Investigating the Impact of Bladder Tumor Resection Surgery through the Urethra on Serum Osmolality and Electrolyte Levels

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Abstract

Introduction: Despite being less invasive than open surgery, transurethral tumor resection has notable side effects, particularly electrolyte disorders resulting from systemic absorption of the irrigation fluid. Several studies have examined the effects of changes in irrigation fluid; however, the findings remain contradictory, and uncertainty surrounds the extent of changes in serum electrolytes and osmolality. Therefore, this study aimed to determine these changes.

Materials and Methods: This observational cross-sectional study included patients aged 20 to 80 years who underwent transurethral resection of bladder tumors (TURBT) at Bahanr Hospital's treatment center in 2022. Patients with tumor diagnoses were registered for analysis. Following the selection of suitable patients, pertinent data, including demographic parameters (age and gender), were extracted and recorded from patient files. Changes in serum electrolytes and osmolality before and after the procedure were then analyzed.

Results: The study investigated 31 patients, consisting of 27 men and 4 women, with an average age of 61.84 ± 10.12 years. The duration of surgery exhibited a significant positive correlation with pre-surgery osmolality ($r = -0.357$, $p < 0.05$) and post-surgery osmolality ($r = -0.428$, $p < 0.05$), as well as with potassium levels in the department ($r = 0.371$, $p < 0.05$). Significant changes in serum levels of sodium, potassium, blood sugar, serum creatinine, and osmolality ($p < 0.01$) were observed during the hospitalization period. Notably, BUN changes during hospitalization were also significant. Furthermore, the average osmolality decreased from 286.82 before surgery to 284.56 after surgery ($p < 0.001$) and increased from 284.56 after surgery to 286.66 during recovery ($p < 0.05$) and 287.08 during the postoperative period ($p < 0.05$). However, no significant differences were observed between preoperative osmolality and recovery ($p = 1$), preoperative osmolality and the postoperative period ($p = 1$), and recovery and the postoperative period ($p = 1$).

Conclusion: The significant increase in potassium and blood sugar levels during hospitalization, despite their inversely related nature, underscores the importance of further investigations to determine the underlying causes.

Key Words: transurethral tumor resection, TURBT, TUR syndrome, serum electrolytes, osmolality..

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INTRODUCTION

Bladder cancer (BC) manifests in two surface forms: non-muscle-invasive and muscle-invasive. Mutations in the urothelial layers trigger rapid growth of cells, leading to wall irritation and potentially involving the bladder's muscle layers. Over time, these cancerous cells can attack the lymph nodes, bones, lungs, and liver, resulting in severe consequences for the patient [1]. While urothelial carcinoma is the predominant pathological type of bladder cancer, other significant types include adenocarcinoma, squamous cell carcinoma, small cell carcinoma, and sarcoma [2-4].

Various treatments have been proposed for BC, depending on its severity. Radical cystectomy, involving the removal of the bladder, prostate, seminal vesicles, peritoneum, end parts of the ureter, and pelvic lymph nodes, is recommended for aggressive forms of the cancer. For non-invasive forms, transurethral resection of bladder tumor (TURBT) is the suggested surgical method [5-7]. Historically, TURBT procedures have utilized Monopolar or Bipolar technology, both of which have significant side effects including blood loss, urinary tract complications, and electrolyte disturbances [8, 9].

During TURBT operations, the use of washing liquid is crucial for removing blood and tumor debris from the surgical site. Liquid options such as glycine 1.5%, glucose 5%, Ringer's or Ringer's lactate, and sodium chloride 0.9% have been employed for this purpose [10-13]. Among these options, serum is regarded as the most ideal due to factors such as ease of access, non-conduction of electric current, non-interference with tumor resection, and minimal systemic absorption [14-16]. However, complete prevention of systemic absorption is impossible, and in 0.78 to 1.4% of cases, absorption of more than 1 to 2 liters of liquid through the bladder wall can result in TUR syndrome. This syndrome presents with manifestations including hypervolemia, decreased serum protein concentration, electrolyte imbalances (e.g., dilutional hyponatremia), hemodynamic and neurological disorders, kidney dysfunction, and lung edema, which if left unmanaged, may even lead to death [14]. Studies have indicated that symptom severity of this syndrome correlates with the volume of liquid absorbed, with the most severe symptoms occurring in volumes above 3 liters [15-18]. Thus, diagnosis of the syndrome relies on clinical and laboratory manifestations, necessitating immediate cessation of the surgical procedure and initiation of appropriate treatment, including possible admission to the intensive care unit (ICU). Given the contradictory results of published studies and the lack of investigation into quantitative changes in serum electrolyte levels and osmolality after TURBT, our study aims to uncover the intricacies of these changes.

METHODS AND MATERIALS

Study Design and Patient Population:

This cross-sectional and observational study focused on patients between the ages of 20 and 80 who underwent TURBT (bladder tumor resection) in 2022 at the Bahnar Hospital treatment center, Iran. The inclusion criteria required patients to have a TCC diagnosis and undergo a TURBT procedure lasting between 30 and 120 minutes. Exclusion criteria included the use of medications that could disrupt serum electrolytes (e.g., lithium, insulin, acetazolamide, diuretics) and a history of underlying diseases that could interfere with the factors under investigation (e.g., diabetes insipidus, SIADH, chronic kidney disease, chronic malnutrition such as anorexia). Additionally, patients had to express their willingness to participate in the research. Patients were withdrawn from the study if they experienced symptoms of TUR syndrome, lacked file information or laboratory results, or refused to participate.

Sample Size: Based on the study by Yousef et al. [15] and the following formula, a minimum sample size of 31 patients was determined:

$$n = \frac{4Z^2\sigma^2}{W^2}$$

$\alpha = 0.05 \rightarrow Z = 1.96$ • Glycine: 134.7 ± 13.4 • Glucose: 135.5 ± 12.9 • Saline: 142.6 ± 12.6

Procedure

After selecting eligible patients and obtaining their consent, relevant data were collected, including demographic parameters (e.g., age, gender), history of TUR surgery, duration of the operation, amount of glycine used during the procedure, amount of normal saline used for recovery and in the department, serum levels of glucose, BUN, creatinine, sodium, and potassium after the surgery, one hour later during recovery, and six hours later in the department. Osmolality was calculated using the formula 2*(Na+) + (serum glucose)/18 + (serum BUN)/1.8. Changes in serum electrolyte levels and osmolality before and after the procedure were recorded and subsequently investigated and analyzed.

Data Analysis

Qualitative variables were described using numbers and percentages, while quantitative data with a normal distribution were described using mean and standard deviation. Quantitative data with a non-normal distribution were described using median and interquartile range. SPSS-26 statistical software was utilized to analyze differences and correlations between the parameters expressing data distribution. Independent samples t-test and repeated measures ANOVA, or their non-parametric equivalents, were employed to assess the correlation of variables at the same time and the extent of changes in serum osmolality and electrolyte levels before and after the surgery. Pearson's Chi-squared test was used to investigate the relationship between qualitative and quantitative variables, while Pearson's r test or its non-parametric equivalents were used to explore the relationship between quantitative variables.

Ethical Considerations

A written letter of introduction was obtained from the university officials to gain access to the research centers. The purpose of the study was explained to all participants, and written consent was obtained from them. Patient information was treated with strict confidentiality by the project manager. The study adhered to ethical guidelines outlined in the Helsinki research and the research ethics committees of the University of Medical Sciences. The project received approval from the Research Council of the Faculty of Medicine.

RESULTS

A total of 31 patients participated in the study, consisting of 27 men (87.1%) and 4 women (12.9%), with an average age of 61.84 ± 10.12 years. The majority of patients had a previous history of TURBT operation (54.84%). The average duration of surgery for these patients was 75.81 ± 25.07 minutes, with an average use of 10.6 ± 3.59 grams of glycine during the procedure. In terms of bladder irrigation, patients received an average of 1.74 ± 0.26 liters of normal saline during recovery and 6.1 ± 0.45 liters of normal saline in the ward. Table 1 presents the serum levels of sodium, potassium, blood sugar, BUN, creatinine, and serum osmolality before and after surgery, during recovery, and in the ward.

Tab.1. Changes in the parameters examined in the study.

Parameter	Before the operation	After surgery	Recovery	Ward
sodium	137.13 ± 2.26	135.94 ± 2.91	136.9± 1.99	136.87 ± 1.89
potassium	4.08 ± 0.36	4.13 ± 0.25	4.29 ± 0.29	4.3 ± 0.34
blood sugar	93.48 ± 21.46	97.42 ± 11.25	99.19 ± 12	104.81 ± 10.65
BUN	19.97 ± 5	18.74 ± 4.17	19.55 ± 4.93	18.92 ± 3.83
Creatinine	1.29 ± 0.2	1.21 ± 0.27	1.24 ± 0.21	1.27 ± 0.18
osmolality	286.82 ± 5.1	284.56 ± 5.7	286.66 ± 4.73	287.08 ± 3.96

The distribution of these parameters was compared based on gender. The results indicated that in men, the serum blood sugar levels after surgery (P < 0.05), during recovery (P < 0.05), and in the ward (P < 0.05) were significantly higher compared to women. However, there were no significant differences between genders in preoperative blood sugar levels or in the serum levels of sodium, potassium, BUN, creatinine, and osmolality before and after surgery, during recovery, and in the ward (P > 0.05).

Regarding the history of TURBT, compared to patients without a history of the surgery, those with a previous TURBT operation had significantly lower serum potassium levels during recovery (P < 0.05) and higher blood sugar levels during recovery and in the ward (P < 0.05). In addition, the serum creatinine levels during recovery and in the ward were significantly higher in patients with a prior TURBT operation (P < 0.05). However, there were no significant differences in the serum levels of sodium, potassium, BUN, osmolality, blood sugar, and creatinine before and after the operation (P > 0.05) among those with and without a history of TURBT (Table 2).

Tab.2. Parameters examined in the study according to gender and previous history of TURBT operation.

Variable		Sex			History of TURBT operation		
		Male	Female	P-value	Negative	Positive	P-value
sodium	Before the operation	137.15±2.21	137±2.94	0.905	136.79±2.15	137.41±2.37	0.452
	After surgery	136.07±2.93	135±2.94	0.5	135.64±3.27	136.18±2.65	0.62
	Recovery	137.04±1.85	136±2.94	0.339	136.5±2.31	137.24±1.68	0.314
	Ward	136.85±1.94	137±1.83	0.887	136.57±1.95	137.12±1.87	0.433
potassium	Before the operation	4.13±0.35	3.75±0.29	0.048*	4.11±0.29	4.06±0.42	0.753
	After surgery	4.14±0.25	4.03±0.21	0.395	4.15±0.24	4.11±0.26	0.632
	Recovery	4.27±0.26	4.43±0.43	0.543	4.43±0.25	4.18±0.27	0.014
	Ward	3.4±0.34	4.35±0.4	0.807	4.26±0.3	4.35±0.38	0.515

blood sugar	Before the operation	95.59±22.24	79.25±2.99	0.159	88.57±7.04	97.53±28.02	0.22
	After surgery	99.26±10.81	85±4.08	0.015*	96.71±7.85	98±13.65	0.757
	Recovery	100.85±11.85	88±5.6	0.044*	93.14±6.83	104.18±13.18	0.008**
	Ward	106.41±10.26	94±6.68	0.027*	99.57±7.37	109.12±11.18	0.01*
BUN	Before the operation	20.33±5.23	17.5±1.91	0.298	19.71±5.33	20.18±4.88	0.803
	After surgery	18.8±4.39	18.38±2.59	0.854	18.11±5.83	19.26±2.09	0.451
	Recovery	19.81±5.23	17.75±0.96	0.444	18.75±6.21	20.21±3.63	0.422
	Ward	19.13±4.05	17.5±1.22	0.437	19.04±5.37	18.82±2.03	0.881
Creatinine	Before the operation	1.28±0.21	1.35±0.1	0.505	1.21±0.17	1.35±0.2	0.062
	After surgery	1.17±0.27	1.45±0.1	0.054	1.14±0.32	1.27±0.21	0.168
	Recovery	1.23±0.21	1.3±0.24	0.57	1.16±0.22	1.31±0.18	0.043
	Ward	1.26±0.17	1.35±0.24	0.353	1.2±0.15	1.33±0.19	0.043
osmolality	Before the operation	287.17±4.93	284.5±.6.45	0.338	285.96±4.36	287.53±5.68	0.405
	After surgery	285±5.57	281.63±6.57	0.277	283.89±5.94	285.12±5.62	0.561
	Recovery	287.13±4.39	283.5±6.45	0.155	285.25±4.75	287.82±4.52	0.134
	Ward	287.35	285.25±4.57	0.33	285.86±4.24	288.09±3.53	0.12

The age variable showed a significant negative correlation with serum potassium levels during recovery (r = -0.405, P < 0.05) and in the ward (r = -0.437, P < 0.05), and a positive correlation with serum creatinine levels in the ward (r = 0.393, P < 0.05). There were no significant correlations with the levels of sodium, blood sugar, BUN, creatinine, osmolality, and potassium before and after the operation (P > 0.05). The duration of surgery positively correlated with serum potassium levels in the ward (r = 0.371, P < 0.05), and inversely correlated with osmolality before surgery (r = -0.357, P < 0.05) and after surgery (r = -0.428, P < 0.05). However, no significant correlations were found with the serum levels of sodium, blood sugar, BUN, creatinine, potassium before and after the operation, potassium during recovery, and osmolality during recovery and in the ward (P > 0.05). The amount of glycine used during the operation showed a significant positive correlation with serum potassium levels in the ward (r = 0.39, P < 0.05). However, no significant correlations were observed with sodium, blood sugar, BUN, creatinine, osmolality, and potassium before and after the operation, and potassium during recovery (P > 0.05). The amount of normal saline used during the recovery section showed no significant correlations with the levels of sodium, potassium, blood sugar, BUN, creatinine, and osmolality before the operation, after the operation, during recovery, and osmolality in the ward (P > 0.05).

During the hospitalization period, significant changes were observed in serum sodium and potassium levels, blood sugar levels, serum creatinine levels, and serum osmolality levels (P < 0.01). However, the changes in BUN during this period were not statistically significant (P = 0.059) (Table 3).

Tab.3. Changes in the parameters examined during hospitalization.

Variable	df	Mean Square	F	P-value	Partial Eta Squared
sodium	1.837	14.155	5.306	0.009	0.15
potassium	2.311	0.533	7.822	<0.001	0.207
blood sugar	1.375	1496.891	7.673	0.004	0.204
BUN	2.083	14.342	2.924	0.059	0.089
Creatinine	3	0.036	3.791	0.013	0.112
osmolality	1.927	64.735	6.049	0.005	0.168

Due to the observed significance of changes in serum sodium and potassium levels, blood sugar level, creatinine level, and serum osmolality level, a post hoc analysis was conducted to further investigate these changes. The results demonstrated that the average serum sodium level decreased significantly from 137.13 before the operation to 135.00 after the operation ($p < 0.001$). Moreover, there was a significant increase in serum sodium level from 135.94 after the operation to 136.9 during recovery ($p < 0.05$). However, the differences between sodium serum levels before the operation and during recovery ($p = 1$) and in the ward ($p = 1$), as well as between postoperative and in the ward ($p = 0.316$), and recovery and in the ward ($p = 1$), were not significant. On the other hand, the average potassium level increased significantly from 4.08 before surgery to 4.31 in the ward ($p < 0.01$). Additionally, there was a significant increase in potassium level from 4.13 postoperatively to 4.29 during recovery ($p < 0.01$) and 4.31 in the ward ($p < 0.01$). However, the differences between preoperative and postoperative ($p = 1$), and recovery ($p = 0.06$), as well as recovery and in the ward ($p = 1$), were not statistically significant (Figure 1).

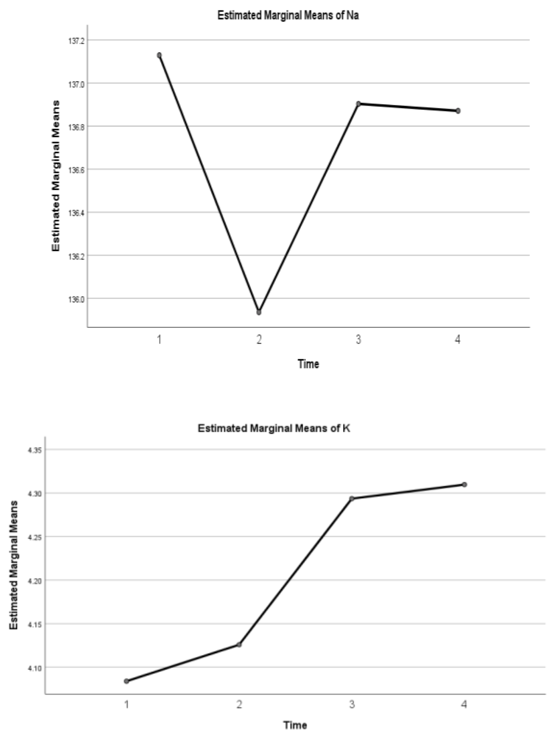

Fig.1. Changes in the average serum levels of sodium and potassium in the time periods examined in the study (time period 1: before surgery, time period 2: after surgery, time period 3: recovery, and time period 4: in the ward).

The average blood sugar level increased significantly to 104.81 in the ward compared to 93.8 before the operation ($p < 0.001$), 97.42 after the operation ($p < 0.001$), and 99.19 during recovery ($p < 0.001$). However, there were no significant differences between blood sugar levels before surgery and after surgery ($p = 1$) or during recovery ($p = 0.59$), as well as between surgery and recovery ($p = 1$). The mean creatinine decreased significantly from 1.29 before the operation to 1.21 after the operation ($p < 0.05$). However, the differences between preoperative serum creatinine levels and recovery ($p = 0.27$) or in the ward ($p = 1$), as well as postoperative recovery ($p = 1$) and in the ward ($p = 0.34$), and recovery and in the ward ($p = 0.85$), were not found to be statistically significant (Chart 2).

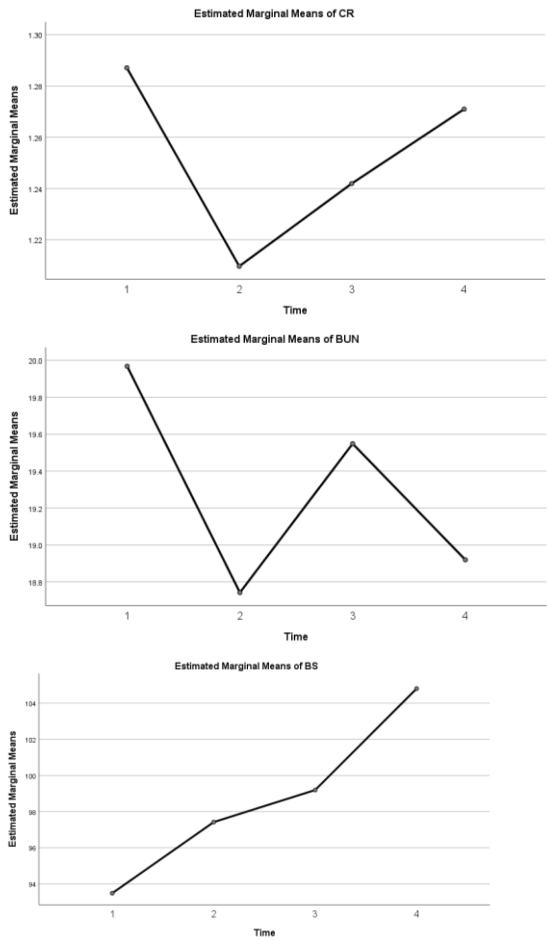

Fig.2. Changes in the average serum levels of sodium and potassium in the time periods examined in the study (time period 1: before surgery, time period 2: after surgery, time period 3: recovery, and time period 4: in the ward).

The average osmolality decreased significantly from 286/82 before surgery to 284/56 after the operation ($p < 0.001$). Furthermore, it increased significantly from

284/56 after the operation to 286.66 during recovery ($p < 0.05$) and 287. 08 in the ward ($p < 0.05$). However, the differences between preoperative osmolality and recovery ($p = 1$) or in the ward ($p = 1$), as well as recovery and in the ward ($p = 1$), were not significant (Figure 3).

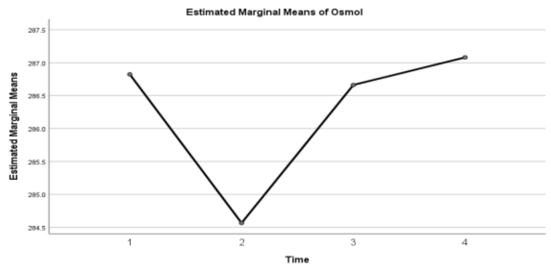

Fig.3. Changes in the average osmolality in the time periods examined in the study (time period 1: before surgery, time period 2: after surgery, time period 3: recovery, and time period 4: in the ward).

Discussion

The use of transurethral resection of bladder tumor (TURBT) as a less invasive alternative to open surgery has been associated with notable side effects, particularly electrolyte disturbances resulting from the systemic absorption of the irrigation fluid (16). Numerous studies have explored the impact of changes in irrigation fluid; however, the findings remain inconsistent, and the extent of alterations in serum electrolytes and osmolality remains uncertain (15, 17). Therefore, this present study aimed to investigate these changes. The results revealed that during TURBT surgery, the absorption of the irrigation fluid (glycine in this study) led to decreased serum sodium levels, subsequently affecting serum osmolality and creatinine levels. Notably, these changes were temporary and returned to baseline levels shortly after the operation.

Regarding gender differences, it was observed that men had higher postoperative, recovery, and in-hospital blood sugar levels compared to women, while preoperative blood sugar levels did not differ between genders. However, it is important to note that the average blood sugar levels in both groups did not reach dangerous levels requiring immediate intervention for diabetes (less than 126 mg/dL). Therefore, it can be inferred that blood sugar level may contribute as a contributing factor to the occurrence of surgery-related complications in men. However, the impact may be mediated by its effect on serum osmolality, which puts individuals at higher risk of transurethral resection (TUR) syndrome. As such, this study did not investigate the association between gender differences and the risk of TUR syndrome and TURBT complications. Further research is needed to thoroughly examine these potential relationships.

In terms of the influence of a history of TURBT, individuals with prior history exhibited lower potassium levels during recovery, as well as higher creatinine and blood sugar levels during recovery and hospitalization. However, the levels of these factors at other time points, as well as serum sodium and blood urea nitrogen (BUN) levels, and subsequently serum osmolality, did not significantly differ compared to those without a history of TURBT. These findings suggest a heightened risk of surgery-related complications in individuals with a history of TURBT. However, this particular aspect has not been thoroughly investigated in previous studies, highlighting the need for future research to definitively determine the association.

Regarding age as a factor, a negative correlation was observed between age and serum potassium levels during recovery and in the hospital section; however, age did not significantly influence other study parameters, including serum sodium, BUN, blood sugar levels (particularly after surgery), except for a positive relationship with serum creatinine levels in the in-hospital section. This relationship is expected considering the age-related increase in creatinine levels. Additionally, the absence of an association between patient age and serum osmolality suggests that age may not significantly impact the risk of complications related to TUR syndrome following surgery.

Regarding minor factors associated with the investigated surgery, the quantity of glycine, saline, and overall irrigation fluids used during and after the procedure had minimal impact on serum levels of sodium, potassium, blood sugar, BUN, and creatinine. Furthermore, increasing the consumption of these substances did not correlate with a higher risk of surgical complications. However, an extended duration of surgery exhibited a significant association with decreased serum osmolality before and after the operation. Although serum levels of sodium, blood sugar, and

BUN were unaffected by this duration, the decrease in osmolality is noteworthy as it raises the likelihood of TUR syndrome. This finding aligns with previous studies conducted by Yousef, Michielsen, and Moharari et al., which highlight that the risk of complications such as electrolyte and hemodynamic disorders and TUR syndrome is linked to the properties of the irrigation fluid rather than its volume (18, 17, 15). Therefore, surgeons and anesthesiologists should consider the duration of contact between the irrigation fluid and the bladder mucosal surfaces, rather than the volume of liquid used, during and after the operation.
Furthermore, we observed a significant decline in sodium levels, which is a key component of serum osmolality, as well as serum creatinine levels post-surgery. However, over time, as the patient recovers from the surgical conditions, these levels return to their baseline values prior to the surgery. This indicates that the risks of electrolyte disorders, hemodynamic disruptions, and TUR syndrome diminish as time passes. Hence, if no complications are observed during or immediately after surgery, it can be concluded with greater confidence that these complications did not occur during hospitalization.

CONCLUSION

In conclusion, the increase in potassium and blood sugar levels during hospitalization, despite their inverse relationship with each other, is a notable finding in this study. However, further research is required to investigate the underlying causes of this phenomenon.

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