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ORIGINAL ARTICLE

# Anterior Chamber Paracentesis Facilitates Laser Peripheral Iridotomy and Restores Vision in Mild-to-moderate Acute Primary Angle-closure Glaucoma

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#### **KEY WORDS:**

acute primary angle-closure glaucoma; anterior chamber paracentesis; intraocular pressure; mannitol infusion; visual acuity **Purpose:** Acute primary angle-closure glaucoma (PACG) is an ocular emergency that commonly presents in Asian populations. For patients with contraindications for mannitol infusion, it is imperative to perform an alternative therapy in order to rapidly decrease intraocular pressure (IOP) and prevent further visual complications. The purpose of this study is to evaluate the therapeutic efficiency of anterior chamber paracentesis (ACP) and mannitol infusion in patients with PACG.

**Methods:** Patients who suffered from their first attack of acute PACG when receiving ACP or mannitol infusion (20%, 300 mL) were included. They were divided into three subgroups: mild, moderate, or severe acute PACG, according to each patient's initial IOP upon presentation (mild group, 45–50 mmHg; moderate group, 50–60 mmHg; severe group, >60 mmHg). IOP at multiple time points, best-corrected visual acuity (BCVA), severity of corneal edema, and waiting time for laser peripheral iridotomy (LPI) were recorded.

**Results:** Compared with mannitol infusion (n = 29), ACP treatment (n = 30) achieved more rapid and effective IOP control within 2 hours, resulted in faster regression of corneal edema (grade:  $0.98 \pm 0.729$  [ACP] vs.  $1.50 \pm 0.720$  [mannitol], p = 0.011), and patients were able to undergo LPI within a reasonable amount of time ( $1.4 \pm 0.93$  days [ACP] vs.  $2.5 \pm 1.17$  days [mannitol], p = 0.0002). All patients who received ACP or mannitol demonstrated improved BCVA within 2 weeks. Intriguingly, ACP restored visual acuity more effectively than mannitol infusion in patients with an initial IOP lower than 60 mmHg. **Conclusion:** ACP effectively treats acute PACG by rapidly stabilizing the anterior chamber. When the

initial IOP is above 60 mmHg, ACP should only be considered when mannitol is contraindicated.

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#### 1. Introduction

Acute primary angle-closure glaucoma (PACG) is an ocular emergency that often presents in Asian populations.<sup>1,2</sup> In Asia, PACG afflicts 3.5 million people and 28 million have gonioscopically narrow anterior chamber angles. Patients in their 60s and 70s are at the greatest risk of developing PACG.<sup>1,3</sup> Patients with acute PACG often suffer from the sudden onset of blurred vision accompanied by severe ocular pain, headache, and even vomiting due to the rapid elevation of intraocular pressure (IOP) that occurs as a consequence of a suddenly occluded drain. Delayed treatment leads to irreversible

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damage to the corneal endothelium, optic nerve, and other intra-ocular structures.  $\!\!\!^4$ 

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Corneal edema, fixed semidilated pupils, and a shallow anterior chamber are the typical signs of acute PACG.<sup>5</sup> Immediate intravenous administration of mannitol, a hyperosmotic agent, is the standard treatment.<sup>6</sup> However, alternative treatments should be considered if the patient is at high risk of a reaction to mannitol, such as congestive heart failure, chronic renal insufficiency, or other systemic illnesses.<sup>7–9</sup>

In order to relieve the symptoms and lower IOP as quickly as possible, immediate anterior chamber paracentesis (ACP) has recently been suggested as an alternative treatment for patients with acute PACG.<sup>10–12</sup> In ACP, the aqueous humor is rapidly drained from the anterior chamber and the intraocular pressure decreases immediately. However, the volume of aqueous humor that should

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be drained is still controversial. In addition, the efficacy of lowering IOP and the visual outcomes that result from ACP are unclear. The aim of this study was to evaluate the therapeutic efficacies of ACP and mannitol infusion in patients with acute PACG, taking into account IOP stabilization, corneal condition, timing of laser peripheral iridotomy (LPI), and visual outcomes.

## 2. Methods

# 2.1. Inclusion and exclusion criteria

Approval from the institutional review board of Wan Fang Hospital of Taipei Medical University was obtained prior to the commencement of this prospective study. We collected cases reports of PACG that occurred during January 2007 to December 2009. The inclusion criteria included the following: 1) first attack of acute PACG; 2) initial presentation of IOP higher than 45 mmHg; 3) confirmation of diagnosis by gonioscopic examination; and 4) symptom onset within 48. hours. Patients were excluded if they had 1) been incompletely followed up within 2 weeks of presenation; 2) been using antiglaucoma medications before ACP or mannitol infusion; 3) previous intraocular surgeries on the same eye; 4) contraindicators for the use of mannitol; or 5) other visionthreatening ocular diseases.

Best-corrected visual acuity (BCVA), IOP, and severity of corneal edema in the affected eye were recorded before treatment. IOP was measured three times at each time point using a pneumotonometer (NIDEK NT-2000, Aichi, Japan). Visual acuity was reported in decimals using the E-chart of an automatic chart projector (NIDEK CP-690). Severity of corneal edema was evaluated according to previously reported criteria<sup>9</sup>: grade 0, no corneal edema; grade 1, only mild corneal haze; grade 2, blurred iris details; and grade 3, iris details are only vaguely visible.

#### 2.2. ACP and mannitol infusion

Patients were randomly divided into the ACP and mannitol groups according to the surgeon's decision. Written informed consent was obtained from each patient before receiving ACP or mannitol. We further divided the patients into three sub-groups within the ACP and mannitol groups based on their initial IOP value (Table 2).

For ACP, patients were placed in the supine position and disinfected with 5% povidone-iodine after the administration of 0.5% Alcaine (Alcon Laboratories, Fort Worth, TX, USA) as a local anesthetic. A sterile 27-gauge needle was inserted into the anterior chamber using the temporal clear-corneal approach. For group 1, 0.05 mL of the aqueous humour was drained, 0.10 mL for group 2, and 0.20 mL for group 3. After ACP, 0.3% topical ciprofloxacin (Alcon) was administered immediately and every 10 minutes for the next 30 minutes. For mannitol treatment, patients received 300 mL of 20% mannitol (60 gm/bottle; Shinlin Sinseng Pharmaceutical Co. Ltd., Taoyuan, Taiwan) via rapid intravenous infusion.

After the administration of ACP or mannitol, the conditions of the eye were recorded daily until LPI could be performed and the cornea became clear (corneal edema: grade 0). Miosis was achieved by administering three drops of 2% pilocarpine (Alcon) within 10 minutes prior to LPI using an Nd:YAG laser (NIDEK YC-1800).

# 2.3. Evaluation of changes in IOP, BCVA, and corneal edema after ACP and mannitol infusion

IOP was measured at 30 minutes, 1 hour, 2 hours, 1 day, 3 days, 1 week, and 2 weeks after ACP or mannitol infusion; BCVA was reevaluated at 30 minutes, 1 day, 3 days, 1 week, and 2 weeks after ACP or mannitol infusion; and the grade of corneal edema was observed daily and 30 minutes before LPI. In addition, complications such as endophthalmitis, intraocular trauma, choroidal effusion, and choroidal hemorrhage were also recorded.

#### 2.4. Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Science version 10 software (SPSS Inc., Chicago, IL, USA). Differences in age, time course of BCVA, time course of IOP, and time between of LPI administration and ACP or mannitol infusion were analyzed using two-tailed, non-paired *t* tests and p < 0.05 was considered statistically significant. The gradient of corneal edema following ACP and mannitol infusion was analyzed using twotailed, Wilcoxon rank sum tests and p < 0.05 was considered statistically significant. Comparisons of the differences between groups 1, 2, and 3, in terms of initial BCVA, initial IOP, and the amount that IOP was lowered by ACP, was carried out using the analysis of variance (ANOVA) test and Tukey's posthoc tests at 95% confidence intervals.

#### 3. Results

According to the inclusion and exclusion criteria, 30 eyes of 30 patients (20 male, 10 female) aged 28–88 years (mean age: 56.5 years) were included in the ACP group; 29 eyes of 29 patients (16 male, 13 female) aged 24–90 years (mean age: 63.2 years) were included in the mannitol group. There were no significant differences in terms of age, BCVA, IOP, and grade of corneal edema between the ACP and mannitol groups at initial presentation. Detailed patient profiles that were composed before ACP and mannitol infusion are summarized in Table 1.

To further analyze the effect of IOP on the therapeutic effects of ACP and mannitol, we divided the patients into three subgroups: mild, moderate, and severe acute PACG, according to IOP at initial presentation as described in the Material and Methods section. No significant differences in initial IOP level, initial BCVA, and initial grade of corneal edema were found between any subgroups of the ACP and mannitol groups (Table 2). Patients with severe acute PACG demonstrated the worst initial BCVA and the most severe corneal edema, followed by patients with moderate and mild acute PACG (Table 2). No complications, such as endophthalmitis, intraocular trauma, choroidal effusion, or choroidal hemorrhage occurred following ACP, and no systemic complications were noted after ACP or mannitol infusion in this study.

#### 3.1. ACP rapidly stabilized IOP

ACP promptly stabilized IOP within 30 minutes, while mannitol gradually lowered IOP (Figure 1A). As shown in Figure 1A, ACP

Table 1	Summery	of patient data	before treatment
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	Mannitol	ACP	P value
Case number (n)	Total = 29	Total = 30	
Gender	M:F = 16:13	M:F = 20:10	
Glaucoma eye	OD:OS = 14:15	OD:OS = 16:14	
Age (y/o) (Mean $\pm$ SD)	$63.2 \pm 7.48$	$56.5\pm7.59$	0.099
Initial BCVA (Mean $\pm$ SD)	$0.16\pm0.103$	$0.14 \pm 0.079$	0.675
Initial IOP (mmHg) (Mean $\pm$ SD)	$54.8\pm3.69$	$\textbf{57.6} \pm \textbf{3.98}$	0.621
Initial gradient of corneal edema (Mean $\pm$ SD)	$2.47\pm0.730$	$2.62\pm0.690$	0.507

ACP: anterior chamber paracentesis; SD: standard deviation; M: male; F: female; BCVA: best-corrected visual acuity; IOP: intraocular pressure; Gradient of corneal edema: 0: no corneal edema; 1: only mild corneal haze noted; 2: iris details blurred; 3: iris details only vaguely visible.

Table 2 Summery of data in each group before treatment

	Mild	Moderate	Severe			
Case number (n)						
Mannitol	10	9	10			
ACP	8	8	12			
Initial IOP (mmH	Ig) (Mean $\pm$ SD)					
Mannitol	$47.9 \pm 1.52$	$53.8 \pm 2.99$	$62.8\pm5.81$			
ACP	$48.8\pm2.50$	$55.4 \pm 3.37$	$65.7 \pm 3.89$			
Initial BCVA (Me	$an \pm SD$ )					
Mannitol	$0.27\pm0.063$	$0.14\pm0.039$	$\textbf{0.04} \pm \textbf{0.010}$			
ACP	$0.27\pm0.041$	$\textbf{0.18} \pm \textbf{0.049}$	$0.03\pm0.017$			
Initial gradient of corneal edema (Mean $\pm$ SD)						
Mannitol	$1.95\pm0.438$	$2.61\pm0.858$	$\textbf{2.89} \pm \textbf{0.580}$			
ACP	$\textbf{2.11} \pm \textbf{0.334}$	$\textbf{2.50} \pm \textbf{0.612}$	$\textbf{3.08} \pm \textbf{0.668}$			

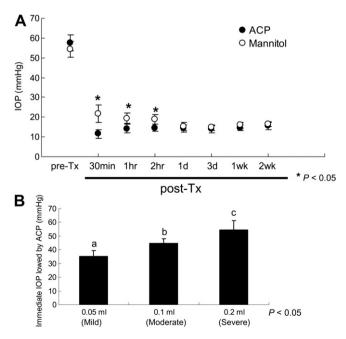
Initial IOP of mild acute PACG: 45 mmHg  $\leq$  mild  $\leq$  50 mmHg.

Initial IOP of moderate acute PACG: 50 mmHg < moderate  $\leq$  60 mmHg. Initial IOP of severe: 60 mmHg < severe.

demonstrated better IOP control than mannitol in the first 2 hours after treatment. In addition, the immediate (30 minutes after ACP) drop in IOP demonstrated by ACP was associated with the volume of aqueous humor that was drained (Figure 1B). The removal of 0.05 mL aqueous humor resulted in an IOP reduction of  $35.3 \pm 4.14$  mmHg, removal of 0.10 mL resulted in a reduction of  $44.76 \pm 3.15$  mmHg, and removal of 0.20 mL resulted in a reduction of  $54.45 \pm 6.69$  mmHg (Figure 1B).

## 3.2. Corneal edema rapidly subsided after ACP

The severity of corneal edema was scored before and 30 minutes after ACP or mannitol infusion. The grade of corneal edema was  $2.62 \pm 0.690$  in the ACP group and  $2.47 \pm 0.730$  in the mannitol group before treatment. However, the grade of corneal edema in the ACP group ( $0.98 \pm 0.729$ ) was significant lower than that of the



**Figure 1** Rapid stabilization of IOP after ACP. (A) ACP demonstrated better IOP control than mannitol infusion in the first 2 hours after treatment (*t* test, \**p* < 0.05). (B) The immediate decrease in IOP caused by ACP was associated with the volume of aqueous humor that was drained (ANOVA with Tukey's post-hoc tests at 95% confidence intervals; different letters represented different levels of significance).

mannitol group (1.50  $\pm$  0.720; p = 0.011) at 30 minutes after treatment (Figure 2A). Changes in corneal edema that occurred in mild, moderate, and severe cases of acute PACG were further analyzed. Before treatment, there were no significant differences in the severity of corneal edema between the three subgroups of the ACP and mannitol groups (Tab. 2). Moreover, after treatment, the gradient of corneal edema in patients with mild acute PACG in the ACP group (0.67  $\pm$  0.750) was significantly lower than that of the corresponding mannitol group (1.17  $\pm$  0.433) (p = 0.004, Figure 2B). The severities of corneal edema in the patients with moderate and severe acute PACG were not significantly different at 30 minutes after mannitol and ACP treatment (moderate acute PACG: mannitol vs. ACP; 1.63  $\pm$  0.744 vs. 1.17  $\pm$  0.683; p = 0.228, respectively, Figure 2C; for severe acute PACG: 1.70  $\pm$  0.856 vs. 1.17  $\pm$  0.707; p = 0.190, respectively, Figure 2D).

#### 3.3. ACP facilitated early LPI

Overall, LPI was performed 2.5  $\pm$  1.17 days after mannitol infusion and 1.4  $\pm$  0.93 days after ACP (p = 0.0002) (Figure 3A). In patients with mild acute PACG, LPI was performed 2.2  $\pm$  0.98 days after mannitol infusion and 1.2  $\pm$  0.84 days after ACP (P = 0.032) (Figure 3B); in patients with moderate acute PACG, 2.8  $\pm$  1.10 days versus 1.6  $\pm$  1.14 days were required, respectively (P = 0.033) (Figure 3C); in severe acute PACG, 2.5  $\pm$  1.44 days versus 1.4  $\pm$  0.90 days were required, respectively (p = 0.043) (Figure 3D).

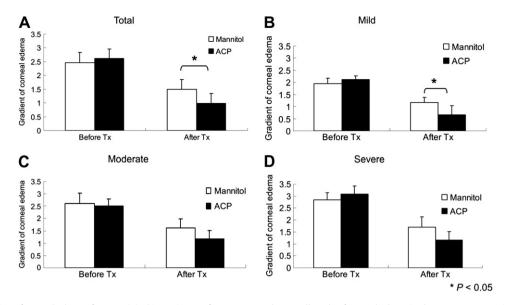
# 3.4. ACP restored visual acuity in patients with an initial IOP of less than 60 mmHg

The time course of BCVA is shown in Figure 4. Overall, there was no significant difference in the prognosis of BCVA between ACP and mannitol treatment (Figure 4A). However, the restoration of visual acuity was different between subgroups. In patients with mild acute PACG, ACP resulted in significantly better visual recovery during the first 2 weeks (Figure 4B). In patients with moderate acute PACG, ACP resulted in a better visual acuity than mannitol, similar to mild group (Figure 4C). Unfortunately, for patients with an initial IOP of greater than 60 mmHg (severe acute PACG), the BCVA of the ACP group was significantly lower than the mannitol group (Figure 4D).

#### 4. Discussion

To the best of our knowledge, this is the first study to show that ACP, when compared to mannitol infusion, more effectively improves the visual acuity of acute patients with PACG and an initial IOP of below 60 mmHg. This was achieved through rapid stabilization of the anterior segment by immediately reducing IOP, rapidly decreasing corneal edema, and allowing LPI to be performed earlier.

In this study, we demonstrated that ACP can effectively control IOP within 2 hours. Upon initiation of ACP, IOP rapidly decreased, followed by a slight rebound, then became stable after 1 hour (Figure 1A), which is compatible with previous reports in the literature.<sup>10</sup> It has been postulated that the main advantage of ACP is its ability to rapidly control IOP and relieve symptoms<sup>10,13</sup>; ACP is, therefore, an alternative therapeutic strategy for PACG patients who are contraindicated for mannitol infusion.<sup>10,11</sup> However, in order to achieve therapeutic effects, the minimum amount of aqueous humor that needs to be drained remains unknown. Although the draining of 0.05–0.2 mL of aqueous humor that should be removed is not clear. We found that IOP reduction was dependent on the volume of drained aqueous humor (Figure 1B). From the results of this study, we suggested that 0.05 mL aqueous humor be

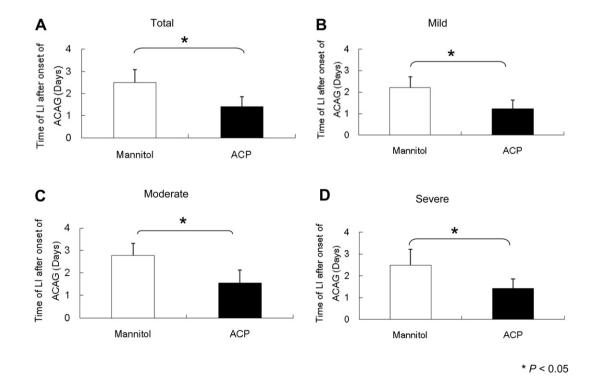


**Figure 2** Rapid regression of corneal edema after ACP. (A) Thirty minutes after treatment, the overall grade of corneal edema in the ACP group was significantly lower than in mannitol group. (B) In patients with mild acute PACG, ACP was more effective in decreasing corneal edema than mannitol. (C, D) In moderate (C) and severe (D) acute PACG, no differences in the severity of corneal edema were found between the ACP and mannitol groups (Wilcoxon rank sum test, \*p < 0.05).

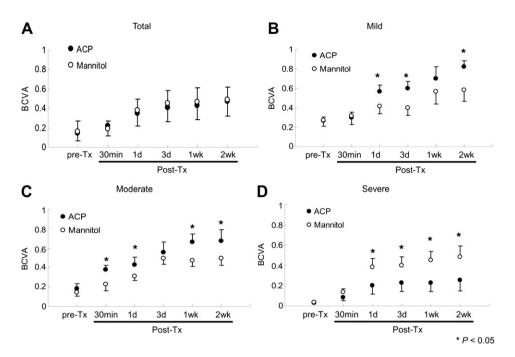
drained from the anterior chamber via ACP in PACG patients with an initial IOP below 50 mmHg; 0.10 mL can be drained from patients with an initial IOP between 50–60 mmHg.

Corneal edema is an important indication of elevated IOP.<sup>3,5</sup> Upon acute IOP elevation, increased pressure on corneal endothelial cells results in irreversible corneal endothelial cell loss.<sup>15–18</sup> In the current study, we showed that the higher the level of initial IOP, the more severe the corneal edema (Tab. 2). The overall grade of corneal edema after ACP treatment was significantly lower than after mannitol infusion (Figure 2A), indicating that ACP more effectively improves the condition of the cornea, especially when the initial IOP is below 50 mmHg (Figure 2B). For patients with an initial IOP above 50 mmHg, the difference in the grade of corneal edema measured 30 minutes after treatment was insignificant between the ACP and mannitol groups (Figure 2C and D), which may have been due to the initial severity of corneal edema in patients with moderate and severe acute PACG.

LPI is the standard therapeutic procedure for treating acute PACG,  $^{5,12,19-21}_{5,12,12}$  and it should be performed as soon as the cornea is clear.  $^{21,22}$  Consequently, rapid regression of corneal edema



**Figure 3** Facilitation of the early application of LPI by ACP. (A) Compared with mannitol infusion, ACP facilitated earlier LPI application in patients with acute PACG. Similar results were found in patients with mild (B), moderate (C), and severe (D) acute PACG (*t* test, \**p* < 0.05).



**Figure 4** Good restoration of visual acuity by ACP when patients presented with an initial IOP below 60 mmHg. (A) In the first 2 weeks after acute PACG, the difference in the overall prognosis of BCVA between the ACP and mannitol groups was insignificant. ACP resulted in significantly better visual recovery in patients with mild (B) and moderate (C) acute PACG, but worse visual outcomes were noted in patients with severe acute PACG (D) (*t* test, \*p < 0.05).

facilitates the early application of LPI. We showed that ACP not only rapidly reduces corneal edema, but also facilitates early LPI application (Figure 3). It has been reported that the early application of LPI stabilizes the anterior segment, thereby avoiding papillary blocks and preventing the recurrence of acute glaucoma.<sup>22-25</sup> Because ACP effectively shortened the waiting time for LPI and prevented prolonged corneal edema, it thereby facilitated the recovery of visual acuity.<sup>26</sup> However, it has been reported that the potential complications of ACP, including choroidal detachment and ischemic-reperfusion injuries that occur during rapid IOP reduction, can hamper the recovery of visual acuity.<sup>27-29</sup> In our study, although there were no significant differences between the mean sequential BCVA of the ACP and mannitol groups (Figure 4A), patients with an initial IOP of below 60 mmHg who underwent ACP treatment showed significantly better visual outcomes than those who received mannitol (Figure 4B and C). Surprisingly, in patients with acute PACG and an initial IOP above 60 mmHg, ACP did not show a significant, beneficial effect on visual outcomes (Figure 4D), despite the fact that ACP still facilitated the early application of LPI in these patients (Figure 3D), thereby indicating the possibility that ischemic-reperfusion injuries are induced by ACP when the initial IOP is higher than 60 mmHg.

Although no patients developed complications such as endophthalmitis, intraocular trauma, choroidal effusion, or choroidal hemorrhage after ACP, patients with severe acute PACG developed more ischemic-perfusion injuries than patients with mild or moderate acute PACG after ACP due to the rapid reduction in IOP and the large volume of aqueous humor that was removed (0.2 mL). In addition, patients with acute PACG and very high IOP presented with extremely shallow anterior chambers, which might have increased the risk of micro-injuries to the corneal endothelium. For these reasons, we suggest that ACP be avoided by patients with acute PACG and an initial IOP that is higher than 60 mmHg unless mannitol infusion is contraindicated.

One limitation of this study is that the measurement of IOP by Goldmann tonometry is not viable due to corneal edema during acute POAG; however, a pneumotonometer is relatively less reliable than the Goldmann standard at very high IOP levels. Besides, the effects of diseases, other than renal dysfunction and heart disease, and medications on the control of IOP, regression of corneal edema, and recovery of visual acuity cannot be ruled out. Surprisingly, there was a higher number of males than females enrolled in this study. The significance of such a gender-specific trend should be investigated. In this study, the effects of ACP on patients with acute PACG and an initial IOP below 45 mmHg were not analyzed. Further studies on this group of patients are required.

We conclude that the immediate application of ACP is a safe and effective therapeutic method for controlling IOP in patients with acute PACG. ACP should be first considered in patients with an initial IOP between 45–60 mmHg because it provides better visual outcomes than mannitol through the rapid stabilization of the anterior segment. We suggest that an adequate volume of aqueous humor that can be drained is 0.05 mL when the initial IOP is between 45–50 mmHg and 0.1 mL when the initial IOP is above 50 mmHg. However, ACP should only be considered in patients with an initial IOP of 60 mmHg or higher when mannitol is contraindicated.

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