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Efficacy of Intravenous 3% Hypertonic Saline Compared to Mannitol 20% for Lowering Intraocular Pressure in Glaucoma Patients

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Abstract

Background: It is essential to reduce acutely raised intraocular pressure before surgery and mannitol has been effectively used for this purpose. Also, intraocular pressure can be decreased by hypertonic saline by pulling fluid osmotically from tissues to the intravascular space.

Aim of Work: To evaluate efficacy of IV infusion of HTS 3% compared to mannitol 20% for decreasing IOP in glaucoma patients.

Material and Methods: 30 patients undergoing glaucoma surgery under general anesthesia were randomly allocated into 2 groups. One group recieved hypertonic saline 3% (3 ml/kg) and the other group received mannitol (0.5gm/kg). Baseline IOP was measured just before infusion then measured 5, 10, 20, 30, 60, 120min after end of infusion.

Results: There was statistical significant decrease in the IOP in both groups at 1 and 2 hours after infusion when collected data were compared to baseline.

Conclusion: This study concluded that IV infusion of HTS 3% seemed to be effective in decreasing IOP in glaucoma patients. It might be considered as a good alternative to mannitol for this purpose.

Key Words: *Hypertonic saline – Mannitol – IOP – Glaucoma.*

Introduction

THE reduction of acutely raised intraocular pressure prior to surgery is often essential [1]. Established systemic medications to reduce IOP rapidly include oral and intravenous acetazolamide, oral glycerol and intravenous mannitol [2]. Hypertonic Mannitol has been effectively used to reduce intracranial pressure in animals and humans [3]. Mannitol has several side effects, including hypotension due to osmotic diuresis and renal affection [4].

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Mannitol 20% was used for reduction of resistantly elevated intraocular pressure [2]. Because the cornea and sclera are more or less rigid, a small amount of fluid drawn from the eye will reduce intraocular pressure, fluid is also pulled from the vitreous with subsequent reduction in IOP. Hypertonic saline can lower intraocular pressure by pulling fluid osmotically from tissues to the intravascular space [5]. Such a reduction has been shown after administration of IVHTS in high doses in cat and human eyes [6]. Corneal edema were treated with topical instillations of 5% hypertonic saline in a water [7]. In their experimental study, Volopich et al. found that hypertonic hydroxyethyl starch is comparable to intravenous Mannitol in lowering the intraocular pressure in healthy normotensive dogs [8].

Harju et al., [6] performed a study on 19 patients with glaucoma and an IOP 30mmHg or higher and concluded that intravenous hypertonic saline solution reduces IOP moderately within minutes for up to 2hr. To our knowledge no studies comparing Mannitol and hypertonic saline in reducing intraocular pressure in glaucoma patients was done.

Patients and Methods

Following the approval of the Ethical Committee of Kasr Al-Ainy Hospital of Cairo University from May 2015 to May 2016 and after obtaining informed and written consent from each patient, a total of 30 patients with glaucoma, with IOP 30mmHg or higher, aging 35-60 years, both genders, ASA I-III were randomly allocated in two groups, 15 each.

- GH (n=15); received IV 3ml/kg hypertonic saline 3% over 30min.

• GM (n=15); received IV 0.5gm/kg Mannitol 20% over 30min.

Subjects were randomly allocated to study groups by a computer-generated random list. Group assignment was sealed in sequentially numbered opaque envelopes that have been opened one hour before infusion to determine which treatment the subject would receive.

However, patients with any active cardiac condition as congestive heart failure, hypertension or pregnant and lactating women were excluded from the study.

All patients included in the study were subjected to history taking in the form of name, age, occupation and any systemic diseases as hypertension or heart failure. Then, examination including appearance and weight was done. IOP was measured with Goldmann Applanation tonometer.

An anticubital 18G venous cannula was inserted and connected to IV line for infusion of either 0.5 gm/kg of 20% mannitol or 3ml/kg of 3% hypertonic saline over 30 minutes. IOP was measured before injection, at 5min, 10min, 20min, 30min, 1h, and 2h after end of infusion and data were recorded.

Sample size:

Based on the assumption that a 25% difference in the mean intraocular pressure is considered a clinically significant difference between the two groups and a common treatment standard deviation of 2.3mmHg 9 and taking power 0.9 and error 0.05, a minimum sample size of 15 patients is calculated for each group.

Statistical analysis:

Categorical variables will be assessed using chi-square or Fischer exact test where appropriate. Normally distributed data will be presented as mean (SD) and will be analyzed using Student's *t*-test and two-way analyses of variance with repeated measures and post hoc Dunnett test as appropriate. Data not normally distributed (tested by Kolmogorov-Smirnov test) will be presented as median (range) and were analyzed with Mann-Whitney U-test or the Kruskal-Wallis test as appropriate. The software SPSS V15.0 for Windows (SPSS, Inc, Chicago, Il, United States) will be used for statistical analysis.

Results

In this study, 30 patients with glaucomatous eyes, who were fulfilling the inclusion and exclusion criteria for the study, were chosen and arranged into two equal groups:

• G_H: Included 15 patients and received 3ml/kg HTS iv infusion over 30min.

• GM: Included 15 patients and received 0.5mg/kg mannitol 20% iv infusion over 30min.

Both groups were compared as regards demographic data and IOP.

IOP was recorded at baseline, 5min, 10min, 20min, 30min, 1h and 2 hours after infusion.

Regarding demographic characteristics, statistical studies between both groups showed no significant differences (Table 1).

As to IOP, when comparing both groups together, there was statistical significant increase in G_H more than GM regarding baseline. There was statistical significant decrease in the IOP in GM more than in G_H at 1 hour and 2 hours recorded data. (p=0.02, 0.03 respectively) Fig. (1) (Table 2).

In addition, within same group comparison at different time intervals, as regards G_H, there was statistical significant decrease in IOP at 5min when compared to baseline up to 2 hours. However, in GM, there was statistical significant decrease in IOP at 10min when compared to baseline up to 2 hours. Fig. (1) (Table 2).

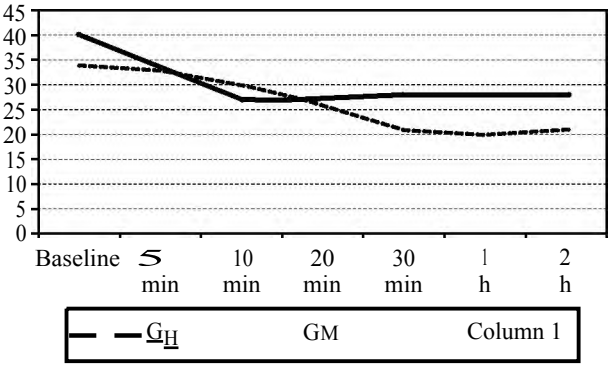

Fig. (1): Comparison between both groups as regards IOP.

Table (1): Comparison between both groups as regards demographic characteristics.

Demographic characteristics	G_H	GM
Age (years)	52 (47-58)	46 (38-53)
Sex (male: female)	7:8	8:7
Glaucoma type: n (%):		
Primary open angle	9 (60%)	8 (53.3%)
Angle closure	5 (33.3%)	6 (40%)
Congenital glaucoma	1 (6.6%)	1 (6.6%)

Numerical data were expressed as median (range).
Categorical data were expressed as n (%).

Table (2): Comparison as regards IOP (mmHg).

IOP (mmHg)	G_H (n=15)	GM (n=15)	*p*-value between both groups	*p*-value relative to baseline
Baseline	40±8.7	34±3	0.017	
5min	34±7.8†	33.8±3	0.9	<0.001
10min	27.6±11†	30.6±4†	0.3	<0.001
20min	27.2±11.3†	26.6±4.6†	0.8	<0.001
30min	28±12.6†	21.8±3.6†	0.07	<0.001
1 hour	28.4±12.6†*	20.2±4.4†*	0.02	<0.001
2 hours	28.4±12.6†*	21.4±4†*	0.03	<0.001

*: Denotes significance relative to the other group. $p<0.05$.
†: Denotes significance relative to the baseline. $p<0.05$.
Numerical data were expressed as mean(standard deviation).
Categorical data were expressed as n (%).
$p<0.05$ was considered to be significant.

Discussion

The reduction of acutely raised intraocular pressure prior to surgery is often essential [1]. Established systemic medications to reduce IOP rapidly include oral and intravenous Acetazolamide, oral glycerol and intravenous mannitol [2]. Mannitol has been effectively used to reduce intracranial pressure in animals and humans [3]. Mannitol has several side effects, including hypotension due to osmotic diuresis and renal affection [4].

Anaesthesiologists use HTS in amounts equivalent to 1-5mmol/kg sodium for treatment of hypovolemic shock and for lowering intracranial pressure [6]. It increases systemic blood volume, raises blood pressure and lowers intracranial pressure by pulling fluid osmotically from tissues to intravascular space [2]. There is no class 1 evidence to indicate that Mannitol is more effective than hypertonic saline in lowering elevated intracranial pressure [10].

In 1988 Worthley et al., [11] first reported the use of hypertonic saline to decrease ICP in 2 patients who didn't improve by mannitol treatment. The reported concentrations of HTS used for decreasing intracranial tension range from 2% to 23.5% [12]. Although it may be more effective in controlling intracranial hypertension than mannitol, unfortunately, it doesn't improve the outcome [13].

The hypertonic saline has been shown to have anti-inflammatory properties. Additionally, it affects the balance between proinflammatory and anti-inflammatory cytokines by decreasing Tumor Necrosis Factor (TNF) alpha production and increasing anti-inflammatory IL-ra and IL-10 [14].

In this study 30 patients were included and were divided into two equal groups, 15 patients each, GH and GM.

Regarding IOP, it was found that IOP started to decrease earlier in GH at 5min after end of HTS infusion and reached maximal decrease at 10-20min after infusion. However, in G M the IOP started to decrease at 10min and reached maximal decrease at 1 hour after infusion.

In consistency with these results, Harju et al., [5] studied the effect of HTS on nineteen patients and found that the IOP lowering effect of the small dose HTS is large enough to be of clinical relevance when IOP is moderately elevated and a fast reduction is desired. Intravenous hypertonic saline reduced elevated IOP in glaucoma eyes a median of 7mmHg within 5min irrespective of baseline IOP. Injection of 0.5mmol sodium/kg was as effective as the double dose. He concluded that the IOP can be lowered safely by HTS preoperatively. The effect lasted for at least 2hrs, enough to complete most surgeries.

Furthermore, Trovinen et al., [15] compared the effect of Intravenous Hypertonic Saline (IVHTS) on Intraocular Pressure (IOP) among patients with Exfoliation Glaucoma (ExG), POAG, and OHT through a prospective, interventional trial. It included patients with an IOP 24-30mmHg with or without topical medication and excluded patients using oral acetazolamide medication, those with heart or kidney failure, dementia or other systemic condition that markedly decreased physical performance. Participants received a bolus of 23.4% HTS through an antecubital vein. Infusion rate was 1ml/s and dosage 1.0mmol/kg sodium in all patients. IOP was measured before bolus injection (baseline), every minute after injection for 10 minutes, and then less frequently for 2 hours. A total of 35 patients participated in this study; 16 ExG, 13 POAG, and 6 OHT patients. The baseline IOP 26.2 (±1.7) mmHg was significantly reduced two minutes after treatment to 22.4 (±2.6) mmHg ($p<0.001$). Maximum IOP reduction was achieved

after 10 minutes, at which time IOP was reduced to 17.3 (±2.9) mmHg (p<0.001), and the mean percentage IOP reduction was 34% (±9).

They concluded that hypertonic saline seems to be an effective and a rapid method to reduce IOP. This reduction seems to be independent of topical medication or glaucoma subgroup. HTS could be a practical method to reduce IOP before or during eye surgery.

Our study concluded that IV infusion of HTS 3% seemed to be effective in decreasing IOP in glaucoma patients. It might be considered as a good alternative to mannitol for this purpose. Infusion of hypertonic saline and mannitol should be encouraged to be used preoperatively in emergency cases of glaucoma.

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مدى فاعلية محلول الملح ٣٪ مقارنة بالمانيتول بهدف تقليل ضغط العين لدى مرضى المياه الزرقاء

إن تقليل ضغط العين المرتفع بصورة حادة قبل إجراء الجراحة بالغ الأهمية. لقد أصبح المانيتول العامل الرئيسى لزيادة الخاصية الأسمولية لقرابة قرن وبقى هو العلاج الذهبى لتقليل الضغط داخل المخ. يستخدم أطباء التخدير محلول الملح المركز عن طريق الوريد لتقليل الضغط داخل المخ وعلى مدار الخمسة والعشرين سنة السابقة قد أصبح محلول الملح المركز أكثر شيوعا كبديل للمانيتول.

أن هدف هذه الدراسة هو تحديد تأثير محلول الملح المركز ٣٪ على ضغط العين لدى مرضى المياه الزرقاء مقارنة بالمانيتول.

هذه الدراسة تشمل ٣٠ عين لدى ١٩ مريض وقد تم توزيعهم عشوائيا لمجموعتين كل منهما ١٥ حالة. المجموعة الأولى مجموعة محلول الملح اللمركز ٣٪ والمجموعة الثانية مجموعة المانيتول ٢٠٪.

وقد كشفت نتائجنا ما يلى:

إنخفاض ضغط العين فى مجموعة محلول الملح المركز ومجموعة المانيتول بصورة ذات دلالة إحصائية.

وقد خلصنا فى هذه الدراسة أن محلول الملح المركز ٣٪ فعال فى تقليل ضغط العين لدى مرضى المياه الزرقاء ويعتبر بديل جيد للمانيتول لهذا الغرض.