Hemolysis in Transurethral Resection of the Prostate Using Distilled Water as the Irrigant

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Background: To investigate the incidence and time course of hemolysis and its clinical effects following transurethral resection of the prostate (TURP) using distilled water as the irrigant.

Methods: Between March 1996 and April 1997, 39 patients who underwent TURP due to benign prostatic hyperplasia (BPH) were randomly included in this study. The levels of plasma hemoglobin, haptoglobin and serum lactic dehydrogenase (LDH) were checked in all patients before, immediately after, and 24 hours after the operation. Serum creatinine and sodium were also checked in 24 patients starting August 1996. Significant hemolysis was identified as simultaneous elevation of plasma hemoglobin (> 10 g/dL), serum LDH and reduction of plasma haptoglobin after TURP.

Results: Among the 39 subjects, hemolysis occurred in 17 (43.6%), whose plasma hemoglobin and serum LDH increased while plasma haptoglobin decreased immediately after operation ($p < 0.05$), but no significant differences between the data before and 24 hours after the operation were noticed. In the hemolysis group, serum creatinine increased while serum sodium decreased immediately after operation ($p < 0.05$), but the data before and 24 hours after the operation had no significant differences. There were no changes in serum creatinine and sodium levels after TURP in patients without hemolysis. The weight of the resected prostate was 42.5 ± 15.5 g in the hemolysis group and 23.3 ± 8.3 g in the nonhemolysis group, while duration of TURP was 68.9 ± 19.6 minutes in the hemolysis group and 34.2 ± 8.4 minutes in the nonhemolysis group. Patients with hemolysis had higher resection weight and longer resection time than those without hemolysis ($p < 0.001$).

Conclusion: Using distilled water as an irrigant for TURP might cause hemolysis, especially in patients with larger prostates and longer resection times. It is necessary to carry out every effort to shorten resection time and avoid extravasation during surgery. [*J Chin Med Assoc* 2006;69(6):270–275]

Key Words: benign prostatic hyperplasia, hemolysis, transurethral resection of the prostate

Introduction

Transurethral resection of the prostate (TURP) is currently the gold standard for the surgical treatment of benign prostatic hyperplasia (BPH). However, since the invention of this operation, there has been continuing debate over its safety. Several papers reported that the lifespan of patients who had undergone TURP was shorter than that of the general population.[1] Although cardiovascular damage during TURP was the suspected cause, it has never been proved.[1–3] A serious complication may occur via accidental perforation of the prostatic capsule with extravasation and systemic absorption of irrigating fluid. The patient may develop mental confusion, uremia or heart failure, the so-called TURP syndrome.[4,5] Brain swelling secondary to hyponatremia well explains mental confusion. Nevertheless, the mechanisms causing uremia and serious cardiovascular events are not well understood.

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Using isotonic irrigant containing glycine, glycerol or other substances may reduce, though not fully, the chance of TURP syndrome. Due to lower cost, distilled water is still widely used in many areas of the world for TURP.[6] It remains important to investigate and prevent TURP syndrome, to which we believe hemolysis to be an important contributor. It has been shown that patients undergoing TURP may absorb a large amount of the irrigating fluid, with as much as 25% of the fluid entering the circulation.[4,7–14] Creevy and Reiser[11] noted intravascular hemolysis induced by absorbed distilled water. Mommsen et al[15] found an increase in plasma hemoglobin and a decrease in serum sodium during TURP. However, the time course of hemolysis following TURP and the correlation between hemolysis and renal functional impairment remain unclear. We conducted this prospective study to evaluate the incidence of hemolysis and its clinical effects following TURP using distilled water as the irrigant.

Methods

Between March 1996 and April 1997, a total of 39 patients, mean age 70.2 years (range, 65–80 years), with symptomatic BPH who underwent TURP using distilled water as the irrigant were included in this study. Patients with carcinoma of the prostate were excluded. Suprapubic cystostomy served as the outlet for continuous irrigation during TURP, and 20 mg lasix intravenous injection was routinely given immediately after surgery. All surgical specimens were weighed and sent for pathologic examination. The duration of resection was recorded from the beginning of resection to the end of the operation.

The level of plasma hemoglobin (g/dL), haptoglobin (mg/dL), and serum lactic dehydrogenase (LDH) (IU/L) were checked before, immediately after, and 24 hours after the operation in all patients. When intravascular hemolysis occurs, red blood cells are destroyed and hemoglobin enters the plasma with an elevation of serum LDH and plasma hemoglobin levels. Plasma hemoglobin is evaluated from the absorbance, at a 540 nm wavelength, of the highly colored hemoglobin solution. Haptoglobin, an $\alpha 2$ globulin, binds hemoglobin in the plasma. Reduction of its level in the plasma represents one laboratory sign of intravascular hemolysis.[16] In addition, serum sodium (mmol/L) and creatinine (mg/dL) were checked in 24 patients, beginning August 1996. Significant hemolysis was defined as simultaneous elevation of plasma hemoglobin (> 10 g/dL) and serum LDH and reduction of plasma haptoglobin.

The software used for statistical analysis was SPSS version 10.0 (SPSS Inc, Chicago, IL, USA) for Windows. We used the paired t test and Pearson's correlation for statistical analysis and considered the differences significant when $p < 0.05$.

Results

Among the 39 subjects, hemolysis occurred in 17 (43.6%). Their plasma hemoglobin and serum LDH levels increased and haptoglobin decreased ($p < 0.001$) immediately after operation, but there were no significant differences between the data before and 24 hours after surgery except for plasma haptoglobin (Table 1; Figures 1 and 2). Serum sodium and creatinine were checked in 11 of the 17 patients. Serum creatinine increased and sodium decreased significantly immediately after TURP ($p < 0.01$), but no significant differences were noticed between the data before and 24 hours after operation (Table 2; Figures 3 and 4). Only one patient needed 3% sodium chloride 200 mL intravenous therapy due to TURP syndrome (sodium: 125 mmol/L immediately after TURP).

Twenty-two of the 39 patients had no significant changes in plasma hemoglobin, haptoglobin and LDH immediately and 24 hours after TURP, and indicated no occurrence of hemolysis (Table 1). Of these 22 patients, serum creatinine and sodium were examined in 13. There were no significant changes in serum sodium and creatinine immediately and 24 hours after surgery in these 13 patients (Table 2).

The weight of the resected prostate was 42.5 ± 15.5 g in the hemolysis group and 23.3 ± 8.3 g in the nonhemolysis group, while duration of TURP was 68.9 ± 19.6 minutes in the hemolysis group and 34.2 ± 8.4 minutes in the nonhemolysis group. Patients with hemolysis had higher resection weight and longer resection time than those without hemolysis ($p < 0.001$).

Significant negative correlation was noticed between plasma hemoglobin and serum sodium in patients of the hemolysis group ($r = -0.69$, $p < 0.05$), but no significant correlation was found in those of the nonhemolysis group ($r = 0.43$, $p > 0.05$). Significant correlation was also noted between serum sodium and creatinine, serum sodium and resection time, and serum creatinine and resection time in hemolysis group patients ($r = -0.74$, -0.68 and 0.68, respectively), but no significant correlation was noticed in nonhemolysis group patients (Tables 3 and 4).

Table 1. Plasma hemoglobin, haptoglobin and serum lactate dehydrogenase (LDH) in hemolysis and nonhemolysis patients before, immediately after, and 24 hours after transurethral resection of the prostate (TURP)

	Before TURP	Immediately after TURP	24 hr after TURP
Hemoglobin			
Hemolysis	3.3 ± 0.8*†	35.2 ± 10.5*	3.6 ± 1.2†
Nonhemolysis	3.1 ± 0.9†	3.4 ± 1.2†	3.2 ± 1.1†
Haptoglobin			
Hemolysis	160.0 ± 88.3*‡	98.4 ± 71.3*	91.7 ± 48.8‡
Nonhemolysis	187.4 ± 75.6†	194.3 ± 80.6†	185.5 ± 82.3†
LDH			
Hemolysis	194.1 ± 22.7*†	306.7 ± 105.1*	217.8 ± 42.5†
Nonhemolysis	197.1 ± 28.8†	211.2 ± 34.7†	209.5 ± 33.3†

**‡p < 0.05; †p > 0.05. Data are expressed as mean ± standard deviation, and paired t test was used for statistical analysis.*

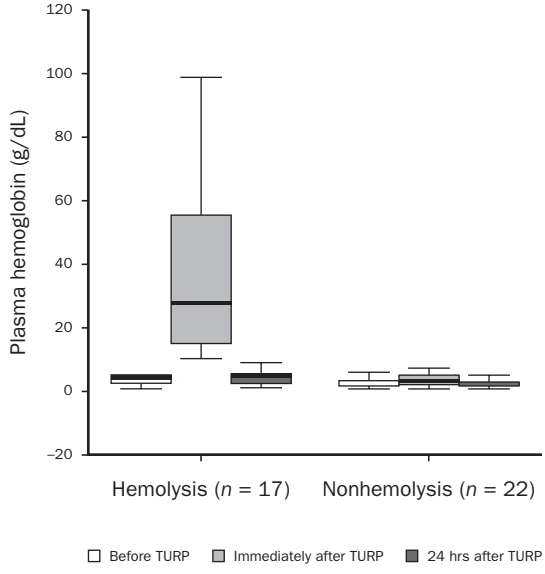

Figure 1. Plasma hemoglobin in hemolysis and nonhemolysis patients before, immediately after, and 24 hours after transurethral resection of the prostate (TURP).

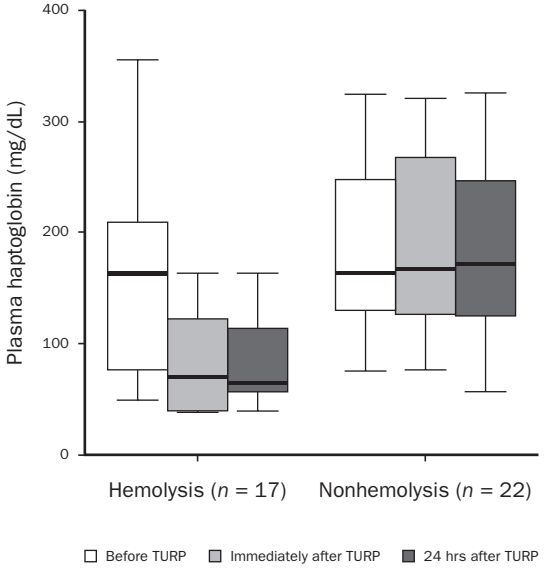

Figure 2. Plasma haptoglobin in hemolysis and nonhemolysis patients before, immediately after, and 24 hours after transurethral resection of the prostate (TURP).

Discussion

The danger of hemolysis following TURP has been emphasized in the past.[17] The irrigation fluids used in TURP range from distilled water to many non-hemolytic irrigants such as glycine, sorbitol, and mannitol solutions. Hemolysis during TURP could happen especially when using distilled water as the irrigating fluid and could be partly prevented by isotonic fluids such as sorbitol or mannitol.[18] The amount of absorbed fluid varied depending on the height of irrigating fluid, the pressure in the prostatic cavity, the time used for resection, the weight of the resected prostate and the skill of the operator.[19,20] The present study also found an increase in the incidence of hemolysis in patients with larger prostates and longer resection times. We routinely used suprapubic cystostomy during TURP to continuously divert irrigating fluid (distilled water) to keep low intravesical pressure and minimize fluid absorption. Therefore, we did not have a control group using different irrigating fluid. Nevertheless, some patients still developed hyponatremia and hemolysis. Heidler[21] also showed that with suprapubic drainage during TURP, significant increase of intravesical pressure still occurred.

Table 2. Serum creatinine and sodium in hemolysis and nonhemolysis patients before, immediately after, and 24 hours after transurethral resection of the prostate (TURP)

	Before TURP	Immediately after TURP	24 hr after TURP
Creatinine			
Hemolysis	0.87 ± 0.11*†	1.14 ± 0.11*	0.95 ± 0.09†
Nonhemolysis	1.07 ± 0.18†	1.03 ± 0.14†	1.02 ± 0.13†
Sodium			
Hemolysis	139.3 ± 2.5*†	132.5 ± 4.3*	139.0 ± 2.5†
Nonhemolysis	140.0 ± 2.2†	139.3 ± 1.8†	139.3 ± 1.5†

$p < 0.05$; †$p > 0.05$. Data are expressed as mean ± standard deviation, and paired t test was used for statistical analysis.

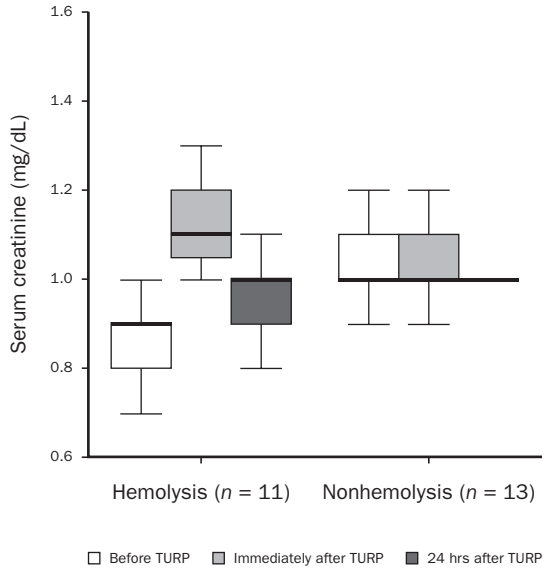

Figure 3. Serum creatinine in hemolysis and nonhemolysis patients before, immediately after, and 24 hours after transurethral resection of the prostate (TURP).

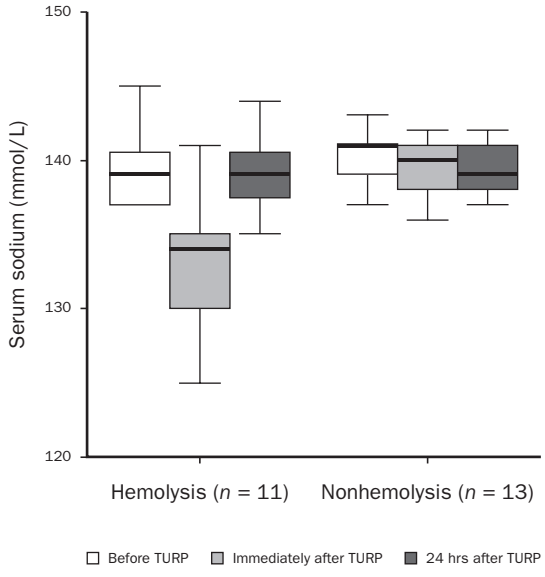

Figure 4. Serum sodium in hemolysis and nonhemolysis patients before, immediately after, and 24 hours after transurethral resection of the prostate (TURP).

Mommsen et al[15] showed that the concentration of serum sodium decreased and plasma hemoglobin increased significantly, but without significant change in haptoglobin level, after TURP by using distilled water as the irrigant. However, in our study, haptoglobin decreased immediately and 24 hours after operation, with all other parameters (including plasma hemoglobin, serum LDH, sodium and creatinine) returning to preoperative levels 24 hours after surgery in patients with hemolysis. The reason for the discrepancy between our observation and Mommsen et al's remains unclear.

The present study showed significant negative correlations between plasma hemoglobin and serum sodium, serum sodium and resection time, and serum sodium and creatinine. Therefore, hemolysis after TURP might lower the level of serum sodium and hence increase the possibility of TURP syndrome and impair renal function. We also found an increase in serum creatinine immediately after TURP in patients with hemolysis, but not in those without hemolysis. In this study, the decrease in renal function was minor and reversible in patients with hemolysis, and there was no significant relationship between serum creatinine and hemolysis parameters, but the detrimental effect of hemolysis on renal function might happen. If hemolysis is severe enough or if patients originally have impaired renal function, renal damage might not be reversible and could lead to acute renal failure, as shown in a previous report.[22]

Table 3. Correlations of plasma hemoglobin, serum sodium and serum creatinine (immediately after transurethral resection of the prostate), resection time, and weight of resected prostate in hemolysis patients*

	Hemoglobin	Sodium	Weight	Time	Creatinine
Hemoglobin	1	–0.69†	0.20	0.36	0.28
Sodium	–0.69†	1	–0.54	–0.68†	–0.74†
Weight	0.20	–0.54	1	0.96†	0.61
Time	0.36	–0.68†	0.96†	1	0.68†
Creatinine	0.28	–0.74†	0.61	0.68†	1

**Data in the table are coefficients of correlation (r) between the parameters in the rows and columns using Pearson's correlation; †significant correlations ($p < 0.05$). Weight = weight of resected prostate; Time = resection time.*

Table 4. Correlations of plasma hemoglobin, serum sodium and serum creatinine (immediately after transurethral resection of the prostate), resection time, and weight of resected prostate in nonhemolysis patients*

	Hemoglobin	Sodium	Weight	Time	Creatinine
Hemoglobin	1	0.43	0.33	0.48	–0.36
Sodium	0.43	1	–0.36	–0.18	–0.53
Weight	0.33	–0.36	1	0.84†	–0.02
Time	0.48	–0.18	0.84†	1	0.10
Creatinine	–0.36	–0.53	–0.02	0.10	1

**Data in the table are coefficients of correlation (r) between the parameters in the rows and columns using Pearson's correlation; †significant correlation ($p < 0.05$) between resection time and weight of resected prostate. Weight = weight of resected prostate; Time = resection time.*

The damaging effects of hemolysis on renal function might be multifactorial. Goodwin et al[16] have suggested that hemoglobinemia may induce renal damage. Hemoglobin itself might occlude renal tubules and cause injury. Besides, reactive oxygen species (ROS) may also injure the kidney following hemolysis. Studies have shown that iron and iron-containing compounds, including hemoglobin, can promote hydroxyl radical formation and lipid peroxidation through Fenton reaction and induce damage, which have been shown to induce hemorrhagic injury of the central nervous system,[23] macular degeneration,[24] and ulcerative colitis.[25] Another study further demonstrated that hemoglobin could stimulate alveolar macrophages to generate ROS.[26] Therefore, it is reasonable to speculate that oxidative stress may occur in TURP and play an important role in the pathogenesis of TURP syndrome. Vesela et al[27] have echoed this concept, reporting that TURP might induce oxidative stress on erythrocytes.

In conclusion, using distilled water as the irrigant for TURP might cause hemolysis, especially in patients with larger prostates and longer resection times. It is necessary to carry out every effort to shorten resection time and avoid extravasation during operation.

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