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Ethanol Monitoring of Irrigating Fluid Absorption in Transurethral Prostatic Surgery

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The ethanol concentration in expired breath (EB-ethanol$_A$) was repeatedly measured in 50 patients undergoing transurethral prostatic surgery in which the irrigating fluid was 1.5% glycine + 2% ethanol in water. EB-ethanol$_A$ was compared at 10-min intervals to the serum sodium concentration, the serum glycine concentration, and the absorbed volume of irrigant. The EB-ethanol$_A$ was found to be related directly to the serum glycine concentration (R^2 = 0.75) and, inversely, to changes in the serum sodium concentration (R^2 = 0.81). The cumulative absorbed volume of irrigant could be predicted from a single EB-ethanol$_A$ reading at the end of each 10-min interval (R^2 = 0.82); the reliability was improved by taking into account the absorption time (R^2 = 0.89). Extravasation of irrigating fluid was indicated by a stable or increasing EB-ethanol$_A$ after the ethanol-tagged irrigant had been discontinued. Ethanol monitoring is a simple and inexpensive method of testing for the presence, and measuring the degree, of irrigant absorption in transurethral prostatic surgery. (Key words: Alcohol. Fluid balance: monitoring. Ions: sodium. Surgery, urologic: prostatectomy.)

ABSORPTION OF IRRIGATING FLUID during transurethral resection of the prostate (TUR) can suddenly evoke a variety of symptoms, such as apprehension, confusion, hypertension, blurred vision, renal insufficiency, and circulatory shock.[1–3] The mortality for this "TUR syndrome" has decreased since the introduction of non-hemolytic irrigating fluids,[4,5] but symptoms due to irrigant absorption still occur in 5–10% of the TURs performed.[1,6] A method for the continuous measurement of irrigant absorption would, therefore, be valuable not only for identifying patients who should receive special intra- and postoperative treatment, but also for indicating when steps should be taken to limit further absorption and, thus, prevent the development of a TUR syndrome. A new and simple method that may be suitable for such monitoring in routine TURs is ethanol tagging of the irrigating fluid, wherein fluid absorption is detected by analysis of ethanol in the expired breath. Hultén *et al.*,[7] who recently described this method of detecting absorption and who used 2% ethanol in 5% mannitol as the irrigating fluid, demonstrated that the bladder is impermeable to ethanol. The fact that mannitol could be detected in serum when ethanol appeared in the exhaled breath indicated that the tracer substance entered the body through absorption of the irrigating fluid.

The purpose of the present study was to assess the value of ethanol monitoring of the irrigant absorption during TUR by examining the relationship between the ethanol content of the expired breath and various common indexes of irrigant absorption, such as change in the serum sodium concentration and the volume of irrigant absorbed.

Materials and Methods

Fifty patients undergoing TUR for benign prostatic hypertrophy (mean age 69 ± 7 (SD), mean weight of resectate 23 ± 12 g; mean resection time 50 ± 19 min; median blood loss 470 ml, range 50–1575) were studied. No patient was debilitated due to pulmonary disease. Premedication consisted of oxazepam 25–50 mg orally. Epidural anesthesia was induced with 8–14 ml of mepivacaine 2% + epinephrine (Carbocain®-adrenalin, Astra, Sweden) using an indwelling catheter. Ringer's acetate solution (ion content in mmol · 1000 ml^{-1}: sodium 130, potassium 4, calcium 2, magnesium 1, acetate 30, and chloride 110) was given in a volume of 10 ml · kg^{-1} during induction of anesthesia and at a rate of between 50 to 150 ml in 10 min during TUR, depending on the blood loss. When blood loss exceeded 500 ml, 100–500 ml of dextran 70 in normal saline (Macrodex®, Pharmacia, Sweden) was also administered (n = 8). No whole blood, packed red cells, plasma, diuretic, or hypertonic saline was given to any patient during the period of study. A Storz 27 Fr. resectoscope and the intermittent technique for filling the bladder were used in all TURs. During resection, the irrigating fluid used was 1.5% glycine + 2% ethanol in water (osmolality 650 mosmol · kg^{-1}; produced by Travenol AB, Sweden). Postoperatively, it was 0.9% sodium chloride. Every 5 min during surgery, an expired breath test was performed with an Alcolmeter® S-D2 (Lions Laboratories Ltd., Barry, Wales). This device measures the ethanol content of the exhaled breath and extrapolates the value to the corresponding blood ethanol concentration based upon the ratio of expired blood/breath ethanol concentration[8] (one part per thousand = 1‰ = 0.1 g/dL = 21.7 mmol · l^{-1}) in steps of 0.05‰ from 0 to 9.95‰. The Alcolmeter was set to read 1.0‰ before each TUR by using a Mini-Nalco calibrating gas (Intoximeters Inc., St. Louis, MO). The patient was instructed

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to inhale and then exhale into the mouthpiece of the Alcolmeter, and a sample was taken at the end of the exhalation. Nose clips were not used. In 15 patients, all measurements specified below were performed every 10 min ("collection period") during TUR, while, in the remaining 35, they were made only after alcohol was detected by the Alcolmeter.

Volumetric Fluid Balance

Before and after use, the irrigating fluid bags were weighed to the nearest gram on a Mettler P-10 electronic scale (Mettler Instruments AG, Zürich, Switzerland). While being used, they were placed 60 cm above the estimated middle of the prostatic fossa. A sterile plastic drape was arranged to collect spillover from the returned irrigating fluid. A volumetric irrigating fluid balance was obtained every 10 min by closing the irrigant inlet, emptying the bladder, and replacing the irrigating fluid bag and the collecting bucket. To each collecting bucket, about 1000 units of heparin was added to prevent clotting. After the return had been stirred with a paddle for 30 seconds, a sample was taken for determination of the irrigant hemoglobin concentration (U-Hb). At each measurement of the volumetric fluid balance, the blood loss was calculated as the product of U-Hb and fluid volume, using the blood hemoglobin concentration (B-Hb) at the end of the collection period as a reference.[9] The volume of irrigant absorbed was obtained as the difference between the volumetric fluid balance and the blood loss.

Blood Samples

Blood for serial determinations of B-Hb, serum sodium concentration (S-Na), and serum osmolality were drawn through a cannula placed in the radial artery at the end of each collection period. The B-Hb and U-Hb were determined on a Coulter Counter S plus (Counter Electronics, Hialeah, Florida), and the S-Na concentration was determined by flame photometry (AutoCal 543, Instrumentation Laboratory, Milan, Italy). For 50 duplicate samples from patients, the coefficients of variation were 1.2% for B-Hb and 0.55% for S-Na. The accuracy of the U-Hb determinations was checked by dispersion of known amounts of bank blood (50–300 ml in 50 ml increments; determination in triplicate) in 3 l of irrigating fluid; the mean deviation from the correct amount of blood was 5 ml. Serum osmolality was measured with a Roebling Micro-osmometer (Herman Roebling, Berlin, Germany) with a coefficient of variation of 0.5%. Serum ethanol and serum glycine were determined serially on samples from collection periods of irrigant absorption. S-ethanol (n = 58) was measured by gas chromatography, using acetonitril as an internal standard; the coefficient of variation was 4%. Serum glycine (n = 25) was determined on a Liquimat III amino acid analyzer (Kontron International, Zürich, Switzerland).

The study was approved by the Ethics Committee of Huddinge University Hospital and Karolinska Institute, Stockholm, and approved as a clinical trial of ethanol-tagged irrigating fluid by the Swedish National Board of Health and Welfare. The method of statistical analysis was stepwise multiple regression (where R^2 is the coefficient of determination). Correlations were included in the presentation when significant by $P < 0.05$. In the presentation, the abbreviation EB-ethanol$_A$ is used for the absolute value of the ethanol concentration in the expired breath as measured by the Alcolmeter, while EB-ethanol$_n$ is used for the incremental change of the ethanol concentration in the expired breath during a specified period of time as measured by the Alcolmeter.

Results

Change in EB-ethanol during 10 Min of TUR

Ethanol was detected in 170 of the 490 tests on expired breath. Data from a representative case are illustrated in figure 1. Four equations describing the relationship between the incremental change in the ethanol concentration in the expired breath (EB-ethanol$_n$) during 10 min of a TUR (a collection period) and other variables are presented in the Appendix. EB-ethanol$_n$ was dependent on the volume of the irrigant absorbed during the same collection period, but was modified by previous absorption and changes in EB-ethanol$_n$ (equations I–III). There was a significant correlation between the change in S-Na concentration during a given collection period and EB-ethanol$_n$ ($R^2 = 0.80$; equation IV). Consideration of past and current changes in S-osmolality did not significantly strengthen these correlations.

Cumulative Absorption

The ethanol concentration in the expired breath (EB-ethanol$_A$) was plotted against the cumulative absorption of irrigant, calculated for each collection period, and against the total change in S-Na following the induction of anesthesia. There was a significant correlation between the cumulative absorption of irrigant and EB-ethanol$_A$ ($R^2 = 0.82$; fig. 2). When absorption continued for many collection periods, the relative change in the EB-ethanol was less for a given amount of absorption; this could be accounted for by taking into consideration the time required for absorption to occur (fig. 3). The correlation between the total change in S-Na following the induction of anesthesia and EB-ethanol$_A$ is shown in fig. 4.

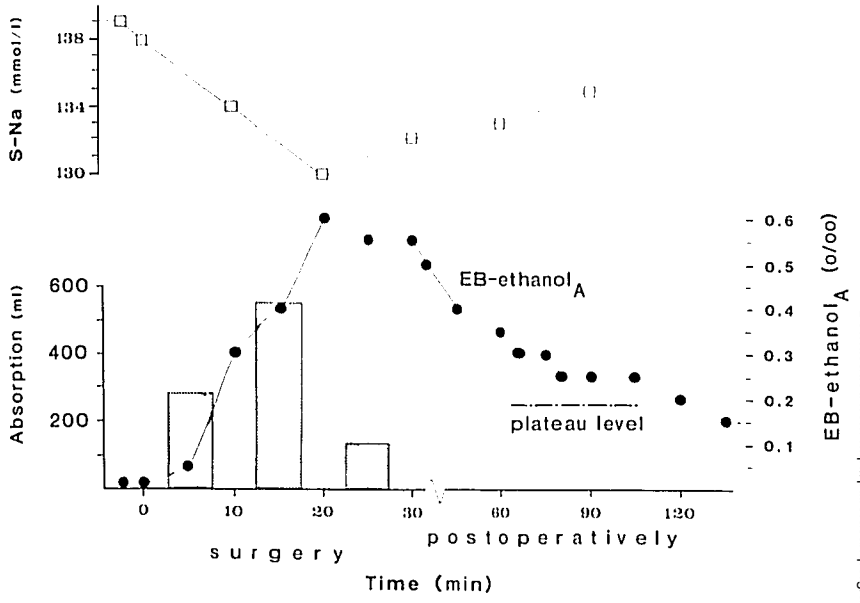

FIG. 1. The volume of irrigant absorbed (bars), ethanol concentration in the expired breath (EB-ethanol$_A$), and serum sodium concentration (S-Na) measured repeatedly during and after TUR in one patient.

S-ETHANOL AND S-GLYCINE

EB-ethanol$_A$ *versus* S-ethanol is plotted in figure 5 and EB-ethanol$_A$ *versus* S-glycine in figure 6. There was a linear correlation between the S-ethanol concentration and the change in S-Na concentration since the beginning of TUR ($R^2 = 0.65$).

BODY WEIGHT AND PREOPERATIVE SERUM CREATININE

Body weight (mean 74 ± 10 kg) had no significant influence on the observed correlations. On the other hand, the preoperative serum creatinine concentration (mean 97 ± 22 μmol/l) had a significant effect on the relationship between the cumulative absorption and EB-ethanol$_A$, an elevated serum creatinine concentra-

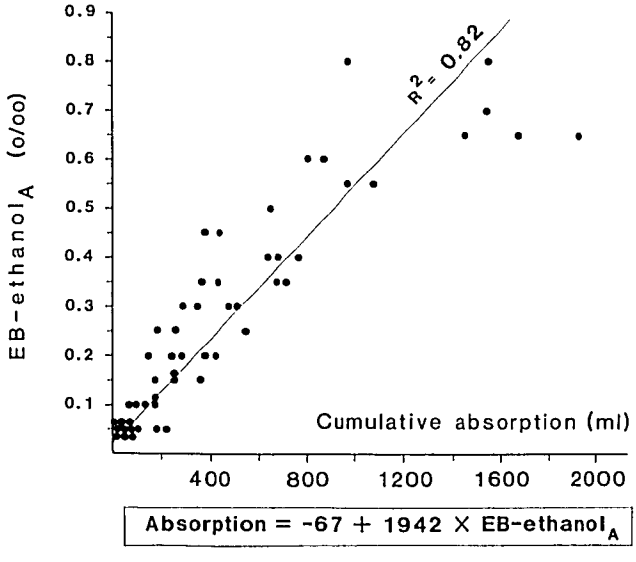

FIG. 2. The ethanol concentration in the expired breath (EB-ethanol$_A$) *versus* the cumulative absorption of irrigant measured at 10-min intervals during TUR.

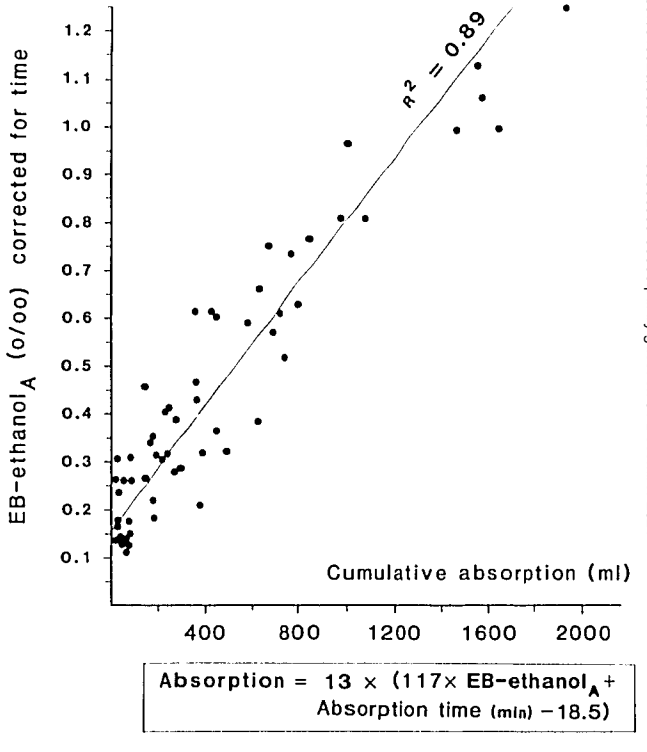

FIG. 3. The same plot as in figure 2, but with a correction factor to take into account time required for the absorption to occur. The linear correlation to EB-ethanol$_A$ in patients with large continuous irrigant absorption was strengthened (the correction factor was: absorption time in minutes divided by 117).

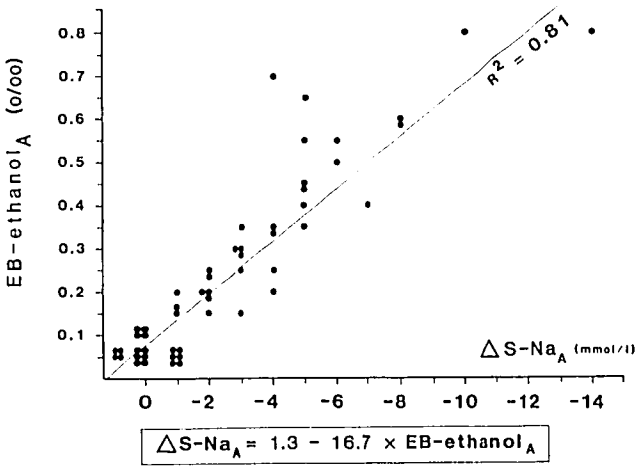

FIG. 4. The ethanol concentration in expired breath *versus* the total change in the serum sodium concentration since introduction of anesthesia. S-Na was measured at the end of each 10-min period during TUR in which ethanol was detected.

tion giving a more pronounced EB-ethanol$_A$ response to absorption.

S-Na and Absorption of Irrigant with no Positive Expired Breath Test

In the 15 patients in whom 10-min determinations of the variables were performed irrespective of the ethanol concentration in the expired breath, the coefficient of variation obtained for the S-Na determinations during collection periods for which the expired breath test was negative (n = 34) was 0.60%, and, thus, practically identical to the values for the 50 duplicate samples from patients.

S-Osmolality

In patients with little, if any, absorption, there were only small changes in S-osmolality during TUR (the coefficient of variation being 0.4–1.0%). Greater absorption, however, was followed by a transient increase in S-osmolality, as much as 15–25 mosmol · kg^{-1}. With regard to the incremental change of S-osmolality in all the collection periods associated with a positive EB-ethanol test (n = 80), there was a significant linear correlation between S-osmolality and the concomitant change in S-Na (inverse relation; $R^2 = 0.40$) and EB-ethanol$_n$ ($R^2 = 0.33$). Of the four blood samples showing hemolysis, only one had been collected during irrigant absorption.

Postoperative Elimination of Ethanol

Except in those patients displaying irrigant extravasation (see below), after completion of the TUR and the change to 0.9% sodium chloride as the irrigant, the EB-ethanol$_A$ decreased over 25–35 min to reach a plateau level approximately half as high as the value recorded at the end of TUR (fig. 1). In the ten patients with the largest absorption volumes (275–1925 ml), the total absorbed volume during TUR was correlated to the EB-ethanol$_A$ plateau level ($R^2 = 0.65$, $P < 0.01$; equation V). The EB-ethanol$_A$ decreased steadily and, in most patients, was not detectable after 1–3 h.

Extravasation of Irrigating Fluid

In the 15 patients for whom 10-min determinations of all the variables were made, there were five collection periods for which the volumetric fluid balance indicated retention of fluid ranging from 75 to 180 ml, although there was no change in EB-ethanol$_A$ or S-Na. This lack

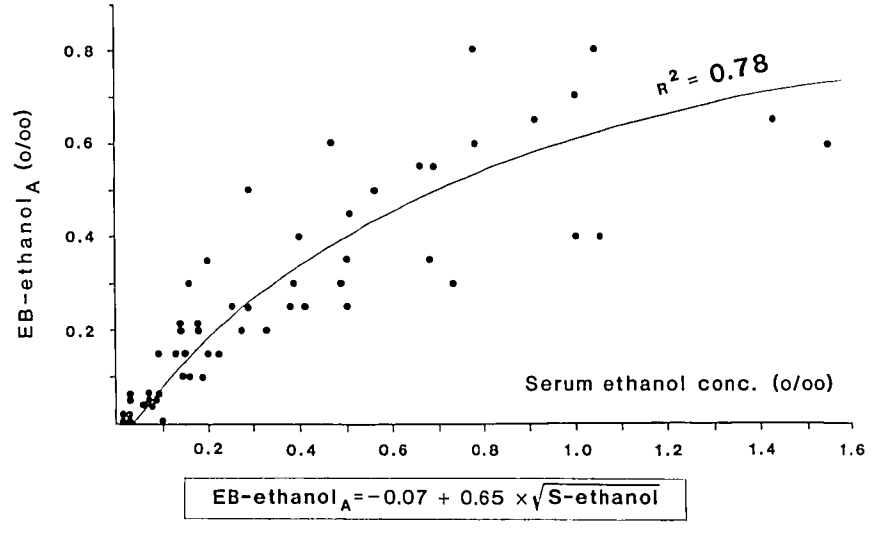

FIG. 5. The ethanol concentration in the expired breath *versus* the serum ethanol concentration at a given time during TUR in which irrigant absorption was recorded.

of a correlation was interpreted as indicating extravasation of irrigating fluid. In the 35 patients, there were three with suspected extravasation. The volumetric fluid balance in these cases indicated massive absorption (about 600 ml in 10 min, 900 ml in 20 min, and 1400 ml in 20 min) associated with no concomitant change in S-Na and only a slight increase in EB-ethanol$_A$, which ranged from 0.10 to 0.15‰. After completion of the TUR, however, the EB-ethanol$_A$ was stable or increased, and there was a postoperative decrease in S-Na of 2–3 mmol/l. In the case of the most pronounced extravasation, reoperation was undertaken 45 min after TUR to drain the absorbed fluid; a *sectio alta* confirmed the diagnosis of irrigant extravasation.

Untoward Effects

Two patients recording EB-ethanol$_A$ values of 0.80‰ claimed upon questioning that they felt "happy" and "extremely well." These effects were ascribed to ethanol; they caused no problems in patient management and subsided with the decrease in EB-ethanol$_A$ upon completion of the TURs. However, one of these two patients (total absorption 1925 ml) complained of nausea 1 h postoperatively. An 83-yr-old patient with an absorption volume of 880 ml and a maximum EB-ethanol$_A$ of 0.60‰ (fig. 1) was more apathetic during absorption than before and, on completion of the TUR, was reported to feel "extremely well." There was a discrete smell of alcohol from patients with irrigant absorption of this magnitude. No other untoward effect that might possibly be related to ethanol was noted.

Discussion

Early detection of irrigating fluid absorption and prompt treatment are important in preventing development of TUR syndrome.[3] Even if absorption elicits no more than mild symptoms, the volume absorbed is important, since it should prompt reduction of the intravenous fluid supplementation. However, the existing methods of measuring absorption are not well suited for routine use. Unless carried out meticulously, the volumetric balance, gravimetric, and radioisotope techniques may not be sufficiently accurate.[10] The first two of these methods require concomitant determination of the blood loss. If they are to help prevent the TUR syndrome, the measurements need to be repeated several times during surgery, and the assistance of additional staff is usually required.

In contrast, ethanol monitoring of irrigating fluid absorption during TUR is easy to perform: the patient inhales and then exhales into the mouthpiece of the Alcolmeter, and the absorption is then estimated from the ethanol concentration shown on the display; the entire procedure requires less than a minute. Detection of absorption using ethanol analysis does not depend upon concomitant determination of blood loss. The tracer substance is usually familiar to the patient and readily accepted. Additional advantages are that ethanol monitoring is non-invasive and the patient is not exposed to the tracer unless absorption has actually occurred.

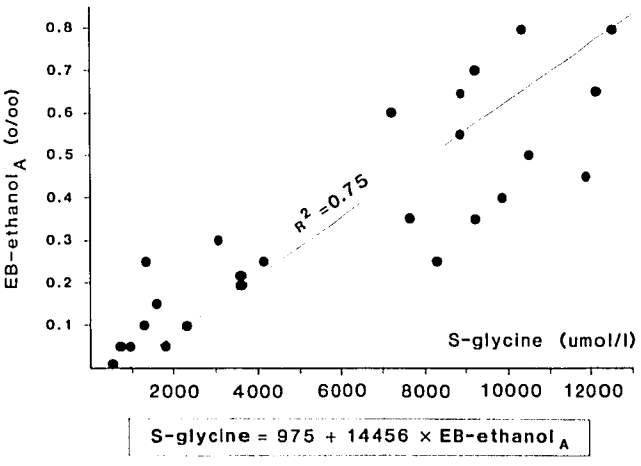

FIG. 6. The ethanol concentration in the expired breath *versus* the serum glycine concentration at the end of 25 collection periods in six patients.

Equipment for analysis of EB-ethanol$_A$ is available at low cost. Such devices are widely used by the police to test automobile drivers suspected of being intoxicated. They are also used in emergency wards to test for the presence of ethanol in intoxicated patients, and are considered very reliable.[8] The EB-ethanol$_A$ is usually expressed in terms of a blood ethanol concentration; the ratio of the ethanol levels in the blood and the expired breath appears to be fairly constant at 2,100/1 at blood ethanol concentrations from 0 to 1.0‰.[8] With higher concentrations, breath values tend to be slightly lower than venous blood values;[8,11] this may be due to uptake of ethanol by the mucosa lining the tracheobronchial tree during exhalation.[11,12] Patients with respiratory disease may have a lower blood:breath partition coefficient of ethanol during exhalation, although it has been argued that this has no systematic effect upon end-tidal breath-ethanol analysis.[12] Nevertheless, the value of ethanol monitoring of irrigant absorption during TUR in patients with pulmonary impairment needs to be evaluated, since such patients were not included in this study.

Absorption detected by the volumetric fluid balance during TUR usually resulted in a prompt increase in the EB-ethanol$_A$, and a simultaneous decrease in the serum sodium level. At the end of TUR, there was typically a two-phase drop in the EB-ethanol$_A$ (fig. 1). However, there were a few cases characterized by a different

pattern; here, the increase of the EB-ethanol$_A$ during absorption, if any, was smaller than in other patients, and, on completion of the TUR, the ethanol concentration remained stable or increased. In one case, the diagnosis of irrigating fluid extravasation was confirmed at re-operation. These results suggest that the pattern of ethanol concentration in the expired breath offers a possibility of distinguishing between the primarily intravascular and extravascular types of absorption. While the EB-ethanol$_A$ did not follow the pattern of irrigant absorption in patients with suspected extravasation, it varied inversely with the serum sodium level at all times. Thus, monitoring ethanol content of the expired breath yields essentially the same information as serial analysis of serum sodium, irrespective of the type of absorption.

The correlations shown in the graphs and presented in the Appendix indicate attenuation of the ethanol response to absorption with time; this means that the incremental increase in the ethanol concentration in the expired breath during a collection period (EB-ethanol$_n$) will be smaller if absorption has also occurred during previous periods. The reason for this will be evident from consideration of the situation where no further absorption occurs; the ethanol concentration in the circulation will then rapidly decrease, owing, in part, to metabolism, but primarily to distribution of the infused ethanol in the total body water. When absorption continues for more than 10 min, diffusion and metabolism of ethanol from the previous time period must be accompanied by some additional absorption if the ethanol concentration in the circulation is to remain constant. In an estimate of the total absorption from an expired breath test during TUR, a correction factor that takes account of time should be applied, especially in the case of massive and prolonged absorption (fig. 3). This continuous distribution of ethanol in the body might explain why the body weight had no significant influence on the relation between EB-ethanol$_A$ and absorbed irrigant volume during TUR, and might also explain the great variance between the ethanol concentrations of the arterial blood and breath samples during surgery (fig. 5).

Although the ethanol-tagged irrigating fluid was well tolerated by the patients, some untoward effects were noted. The postoperative nausea experienced by the patient with an absorption volume of 1925 ml may have been due to metabolic effects of glycine.[13] Two patients displayed mild euphoria that was probably due to the ethanol; the absence of any signs of intoxication by water or glycine in these patients indicates that, at concentrations associated with massive absorption, the ethanol may be more toxic than both glycine and water. We considered this situation to be unacceptable, and, in the TURs performed during the last 10 months, we have, therefore, been using 1.5% glycine + 1% ethanol-tagged irrigating fluid. According to *in vitro* tests performed by the manufacturer, neither the 1 nor 2% ethanol + 1.5% glycine is hemolytic.

The addition of ethanol to an irrigating fluid considerably increases its osmolality. The absorption of irrigant was followed by a transient increase in the serum osmolality. Inasmuch as 1.5% glycine + 1% ethanol is still hypertonic, we foresee the possibility of reducing the glycine content of the irrigant where ethanol is used as a tracer.

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References

1. Harrison RH, Boren JS, Robison JR: Dilutional hyponatremic shock: Another concept of the transurethral prostatic resection reaction. J Urol 75:95–110, 1956
2. Norris HT, Aasheim GM, Sherrard DJ, Treman JA: Symptomatology, pathophysiology and treatment of the transurethral resection of the prostate syndrome. Br J Urol 45:420–427, 1973
3. Valk WL, Mebust WK: Water intoxication, Benign Prostatic Hypertrophy. Edited by Hinman F Jr. New York, Springer-Verlag, 1983, pp 851–854
4. Creevy CD: Hemolysis and transurethral resection. Surgery 39:180–188, 1956
5. Emmett JL, Gilbaugh JH, McLean P: Fluid absorption during transurethral resection: Comparison of mortality and morbidity after irrigation with water and non-hemolytic solutions. J Urol 101:884–889, 1969
6. Rhymer JC, Bell TJ, Perry KC, Ward JP: Hyponatraemia following transurethral resection of the prostate. Br J Urol 57:450–452, 1985
7. Hultén JO, Jorfeldt LS, Wictorsson YM: Monitoring fluid absorption during TURP by marking the irrigating solution with ethanol. Scand J Urol Nephrol 20:245–251, 1986
8. Gibb KA, Yee AS, Johnson CC, Martin SD, Nowak RM: Accuracy and usefulness of a breath alcohol analyzer. Ann Emerg Med 13:516–520, 1984
9. Hagstrom RS: Studies on fluid absorption during transurethral prostatic resection. J Urol 73:852–859, 1955
10. Madsen PO, Kuni H, Naber KG: Various methods of determining irrigating fluid absorption during transurethral resection of the prostate. Urol Res 1:70–78, 1973
11. Wright BM, Jones TP, Jones AW: Breath alcohol analysis and the blood:breath ratio. Med Sci Law 15:205–210, 1975
12. Haas H, Morris JF: Breath-alcohol analysis in chronic bronchopulmonary disease. Arch Environ Health 25:114–118, 1972
13. Alexander JP, Pollard A, Gillespie IA: Glycine and transurethral resection. Anaesthesia 41:1189–1195, 1986

Appendix

Equations Describing Incremental Changes in EB-ethanol

The linear correlation between the absorption$_n$ (in ml) during a collection period (10 min) of TUR and the change in

ethanol concentration in the expired breath (EB-ethanol$_n$; in ‰) is described by the expression (n = 80):

$$\text{Absorption}_n = 57 + 1051\ \text{EB-ethanol}_n\ (R^2 = 0.56) \quad (I)$$

This correlation is strengthened on inclusion of the absorption volumes for the previous two collection periods (absorption$_{n-1}$ and absorption$_{n-2}$) (liters):

$$\text{EB-ethanol}_n = 0.03 + 0.63\ \text{absorption}_n - 0.16\ \text{absorption}_{n-1} - 0.29\ \text{absorption}_{n-2}\ (R^2 = 0.72) \quad (II)$$

The modification of the EB-ethanol$_n$ response to absorption by previous changes in EB-ethanol (EB-ethanol$_{n-1}$ and EB-ethanol$_{n-2}$) is described by the expression:

$$\text{Absorption}_n = 1100\ \text{EB-ethanol}_n + 533\ \text{EB-ethanol}_{n-1} + 413\ \text{EB-ethanol}_{n-2}\ (R^2 = 0.80) \quad (III)$$

The correlation between the EB-ethanol$_n$ (‰) and the change in S-Na (mmol/l) during a collection period is described by the expression:

$$\text{EB-ethanol}_n = 0.05 - 0.05\ \text{S-Na}_n\ (R^2 = 0.80) \quad (IV)$$

This correlation was not improved by taking into account previous changes in S-Na or previous absorptions.

Equation for Retrospective Estimation of Absorption

A retrospective estimate of the absorbed volume (litres) during TUR could be obtained from the EB-ethanol$_A$ plateau value (appearing about 30 min after completion of TUR) in the ten patients with the largest absorption volumes (275–1925 ml);

$$\text{Absorption} = \nabla + 0.2 + 3\ \text{EB-ethanol}_A\ (R^2 = 0.65) \quad (V)$$