antiglaucomatous medications were still administered: 2% pilocarpine 1 drop after injection and then four times every hour, 0.5% timolol maleate gellan 1 drop after injection and then twice daily. Each patient also received oral acetazolamide, 500 mg continuing the previous therapy (twice daily) and slow intravenous 20% mannitol (about 4 hours after the first injection). Intraocular pressure was measured by applanation tonometry before intravenous injection, immediately after intravenous injection, 15 and 30 minutes, and 1, 2, 4, 12, and 24 hours after intravenous injection. Visual acuity, corneal edema, pupillary size and reaction were documented 1, 2, 4, 12, and 24 hours after the intravenous injection. Gonioscopy was performed at 1 and 24 hours after the intravenous injection. Definitive laser iridotomy was carried out between 24 and 48 hours after intravenous injection. Patients were followed up for any complications arising from the treatment.

The blood pressure and heart rate were also recorded at the following times: basal, just before, immediately after the intravenous injection, 5 minutes later and 15 minutes later.

For comparison, another consecutive series of acute PACG patients fulfilling the same inclusion and exclusion criteria received the same medical treatment, from October 2005 to April 2006. This second series of patients was also recruited at the Eye Hospital of Wenzhou Medical College. The patients received the same treatment as the study group except intravenous injection. These patients had their intraocular pressure documented at presentation and before the second cycle of general medication, at 15 and 30 minutes, and 1, 2, 4, 12, and 24 hours after the second cycle medication.

They signed an informed consent allowing us to make the preceding intraocular pressure measurements. The intraocular pressure profiles and symptoms of this group of patients were compared with the series of patients receiving immediate intravenous injection of lidocaine and medications.

Results

Six eyes of five patients with their first acute PACG were recruited into the study. The demographics of this group of patients are summarized in Table 1. The duration of attack before presentation, as determined by the onset of symptoms, ranged from 18 to 68 hours (mean 39.6±19.31 SD). All five patients had severe eye pain. Three patients also were seen with nausea and vomiting, whereas another patient had nausea and headache. All five patients had no previous history of glaucoma or other eye treatments. All five patients were of Chinese ethnic origin, with dark brown irides. Iris bombé was seen in all patients, indicating the presence of pupillary block in all patients. All five patients had a fixed, middilated pupil of 4 to 7 mm (mean ± SD, 5.58±1.07 mm).

The intraocular pressures of all six eyes at various time points are presented in Table 2 (with the control eyes). All five patients had immediate relief of ocular pain, headache, nausea, and vomiting after intravenous injection, with no recurrence of pain over the next 24 hours.

Table 3 summarizes the grading of corneal edema in the six eyes at various time points.

The pupils were "unreactive" to "very sluggish" in all six eyes before intravenous injection. All six eyes showed constrictive response to the topical pilocarpine at 2 hours after intravenous injection. Table 4 summarizes the pupil sizes of these patients at various time points.

On repeating gonioscopy at 1 hour after intravenous injection, it was interesting to note that the drainage angle had already opened up to Shaffer grade I in one patient. The drainage angle remained closed in all other patients at 1 hour after gonioscopy. At 24 hours after intravenous injection, the drainage angle was Shaffer grade II in two patients and grade I in one patient. The drainage angle remained very narrow in all other patients at 24 hours.

Table 1 The demographics of the two consecutive series of eyes with acute primary angle-closure glaucoma

Treatment groups	Intravenous injection + medical therapy	Medical therapy alone
Number of eyes	6	6
Number of patients	5	6
Age/yrs (mean ± 1 SD)	56.60±10.01	57.50±8.19
Age range/yrs	46 to 69	48 to 68
Male/female	1:4	2:4
Left/right eyes	2:4	3:3
Duration of attack/hrs (mean ± 1 SD)	39.60±19.31	39.33±18.40

SD=standard deviation.

The visual acuity at presentation ranged from 20/50 to counting fingers. Five of the six eyes had visual acuity of 20/200 or less at the time of presentation. At just 1 hour after intravenous injection, the visual acuity ranged from 20/50 to 20/200. The eye with the worst visual acuity of 20/200 at 1 hour had a preexisting age-related macular degeneration. At 2 hours, the visual acuity ranged from 20/30 to 20/100. The visual acuity at 2 hours was already comparable to those of the fellow eyes in those patients with unilateral attack (range, 20/30–20/70), with cataract explaining the poorer of these visual acuities.

Table 5 summarizes blood pressure and heart rate before and after intravenous injection.

For comparison, another consecutive series of six eyes with acute PACG (six patients) fulfilling the same inclusion and exclusion criteria received the continued medical treatment and were recruited between October 2005 and April 2006. The demographics of this group of patients are summarized alongside those of the intravenous injection patients in Table 1. There were no statistically significant differences in age (P=0.164), duration of attack (P=0.681), and the initial intraocular pressure (P=0.954) between this group of patients and the series receiving intravenous injection using the t-test. All six patients were initially seen with severe eye pain. Five of the six patients also had nausea and vomiting at presentation. All six patients were of Chinese ethnic origin, with dark brown irides. The mean intraocular pressure profile of this group of patients is plotted alongside the mean intraocular pressure profile of the five patients treated with immediate intravenous injection in Table 2. Three of the six patients receiving medical treatment alone still had ocular pain at 1 hour after commencement of treatment.

All six patients with nausea and vomiting at presentation had their nausea and vomiting resolved by 1 hour after the start of medical therapy.

Discussion

Pretreatment with lidocaine partially blunts the intraocular pressure increase from succinylcholine, and blunts the further increase from intubation. In clinical conditions we also found that intravenous lidocaine can help topical pilocarpine contract the pupil quickly during the surgery.

On the basis of these findings, we have postulated that a combination of both intravenous injection of lidocaine and intraocular pressure-lowering medications in a situation with grossly raised intraocular pressure which cannot be aborted by routine primary antiglaucoma medication in a limited time—as in acute PACG—should result in both an immediate and sustained control of intraocular pressure. The unique advantage of intravenous injection of lidocaine,

Table 2 Intraocular pressures (mmHg) in the eyes of the two groups with or without intravenous injection

injection *Eyes*	At presentation	4 hrs (before injection)	4.5 hrs (0.5 hrs after injection)	5	6	8	16	28
1	73	56	45	38	28	10	10	8
2	70	58	40	36	31	22	14	15
3	66	49	41	35	24	16	15	14
4	60	51	35	30	19	12	10	11
5	58	47	39	32	26	15	15	14
6	55	44	37	29	18	15	14	13
Mean	63.67	50.83	39.50	33.33	24.33	15	13	12.50
1 SD	7.12	5.34	3.45	3.56	5.09	4.1	2.37	2.59
Comparison eyes	At presentation	4 hrs	4.5 hrs	5	6	8	16	28
1	72	56	48	42	34	38	Trabeculectomy	
2	68	49	45	41	32	36	argon laser peripheral iridoplasty	
3	67	55	49	35	21	12	10	11
4	64	43	39	38	30	22	argon laser peripheral iridoplasty	
5	56	48	45	35	31	15	15	14
6	52	42	38	31	25	15	14	13
Mean	63.17	48.83	44.00	37.00	28.83	23.00		
1 SD	7.65	5.85	4.56	4.15	4.88	11.35		
t	0.12	0.62	1.93	1.64	1.57	1.62		
P	0.96	0.85	0.37	0.74	0.94	0.017		

SD=standard deviation.

in addition to the conventional topical and systemic medical regimen, in the management of acute PACG lies in the rapidity of intraocular pressure control and almost instantaneous relief of the severe symptoms. All five patients receiving intravenous injection had immediate relief of severe ocular pain, headache, nausea, and vomiting, with no recurrence of the symptoms. This is welcomed by every patient.

In comparison, three of the six patients receiving medical treatment alone still had ocular pain 1 hour after commencement of treatment, and three of the six patients had accepted argon laser peripheral iridoplasty or trabeculectomy because of the uncontrolled intraocular pressure. The results indicate that intravenous injection of lidocaine may help lower the intraocular pressure and relieve the symptoms in PACG. The intraocular pressure approximately one third of the patients does not return to the normal level in our clinical practice. When the combination of topical and systemic medications fails to decrease the intraocular pressure, surgery, anterior chamber paracentesis or laser peripheral iridotomy may be the selected choice. In an eye with acute PACG, the anterior chamber is already very shallow. Immediate argon laser peripheral iridoplasty can lower intraocular pressure and relieve symptoms in

Table 3 The grading of corneal edema in the six acute primary angle-closure glaucoma eyes treated by intravenous injection at various time points

Grading of corneal edema at various time points in relation to intravenous injection						
Eyes	At presentation	1 hour	2 hours	3 hours	12 hours	24 hours
1	3.0	2.0	1.5	1.5	0.0	0.0
2	3.0	2.5	1.5	1.0	0.0	0.0
3	3.0	2.5	0.5	0.0	0.0	0.0
4	2.5	2.0	0.0	0.0	0.0	0.0
5	2.5	2.0	1.0	1.0	0.0	0.0
6	2.5	1.5	0.0	0.0	0.0	0.0

Grading for corneal edema: grade 0- no corneal edema; grade 1- only mild corneal haze noted; grade 2-iris details blurred; grade 3-iris details only vaguely visible; grade 4-iris details not visible.

Table 4 The pupil sizes in the six acute primary angle-closure glaucoma eyes treated with intravenous injection at various time points

Pupil sizes at various time points in relation to intravenous injection /millimeter						
Eyes	At presentation	1 hour	2 hours	3 hours	12 hours	24 hours
1	7.0	3.0	2.0	2.0	2.0	1.5
2	5.0	4.0	3.5	3.5	2.0	2.0
3	5.5	3.5	3.0	3.0	3.0	2.5
4	6.5	4.5	2.5	2.0	2.0	1.5
5	5.5	3.0	2.5	1.0	1.0	1.0
6	4.0	3.5	2.0	1.0	1.0	1.0
Mean	5.58	3.58	2.58	2.08	1.83	1.58
SD	1.07	0.58	0.58	1.02	0.75	0.58

SD=standard deviation.

acute PACG almost as rapidly [11–13], but the argon laser may not be performed on the some edema cornea. The effect of anterior chamber paracentesis is expected to be transient [7]. Paracentesis may make the anterior chamber even shallower, thus allowing the iris–lens diaphragm to come further forward. This may result in malignant glaucoma or aggravate a preexisting aqueous misdirection. It is envisaged that ophthalmology residents or nurses may also be competent enough to perform an effective and safe intravenous injection.

We report on a series of patients with attack of acute angle-closure glaucoma who were aborted dramatically with intravenous lidocaine treatment. An extensive literature search using MEDLINE found no previous descriptions of this. We speculated that the underlying mechanisms for the reduction in intraocular pressure following intravenous lidocaine may stem from a direct effect on cerebral reflex sympathetic response, changes in intraocular circulation, or alterations in ocular muscle tone. A clinical observation we have also noted is the heightened sensitivity of the pupil to pilocarpine-induced miosis following intravenous lidocaine. The immediate decrease in intraocular pressure can promptly relieve the pain and help sleep in the patients, which leads to further reductions in intraocular pressure. The effect of lidocaine in reduction of intraocular pressure may be multifactorial, but the result was obvious in these patients.

Most of the side effects of injected lidocaine were related to the cardiovascular system and nervous system. So we monitored the blood pressure and heart rates as objective indicators, and at the same time observed the other possible responses to the injection. To minimize systemic exposure and toxicity, a low dosage of lidocaine was used in all patients. Although we encountered no complications in this small series of patients, certain potentially serious complications are conceptually possible from intravenous injection of lidocaine, so this method should be performed under careful monitoring. In this study, small-dosage lidocaine obtained positive results; it is still unknown whether a medium to high dose may be more helpful.

In conclusion, this preliminary study suggests that intravenous injection of lidocaine, in addition to the conventional systemic and topical intraocular pressure-lowering medications, can much more rapidly control intraocular pressure and relieve symptoms in patients with acute PACG. Intravenous injection of lidocaine seems to be safe in this pilot study. A large-scale prospective trial, with longer follow-up, seems warranted to more clearly define its role in treating acute PACG.

Table 5 Blood pressure and heart rate (HR) in the five patients treated with intravenous injection

	Patients at presention		Just before		Immediately after		5 minutes		15 minutes	
	BP(Kpa)	HR(times/min)	BP	HR	BP	HR	BP	HR	BP	HR
1	18.0/11.0	85	18.5/10.5	83	18.0/10.0	75	18.5/10.0	78	17.0/9.0	75
2	14.0/8.5	65	15.0/8.0	77	15.0/8.0	80	14.5/7.5	75	15.0/8.0	70
3	19.0/10.5	70	18.0/10.5	75	18.0/10.5	78	18.5/10.0	83	18.0/9.5	76
4	16.5/9.0	82	16.0/9.0	85	15.5/8.5	68	15.0/8.0	67	15.0/8.5	80
5	15.0/8.0	75	14.0/7.5	76	14.5/7.0	78	15.0/8.0	70	15.5/8.0	65
Mean	16.40/9.40	75.40	16.30/9.1	79.20	16.00/8.80	75.80	16.20/8.70	74.60	16.00/8.60	73.20
SD	2.07/1.29	8.26	1.92/1.39	4.49	1.87/1.44	4.71	1.89/1.20	6.35	1.41/0.765	5.81

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