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REVIEW ARTICLE

Fluid absorption in endoscopic surgery

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Fluid absorption is an unpredictable complication of endoscopic surgery. Absorption of small amounts of fluid (1–2 litre) occurs in 5–10% of patients undergoing transurethral prostatic resection and results in an easily overlooked mild transurethral resection (TUR) syndrome. Large-scale fluid absorption is rare but leads to symptoms severe enough to require intensive care. Pathophysiological mechanisms consist of pharmacological effects of the irrigant solutes, the volume effect of the irrigant water, dilutional hyponatraemia and brain oedema. Other less widely known factors include absolute losses of sodium by urinary excretion and morphological changes in the heart muscle, both of which promote a hypokinetic circulation. Studies in animals, volunteers and patients show that irrigation with glycine solution should be avoided. Preventive measures, such as low-pressure irrigation, might reduce the extent of fluid absorption but does not eliminate this complication. Monitoring the extent of absorption during surgery allows control of the fluid balance in the individual patient, but such monitoring is not used widely. However, the anaesthetist must be aware of the symptoms and be able to diagnose this complication. Treatment should be based on administration of hypertonic saline rather than on diuretics. New techniques, such as bipolar resectoscopes and vaporizing instead of resecting tissue, result in a continuous change of the prerequisites for fluid absorption and its consequences.

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Many endoscopic surgical procedures require the use of an irrigating fluid to dilate the operating field and to wash away debris and blood. A potential complication of such irrigation is systemic absorption of the fluid to the extent that overt symptoms are produced. The consequences depend on the rate, volume and nature of the fluid absorbed.

History

Fluid absorption was described, in 1947, as the cause of renal damage after transurethral resection of the prostate (TURP). The sterile water used for irrigation apparently caused intravascular haemolysis when absorbed. Within a few years, the modern non-electrolyte solutions containing glycine, mannitol or sorbitol were introduced to prevent haemolysis, without dispersing the electric current used for cutting with the resectoscope. However, other adverse effects due to fluid absorption soon became apparent. They arose in both the cardiovascular and nervous systems and, in the late 1950s, became known as the 'transurethral resection (TUR) syndrome'. Since then, several hundred life-threatening[32 60 96] and even fatal[5 12 69 87 100] TUR syndromes have been reported. Severe events are associated with absorption of >3 litre of fluid.

The TUR syndrome can occur with other operations including transcervical resection of the endometrium (TCRE),[15 28 72] TUR of bladder tumours,[20 38] cystoscopy,[109 127] arthroscopy,[69] rectal tumour surgery, vesical ultrasonic lithotripsy and percutaneus nephrolithotripsy.[19 24 115]

Mechanisms

Irrigating fluid is most frequently absorbed directly into the vascular system when a vein has been severed by electrosurgery. The driving force is the fluid pressure, which needs to exceed the venous pressure of ≈1.5 kPa.[66] The period of time that the fluid pressure exceeds 2 kPa (15 mm Hg) increases significantly with the absorbed volume.[41 77] Major fluid absorption rarely stops once initiated and often coincides with a decrease in arterial pressure.[48]

Extravasation occurs after instrumental perforation of the prostatic capsule during TURP, the uterine wall in TCRE,[89] or the bladder wall during cystoscopy[127] and TUR of bladder tumours.[20 38] Several litres of irrigating fluid are rapidly deposited in the periprostatic, retroperitoneal or intraperitoneal spaces. The fluid pressure only needs to exceed the intra-abdominal pressure of ≈0.5 kPa for extravasation to occur.[67]

Extravasation is more common during renal stone surgery,[24 115] while direct intravascular absorption is the more common during TURP[31 34 45 48] and TCRE.[89]

Risk factors

Smoking is the only patient factor known to be associated with large-scale fluid absorption during TURP.[43] Patients with prostate cancer who undergo TURP have the same incidence of fluid absorption as those with benign tissue.[48]

Fluid absorption increases with the extent of the resection as the exposure is prolonged.[48] Visual indications of fluid absorption to the surgeon are usually lacking, although capsular perforation,[103] which occurs in at least 10% of the TURPs, or apparent damage to a venous sinus increases the likelihood of its occurrence.

During TCRE, fluid absorption occurs more often during resection of fibroids.[71 113] Variable amounts of fluid are extravasated via the Fallopian tubes[88] but previous sterilization does not alter total absorption.[15 89]

Incidence

Mild to moderately severe TUR syndrome occurs in between 1 and 8% of TURPs performed.[25 31 34 111 121] Certain smaller patient series have a higher incidence,[4 7 99] while others do not report any cases.[26] One problem is that few studies use a clear definition of the TUR syndrome. High variability in fluid absorption and patient's responses makes it necessary to include up to 400 patients in any meaningful examination of the incidence of the syndrome. The use of a checklist to grade symptoms is recommended (Table 1).[54 55 92]

An alternative approach is to measure the amount of absorbed fluid and the number of patients who develop symptoms. The likelihood of symptoms developing can then be described in terms of 'risk' for increasing volumes of absorbed fluid (Figs 2 and 3). Such data allows valid comparison of the incidence of symptoms with various irrigating fluids.

Absorption in excess of 1 litre of glycine solution, which is associated with a statistically increased risk of symptoms,[92] has been reported in 5–20% of the TURPs performed (Fig. 1). Extravasation is the cause in ∼20% of these patients.[54 55 92]

Fluid absorption is slightly more common during TCRE than during TURP,[15 28 72] the average being 400–700 ml. Istre[71] reported absorption to be in excess of 1.5 litre in 9% of patients, but there also appears to be a learning curve. In larger case series, the incidence of the TUR syndrome may be <1%.[73]

In one study, fluid absorption exceeded 1 litre in 7% of patients undergoing percutaneous renal stone surgery.[19] Gehring and co-workers detected fluid absorption in all 31 patients who underwent this operation, and those with extravasation required more opioids and had a longer hospital stay.[24] Four of them remained in the ICU for more than 1 day.

Symptoms of glycine absorption

The incidence and severity of symptoms for increasing amounts of absorbed fluid have been best established for glycine solution. In one retrospective analysis,[92] patients who absorbed 0–300 ml of glycine solution had an average of more than one symptom. This increased to more than two when 1–2 litre had been absorbed, to more than three when 2–3 litre had been absorbed, and to more than five for volumes >3 litre. The odds ratio for symptoms to develop was 7 for TURPs during which 1–2 litre of glycine had been

Table 1 A checklist used to define and score symptoms included in the TUR syndrome. In three studies,[54 55 92] the number and severity of symptoms showed a statistically significant increase as more irrigating fluid was absorbed. HR, heart rate; SAP, systolic arterial pressure

Symptom	Severity score		
	1	2	3
Circulatory			
Chest pain	Duration <5 min	Duration >5 min	Repeated attacks
Bradycardia	HR decrease 10–20 bpm	HR decrease >20 bpm	Repeated decrease
Hypertension	SAP up 10–20 mm Hg	SAP up >30 mm Hg	Score (2) for 15 min
Hypotension	SAP down 30–50 mm Hg	SAP down >50 mm Hg	Repeated drops >50 mm Hg
Poor urine output	Diuretics are needed	Repeated use	Diuretics ineffective
Neurological			
Blurred vision	Duration <10 min	Duration >10 min	Transient blindness
Nausea	Duration <5 min	Duration 5–120 min	Intense or >120 min
Vomiting	Single instance	Repeatedly, <60 min	Repeatedly, >60 min
Uneasiness	Slight	Moderate	Intense
Confusion	Duration <5 min	Duration 5–60 min	Duration >60 min
Tiredness	Patient says so	Objectively exhausted	Exhausted for >120 min
Consciousness	Mildly depressed	Somnolent <60 min	Needs ventilator
Headache	Mild	Severe <60 min	Severe >60 min

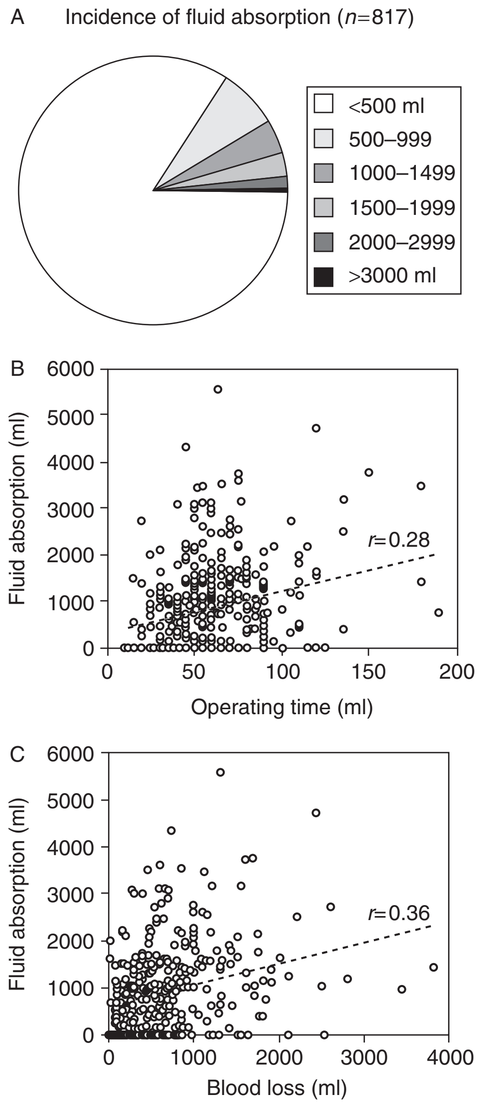

Fig 1 The incidence of fluid absorption during transurethral prostatic resection as measured by the ethanol method in 817 consecutive patients, summarized from two studies.[54 55] The uptake exceeded 500 ml in 16% of the operations performed (A). The amount of absorbed fluid is difficult to predict from the extent of surgery, although it does become more common and more pronounced in prolonged (B) and bloody operations (C). The *x*–*y* plots show data on 375 patients from three studies,[54 55 92] all of those who had fluid absorption and a minority of the patients with zero absorption.

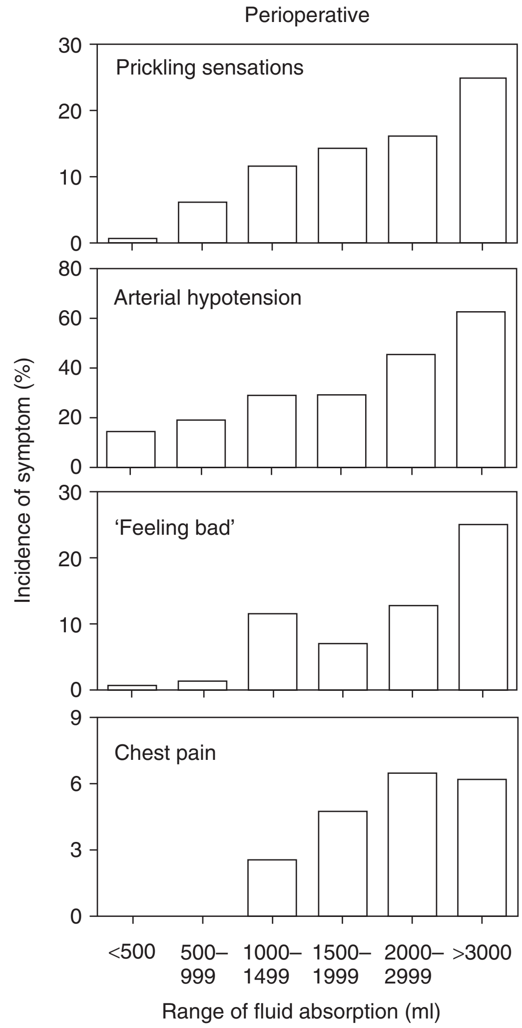

Fig 2 The incidence of prickling sensations, arterial hypotension, feelings of uneasiness and chest pain with increasing amounts of absorption of glycine 1.5% during TURP. The absorption was measured by ethanol 1%. Data are summarized from three studies[54 55 92] using the checklist shown in Table 1.

absorbed. Further increases mainly comprised neurological symptoms. This dose-dependent increase in the number of symptoms arising has been corroborated in subsequent prospective studies.[54 55] A pooled analysis of the incidence of various symptoms, based on these three studies which were carried out in the same way, shows that the TUR syndrome has a progressive nature.

Perioperative

The patient sometimes reports transient prickling and burning sensations in the face and neck, becomes restless and complains of headache. The most consistent signs are bradycardia and arterial hypotension (Fig. 2). 'Feeling bad' is slightly more common than perioperative nausea, which is reported by 5–10% of the patients. Chest pain occurs in 5% of the patients who absorb >1 litre, and is more likely if the blood loss is small.[98] Hypertension is statistically unrelated to fluid absorption.

Postoperative

The most common signs and symptoms are nausea and arterial hypotension followed by vomiting and low urinary output, all of which become more frequent as more irrigating fluid is absorbed (Fig. 3). Visual disturbances are reported by 10% of the patients who absorb >500 ml of glycine solution. Arterial hypertension becomes less common when more irrigating fluid is being absorbed. Depressed consciousness

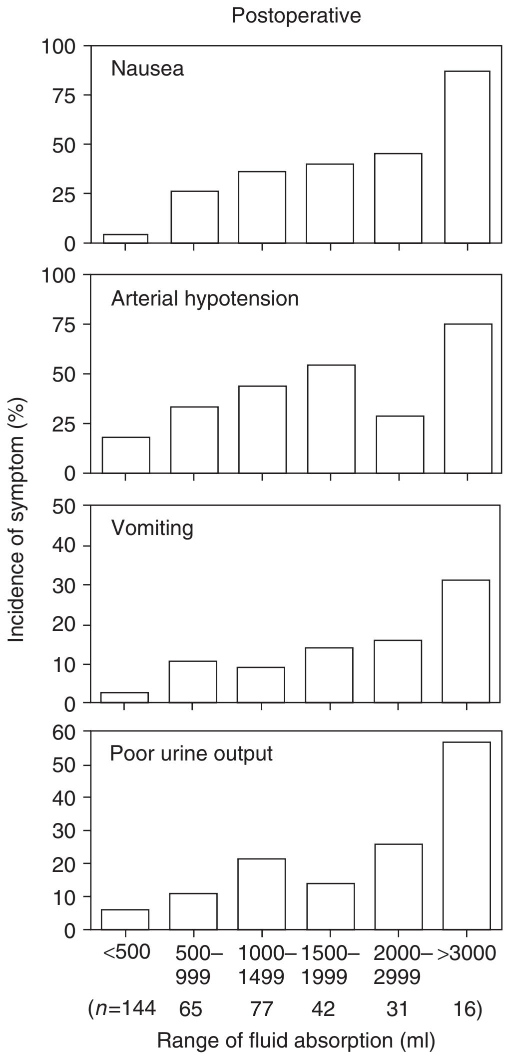

Fig 3 The incidence of nausea, arterial hypotension, vomiting and poor urinary output with increasing amounts of absorption of glycine 1.5% after TURP. The absorption was measured by ethanol 1%. Data are summarized from three studies using the checklist shown in Table 1.

develops in ≈5% of the patients after absorption of >1 litre of fluid. Diarrhoea occurs in 20% of those who absorb >3 litre.

Abdominal pain is reported by 10–20% of patients who absorb >1 litre of fluid. This symptom is strongly related to extravasation, which is also associated with a higher incidence of arterial hypotension and poor urinary output.[37]

The clinician should be aware of a mild TUR syndrome, which is easily overlooked. This presents with nausea and often a sudden reduction in arterial pressure 30–45 min after the operation.[54 55 92] Serum sodium is lowered 5–10 mmol litre^{-1}.[34 72]

The ‘mini-mental’ status test shows that glycine absorption has a strong association with transient confusion after TURP.[83] Apparent confusion may occur in response to absorption of 1–2 litre,[114] but is more consistent with larger absorption volumes[4 25] and might proceed to depressed consciousness[33 102 115] and coma.[60 100 116]

The incidence of acute myocardial infarction during TURP is between 1 and 3%.[70] Evidence of cardiac ischaemia, using Holter ECG, was found in 25% of TURP patients, mostly in those with known cardiovascular disease.[124] A marginal increase in cardiac enzymes occurred in 7% of all TURP patients,[70] but the incidence was higher in patients with glycine absorption.[49]

Severe TUR syndrome is rare but well described in the literature. A review of 24 severe cases (glycine 1.5%) showed that neurological symptoms occurred in 92%, cardiovascular symptoms in 54%, visual disturbances in 42%, digestive tract signs in 25% and renal failure in 21%. The mortality was 25%.[100]

Pharmacokinetics and pharmacodynamics

Glycine is a non-essential amino acid which was introduced in 1948 as an irrigating fluid solute (usually 1.5%) with low cost and lack of allergic reactions. The plasma concentration in humans is 0.3 mmol litre^{-1}, which is raised 25-fold on administration of 1 litre of this fluid. The distribution half-life is only 6 min,[51] while the terminal half-life is between 40 min and several hours.[33 51 56] The half-life is dose-dependent[36] which is probably due to intracellular accumulation of glycine.[86] Penetration into the central nervous system is restricted,[126] but may be clinically important.[112]

Elimination of glycine occurs primarily in the liver, yielding ammonia. Only 5–10% of an excess dose is excreted unchanged in the urine, promoting an osmotic diuresis.[56] The plasma concentration and urinary excretion of other non-essential amino acids are also increased.[32 33]

Visual disturbances correlate with a plasma glycine concentration of 5–8 mmol litre^{-1} [44 82] while higher concentrations produce transient blindness.[120] Nausea and vomiting develop when the plasma glycine concentration exceeds 10 mmol litre^{-1}.[25 33] Concentrations measured in fatal TUR syndromes have been 21 and 80 mmol litre^{-1}.[5 96]

Mannitol is an isomer of glucose used as a 3 or 5% solution. After a short distribution phase, mannitol spreads throughout the extracellular fluid space. The elimination half-life is ∼100 min[51] but can be twice[85] and even four times[1] longer in TURP patients with a moderately elevated serum creatinine concentration.

Mannitol is not metabolized and is excreted unchanged in the urine,[1] promoting an osmotic diuresis. This effect makes it inappropriate to combine irrigation with mannitol 5% and postoperative diuretic therapy.[75 85] However, mannitol is not diuretic in a 0.5–1% concentration as an irrigating fluid mixed with 2–3% sorbitol.[84 87]

A maximum concentration of 2 g litre^{-1} was measured in 10 volunteers who received 1.2 litre of mannitol 3%.[51] Plasma concentrations >4 g litre^{-1} were associated with bradycardia and hypotension after TURP[75] while other authors found few or no symptoms after absorption of mannitol 5%,[1] a fact probably attributable to the isotonic nature of mannitol 5%.

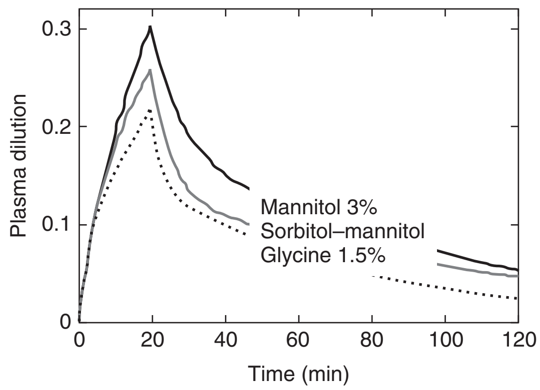

Fig 4 Computer simulation of the plasma dilution resulting from experimental infusion of 1.5 litre of three irrigating fluids for more than 20 min in 10 volunteers. There are only small differences between the fluids despite the differences in half-life of the solutes. Calculation is based on data from ref. 51.

Sorbitol is metabolized to fructose and glucose in the liver and has a distribution half-life of 6 min and a terminal half-life of 33 min.[51] As for glycine, 5–10% of an infused load is excreted unchanged by the kidneys. Plasma sorbitol concentrations corresponding to 2 litre of absorbed fluid have been reported after TURP without associated untoward effects. However, in five patients with TUR syndrome (of whom two died), the total serum concentration of irrigant solutes was between 5.4 and 12.0 g litre^{-1} when irrigation was performed with a mixture containing sorbitol 2.7% and mannitol 0.54%.[87] The major portion of this solute concentration can be attributed to sorbitol.

Water in irrigation fluids

The fluid volume in which the solutes are dissolved adds to the symptoms of fluid absorption. The volume expansion of the intravascular space and dilution of the plasma has been quantified in volunteers. Mannitol 3% expands the plasma more than glycine 1.5%[104] while sorbitol–mannitol takes an intermediate position (Fig. 4).

The lower osmolality of irrigating fluid compared with plasma means that irrigant water enters the cells very quickly after absorption takes place. Glycine and sorbitol enter the cells and, by virtue of osmosis, bring water intracellularly. Cellular oedema develops with a delay related to the half-life of the solute and, together with urinary excretion and surgical haemorrhage, reduces the extracellular overhydration.[104 105]

General pathophysiology

Haemodynamics

Fluid absorption causes a transient hypervolaemia with an increase in central pressures, which plateaus within 15 min.[32 35] Shortness of breath, uneasiness, chest pain and pulmonary oedema may develop on the operating table,[14 21 32] particularly during operations associated with a small blood loss.[35]

Hypervolaemia is followed by a longer and more problematic hypokinetic haemodynamic phase, which is characterized by low cardiac output, hypovolaemia and low arterial pressure.[8 14 105 110] Factors promoting the haemodynamic changeover include natriuresis, osmotic diuresis and, with glycine and sorbitol, intracellular uptake of water. Hyponatraemia, hypocalcaemia,[13 14] low serum osmolality,[100] acute lowering of the body temperature[23] and release of prostatic substances[118] or endotoxins[111] may also contribute. Therefore, bradycardia and a marked decrease in systolic arterial pressure down to 50–70 mm Hg at the end of, or just after, the operation is often the first sign suggesting TUR syndrome.[4 14 110] Pulmonary oedema might also develop late, indicating that serum sodium is <100 mmol litre^{-1} [11 102] in coexistence with severe hypo-osmolality.[18]

Heart

Disturbances of cardiac function due to excess water might be an important cause of cardiovascular collapse. Depression of the conductivity system, bradycardia, and depression of the ST segment and T wave is common also in humans with massive fluid absorption.[4 49 87 96 102]

Animal studies have shown damage to the myocardial histoskeleton in association with irrigating fluids and that glycine in particular causes hypoxic lesions in the subendocardium[50 52 57 105] (Fig. 5) and an acute increase in the weight of the heart.[93 105] The ECG shows a bradycardia with prolongation of the PQ time, widening of the QRS complex and reduction of the QRS amplitude, all of which correlate with the outcome.[93]

Blood

Dilution of plasma proteins rarely exceeds 25%, but might reach 40–50% in a severe case.[32] Hyponatraemia (<120 mmol litre^{-1}) may cause muscle weakness, muscular twitches, epileptic seizures and shock.[25 99] This key finding is often accompanied by reduction of serum osmolality of 10–25 mosmol kg^{-1}, as most irrigating fluids are hypo-osmolar (200 mosmol kg^{-1}). Ghanem and Ward[25] reported a strong correlation between low serum osmolality and symptoms and Desmond[18] between osmolality and pulmonary oedema. Serum potassium often increases transiently by 15–25% in response to fluid absorption, particularly after absorption of glycine.[56 82] The hyperkalaemia is probably related to intracellular uptake of the irrigant solute.

Absorption of a volume large enough to cause TUR syndrome is accompanied by metabolic acidosis with pH levels ranging from 7.10 to 7.25.[63 127] Hypoxia has also been reported,[28] but it is less consistent and is more common in women.[2 28]

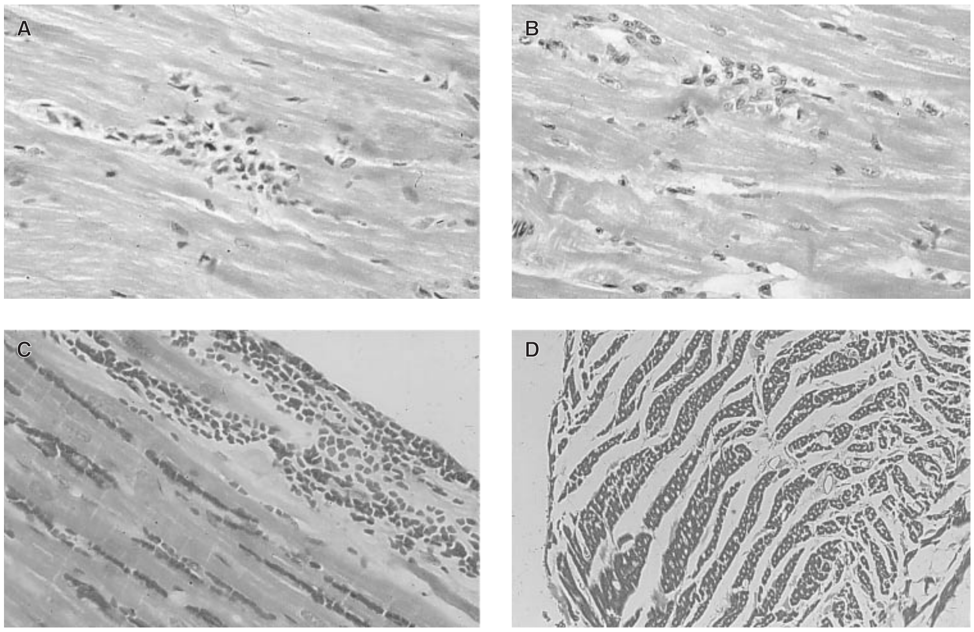

Fig 5 Cardiac pathology in animals infused with irrigating fluid. Light microscopy is used with haematoxylin–eosin stain, with the permission of Professor Jovan Rajs, Karolinska Institute. (A) Focal myocarditis in the heart of a mouse after receiving glycine 1.5%. (B) Focal necrosis of myocytes with inflammatory reaction in a rabbit from glycine 1.5%. (C) Vasodilatation and haemorrhage in the subendocardium in a mouse given mannitol 5%. (D) Extreme interstitial dilatation in the myocardium of a rabbit sacrificed 2 h after being treated with 100 ml kg^{-1} of glycine 1.5%.

The incidence of urosepsis seems to be increased by i.v. fluid absorption during TURP[54] and by extravasation in percutaneous nephrolithotripsy.[24]

Brain

Brain oedema is a serious problem and cerebral herniation developing a few hours postoperatively[5,100] is a major cause of death from fluid absorption, in addition to cardiovascular or respiratory collapse.[12,87,96] Signs of cerebral oedema on CT scans were found after absorption of as little as 1 litre of glycine 1.5% during TCRE[72] while this did not occur in younger male volunteers.[104] However, lowering of the serum osmolality in response to larger amounts of glycine solutions raises the intracerebral pressure in experimental animals[105] and in TURP patients.[78]

The patient may become comatose after glycine absorption without having cerebral oedema, but with signs of metabolic encephalopathy with,[98] or without,[127] a marked increase in blood ammonia, arising from the metabolism of glycine.

Kidney

Moderate amounts of irrigating fluid (up to 2.5 litre) induce osmotic diuresis, which results in absolute losses of sodium from the body (40 mmol $litre^{-1}$ urine).[51,112] With larger amounts of irrigating fluid, they ultimately swell, which promotes anuria.[50,119] In extravasation, failure to void correlates with arterial hypotension,[37,92] which causes anoxia of the renal tubular cells.

Extravasation

Abdominal pain, which may radiate to the shoulder, is a common first sign of extravasation.[37] Extracellular electrolytes diffuse into the pool of deposited irrigating fluid[6,90] and the hyponatraemia is most pronounced 2–4 h later.[37] This movement of electrolytes is followed by hypovolaemia, with bradycardia and arterial hypotension.[6,38,115] Extravasation may go undetected until the next day, because of the slow development.[127]

Fluid-specific pathophysiology

Certain features of the pathophysiology are unique to each irrigating fluid.

Glycine is an inhibitory neurotransmitter in the retina. An excess amount slows down the transmission of impulses from the retina to the cerebral cortex. Prolongation of visual-evoked potentials and deterioration of vision occur after absorption of as little as a few hundred millilitres of glycine 1.5%.[44,79,82] More pronounced absorption, corresponding to glycine concentrations of 7–8 mmol $litre^{-1}$, abolishes the oscillatory potentials on the electroretinogram.[120] There are clinical reports of transient blindness after absorption of glycine during most types of endoscopic surgery. Intraocular pressure,[99] fundoscopy, pupillary reflexes and brain CT scan are normal, while the pupils may be dilated. The blindness resolves within 24 h.

Prickling sensations and facial warmth are early signs of glycine absorption.[56]

Vasopressin is released as a specific response to glycine in doses exceeding 25–30 g[32 112] leading to water retention and restoration of the serum sodium after fluid absorption more difficult.

Hyperammonaemic encephalopathy may develop as ammonia is an intermediate product in glycine metabolism. Blood ammonia concentrations >100 μmol litre^{-1} (normal range 10–35) are associated with neurological symptoms, and values up to 800 μmol litre^{-1} have been reported.[63] Ammonia is released from the liver and kidneys and removed in the head and limbs. The blood concentration correlates with the glycine dose and symptoms such as confusion.[56] Interindividual variability is great, however, and patients may show neurological symptoms after absorbing large amounts of glycine 1.5% while still having a normal blood ammonia concentration. Only 15–20% of volunteers show an increase in blood ammonia when challenged by a glycine overload.[53] There is a vague correlation between hyperammonaemia and visual disturbances,[44 82] while these factors are independent from cerebral oedema. Other metabolic products of glycine have also been associated with neurological symptoms. Among them are glycolic acid and glyoxilic acid, which accumulate in the cerebrospinal fluid,[97 98] and glutamate (glutamic acid), the elevation of which shows a time-course similar to the symptoms.[33] Some of the metabolic symptoms of glycine absorption can be recognized in hyperglycinaemia, which is a rare disorder of amino acid metabolism characterized by episodes of ketosis and metabolic acidosis that may proceed to coma.

Oxalate is an end-product of glycine metabolism, but studies in volunteers and TURP patients refute the assertion that glycine markedly increases oxalate excretion.

Allergic reactions to *mannitol* are very rare. Mannitol concentrations >5% are often used for purposes other than irrigation and entail the risk of acute renal failure in dehydrated patients.[64]

Metabolic complications of *sorbitol* are due to a primary metabolite, fructose. Rapid administration of fructose, compared with absorption of 5 litre of sorbitol 5% for more than 30 min, causes lactic acidosis.[9] Fructose might also induce coma in patients with liver disease.[125] Infusion of sorbitol has lead to death of patients with intolerance to fructose, because of lack of the aldolase B enzyme.[106] Finally, hypoglycaemia develops in young patients with fructose-1,6-diphosphatase deficiency who are given sorbitol.

Normal saline is used for irrigation with the bipolar resectoscope. Although cerebral oedema is unlikely, infusion of 25 ml kg^{-1} of isotonic electrolyte solution for more than 15 min in women caused sensations of swelling in the hands and face, slight dyspnoea, abdominal sensations and analgesia around the lips.[46] Twice the volume infused for more than 1 h was followed by mental changes and discomfort from swelling.[123] Moreover, normal saline causes hyperchloraemic acidosis due to its excessive content of chloride.[122]

Because of the greater plasma volume expansion,[112] acute volume overload is more likely during absorption of normal saline compared with other irrigating solutions. Pulmonary oedema is a reported consequence.[29]

Sterile water is often used for cystoscopy as it offers the surgeon a very clear view of the operating field. Warnings against using sterile water for irrigation during electrosurgery are based on both animal experiments[119] and clinical experience;[80] but, more recently, several authors have recommended the fluid for limited resections.[30 68 81] Although there is no agreement about how much sterile water is needed to cause renal failure, damage requiring chronic haemodialysis still occurs with accidental and unexpected absorption of sterile water.[20] Serum potassium might also increase precipitously.

Sterile water could be expected to promote cerebral oedema more vigorously than other electrolyte-free irrigating fluids.

Comparing outcomes

The clinician has an interest in knowing which irrigation fluid is associated with the least danger if fluid absorption occurs. This issue was studied by Hahn's group during the 1990s. A consistent finding in these studies was the poor performance of glycine 1.5%.

Animals

Zhang and colleagues[128] studied rat cardiac myocytes and found that 99% of cells were viable after being mixed with sorbitol 2% or mannitol 1%, while only 83% of them were viable after glycine 1.5%.

In live mice, i.v. infusion of irrigating fluids was associated with survival in 20% (glycine 1.5%), 32% (sorbitol 2% with mannitol 1%) and 60% (mannitol 5%).[91] Survival after glycine administration was dependent on both the glycine dose and the accompanying fluid volume after both i.v.[129] and intraperitoneal[95] administration. Isotonic glycine 2.2% was associated with the poorest outcome. Glycine 1.5%, 100 ml kg^{-1} for more than 60 min, was fatal in two out of seven rabbits, while no animal died after mannitol 3% or sorbitol–mannitol.[50] Glycine solution induced the greatest increase in cardiac weight and tissue damage in the heart, kidneys, liver and brain. Maatman and colleagues[76] reported microscopic damage to the liver and kidney of rats given glycine 1.5% by i.v. and retroperitoneal infusion, while the histology was normal after Ringer's solution and water. The water content of the mouse hearts increased markedly after infusion of glycine 1.5%, but not after normal saline or glycine 1.5% in normal saline.[93]

In pigs, mannitol 5% increased the blood volume more than glycine 1.5%, and maintained the haemodynamic profile better during infusion.[105] The intracranial pressure doubled during infusion of glycine 1.5%, but was unchanged in response to mannitol 5%. The peripheral vascular resistance was increased during infusion of glycine 1.5% in sheep[112] and pigs.[105] For both fluids, cardiac output and aortic blood flow decreased by as much as 50% after the infusion was completed.[105] A similar cardiodepression has been observed in dogs given glycine 1.5%.

Volunteers

In studies based on infusing ~1 litre of irrigating fluid for more than 20–30 min, glycine 1.5% elicits more symptoms than mannitol 3% and 5%,[56 104] while glycine 2.2% is worst.[56] Glycine, but not mannitol 3% or sorbitol–mannitol solutions, reduces cardiac output by increasing peripheral resistance.[84] The diastolic and mean arterial pressures become slightly increased.[56 84 104]

Ethanol, which can be added to the fluid to allow monitoring of fluid absorption, has no effect on the fluid balance in prostatectomy patients given glycine 1.5%. Ethanol readily enters the cells and only slightly increases the resistance to haemolysis.[55] The breath ethanol concentration is practically identical regardless of whether the ethanol is added to glycine 1.0%, glycine 1.5% or mannitol 3%.[56 84 104]

Clinical

In a two-centre evaluation, glycine 1.0% had the same incidence of symptoms as glycine 1.5%,[55] but mannitol 3% had a significantly lower incidence of symptoms, such as nausea, than glycine 1.5%.[54] Cardiovascular events did not differ between the fluids. Inman and colleagues[70] found no difference, based on 205 patients, in symptoms and cardiac enzymes between glycine 1.5% and sorbitol–mannitol.

Measuring fluid absorption

Fluid absorption can be quantified by measuring serum sodium in all cases where the solution lacks electrolytes. The method is best applied repeatedly during surgery, but is rarely used clinically because of practical problems and invasiveness. As a rule, serum sodium is only measured at the end of surgery. The hyponatraemia then correlates with the amount of absorbed fluid, although smaller absorption events may be blurred by variability and the sodium content of other infusions. Serum sodium is also a poor guide to the degree of extracellular overhydration during the post-operative phase.[42]

Volumetric fluid balance is based on the calculation of the difference between the amount of irrigating fluid used and the volume recovered. Positive values are regarded as absorption. The accuracy is hampered by many factors, including variations in bag-to-bag content, spillage, blood loss and urinary excretion. Haemodilution during surgery should be considered in the blood loss figure to accurately account for the plasma loss. All these factors make volumetric balance an unreliable tool,[94] and it must be refined to be accurate.[31 34 45] Volumetric fluid balance is more useful during TCRE as the confounding influence of blood loss is much smaller than during TURP (Fig. 6).[58]

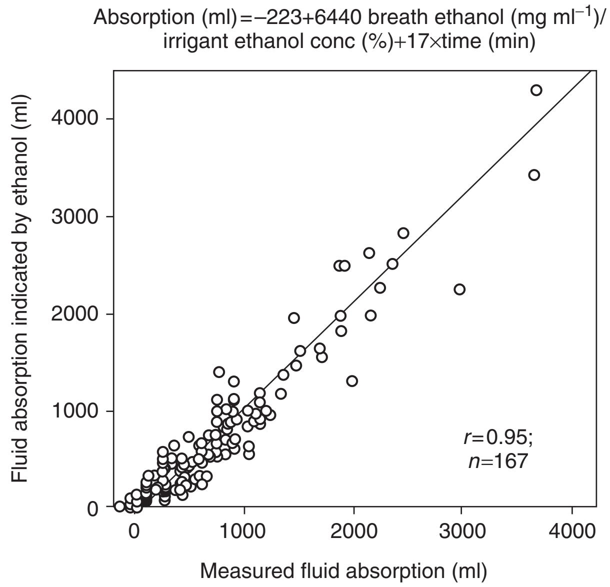

Fig 6 Early graph, from 1989, showing the fluid absorption as indicated by careful measurements of the volumetric fluid balance corrected for blood loss at the end of any 10 min period of TURP *vs* the fluid absorption as obtained by a regression equation based on the expired breath ethanol concentration, the ethanol concentration in the irrigating fluid and the period of time during which ethanol has been detected. Most of the data are from refs 31 and 34.

Gravimetry implies that the patient is operated on on a bed-scale and that an increase in body weight implies fluid absorption. The method must take blood loss and all i.v. infusions into account, and recordings should be made when the bladder is empty. Coppinger and colleagues[16 108] have shown that the gravimetric method is quite accurate, when incorporating modern transducers and potential errors are considered.

Central venous pressure increases transiently on intravascular administration of irrigating fluid, but the method is relatively insensitive because 500 ml must be absorbed within 10 min to increase the pressure by 2 mm Hg.[45] The result is also affected by blood loss and other fluid therapy[111] but it may be recommended for poor-risk patients.[18]

Measurement with *isotopes* was long considered to be the most reliable method to quantify fluid absorption,[77] but modern safety precautions make them difficult to apply. Isotopes are a sensitive tool for detecting low-grade absorption.

Ethanol is based on the same principle as isotopes that a tracer is added to the irrigating fluid and that the body concentration measured is an index of fluid absorption. Measurements of the ethanol concentration in the exhaled breath can be made during surgery with relatively little effort. The first clinical trial used glycine 1.5% with ethanol 2%,[31] but later studies concluded that 1% was suitable for clinical use.[34] The sensitivity is ~75 ml per 10 min of surgery, and any further elevation of the breath ethanol concentration implies that more fluid is being absorbed (Fig. 6). Ethanol monitoring method can be applied during both spinal and general anaesthesia and in patients with poor lung function. The method has been well evaluated worldwide. Two reviews are available.[39 40]

Absorption of fluid directly into the bloodstream is accompanied by a prompt decrease in serum sodium, elevation of the central venous pressure and an increase in the serum or breath concentration of any marker present in the fluid. These elevations correlate with the volume of absorbed irrigant fluid as obtained by gravimetric weighing and very careful measurements of volumetric balance.

Extravasation is detected immediately only by gravimetric weighing and volumetric fluid balance, while serum sodium and breath ethanol become apparent 15–20 min later.[37] The maximum concentrations are approximately one-third of those indicated by intravascular absorption, and a further increase after the operation is characteristic.[39]

Prevention

Several methods have been proposed to reduce the risk of fluid absorption and its associated dangers. None of them is capable of eliminating the complication.

Education

Fluid absorption varies between surgeons and depends on their skill in avoiding prostatic capsule perforations and the opening up of venous sinuses. However, studies do not support that experienced surgeons have less fluid absorption during their operations[61 74] but those who obtain immediate feedback via ethanol monitoring learn how to operate with less fluid absorption.[74]

Spinal anaesthesia does not reduce absorption[48] but allows early detection of gross changes in mental status. This approach offers limited possibilities to interact with the absorption process as symptoms require the build-up of a considerable absorption volume.

Reduction of surgical time

It is a common belief that dangerous fluid absorption during TURP is prevented by keeping the operating time below 1 h.[18] However, massive absorption has been described after as little as 15 min of surgery (Fig. 1).[34 48 87]

Lowering the fluid bag

Placing the irrigating fluid bag at 60 cm above the operating table was advocated early on as a method of controlling fluid absorption.[77] However, two studies comprising nearly 600 patients could not demonstrate any correlation between bag height and fluid absorption during TURP.[47 117] The reason is probably that the urologist tends to operate at a certain fluid pressure, which might be much lower than the maximum possible pressure indicated by the bag height.[22]

Low-pressure irrigation

Performing TURP with a low fluid pressure, below the critical pressure for intravascular absorption, would limit the risk. This can be achieved by applying a suprapubic evacuation instrument (Reuter's trocar)[101] or a special channel in a resectoscope (the Iglesias technique).

Several authors have found irrigation using the suprapubic trocar to be efficient,[65] while others have not. There is even more widespread scepticism about the effectiveness of the Iglesias method. Heidler[59] reported development of severe hyponatraemia in 3 out of 30 patients undergoing TURP using an Iglesias resectoscope. In contrast, only 1 patient out of 60 developed severe hyponatraemia when the pressure was maintained below 2 kPa using the suprapubic trocar. In another study, the trocar maintained a low pressure (<1.5 kPa) only in half of the operations.[41] Five mild TUR syndromes occurred in 500 patients using this evacuation device.[121] The variable effectiveness is probably because of outflow obstruction by blood clots, which raises the fluid pressure. Low-pressure irrigation is probably more efficient if combined with monitoring of the intravesical pressure.[62]

Bipolar resectoscope

A bipolar technique allows the use of normal saline for irrigation, which will influence the signs of TUR syndrome. The incidence of mental changes and abdominal pain will be similar to that with sorbitol–mannitol irrigation,[46 122 123] and vascular overload resulting in pulmonary oedema could be expected as a more common problem.[29]

Vaporization

Alternative techniques to TURP have been developed, one of them being vaporization of the prostate. Fluid absorption and blood loss are less pronounced during this operation, but fluid absorption of up to 3 litre may still occur.

Drugs

Vasoconstrictor with vasopressin injected at the operating site is claimed to reduce fluid absorption during TCRE[27] and might possibly have the same effect during TURP.[107] During TCRE, pretreatment with hormones to reduce endometrial thickness affects the risk of fluid absorption in many, but not in all, studies.[113]

Treatment

Visual disturbances resolve spontaneously within 24 h and need no treatment.[32 79] Mild adverse events are treated by supportive measures, including antiemetics. Hypertension is likely to be transient. The cardiovascular collapse can be reversed if treatment is instituted promptly. Bradycardia and hypotension should be treated with atropine, adrenergic drugs and i.v. calcium.[110] Although fluid restriction was recommended previously,[8] plasma volume expansion is indicated as hypovolaemia and low cardiac output develops as soon as irrigation is discontinued.[32 35 105 110 119]

Specific treatment includes hypertonic saline, which is indicated when several symptoms develop or the serum sodium concentration is <120 mmol litre^{-1}. Both experimental[10 21] and clinical[3 25 60 102] studies support the use of this treatment, although serum sodium concentrations down to ~100 mmol litre^{-1} may be fatal.[87] Patients who do not receive hypertonic saline, or with a delay of several hours, more frequently suffer residual neurological damage or die.[2 25]

Warnings about pontine myelinolysis resulting from rapid correction of hyponatraemia originally pertained to chronic hyponatraemia, but recent studies question rapid correction also in acute hyponatraemia. Raising the serum sodium concentration by 1 mmol litre^{-1} h^{-1} may be taken as a safe rate.[2] Hypertonic saline combats cerebral oedema, but it also expands the plasma volume, reduces cellular swelling and increases urinary excretion without increasing the total solute excretion. In the past, there was a fear of hypertonic saline inducing pulmonary oedema,[8 87] but this has not been seen in clinical experience.

The primary indication of i.v. furosemide is to combat acute pulmonary oedema and to induce diuresis when this does not occur spontaneously. In other situations, the best practice is probably to withhold this until the patient is haemodynamically stable and hypertonic saline is infused. No studies support its routine use in the treatment of fluid absorption. In fact, furosemide after TURP aggravates the hyponatraemia and hypovolaemia.[17] Early treatment with furosemide is based on the belief that hyponatraemia is solely due to fluid overload which dilutes the extracellular fluid space.[18 87] One hour after surgery, however, the hyponatraemia following moderate-sized absorption (up to 1.3 litre) is entirely because of natriuresis, while half of the hyponatraemia is explained by these factors in large-scale absorption.[42]

Extravasation is treated with the similar measures. Great care should be taken to counteract arterial hypotension and oliguria.[37] Morbidity and mortality can also be reduced by surgical drainage of the retroperitoneal fluid, but this is only necessary after massive absorption.[37] Such drainage also removes extracellular electrolytes that have diffused into the fluid pool,[90] which makes hypertonic saline a valuable remedy when drainage is performed.[10]

Conclusions

Fluid absorption is a complication inherent in many endoscopic procedures that can be limited by technical means but never prevented. The past decade has provided better insight into the incidence of fluid absorption, how various irrigating fluids compare and the gradual increase in the number and type of symptoms occurring when more fluid is being absorbed. Mild TUR syndrome should be better recognized and it should be noted that most symptoms appear 30–45 min after surgery is completed. At that time, the hyponatraemia is explained by natriuresis and not by dilution. However, symptoms related to fluid absorption develop in 3–5% of patients. Neurological symptoms are prominent whem glycine 1.5% is used. Some patients develop a severe TUR syndrome which involves a hypokinetic circulation and damage to the heart. Their treatment should be based more on hypertonic saline than on furosemide.

To control fluid absorption, the surgical training should be guided by immediate feedback about fluid absorption. The surgeon should be notified about ongoing fluid absorption whenever it exceeds 1 litre. This allows steps to be taken to prevent excessive absorption. Treatment can be instituted early and the optimal concentration of postoperative care be chosen. The most viable methods to monitor fluid absorption are ethanol monitoring and gravimetric weighing. Little is yet known about the risks associated with alternative resection techniques, such as the bipolar resectoscope.

Supplementary data

The complete list of 320 references is available as supplementary data to the online version of this article, at www.bja.oxfordjournals.org.

References

1 Allgén LG, Norlén H, Kolmert T, Berg K. Absorption and elimination of mannitol solution when used as an isotonic irrigating agent in connection with transurethral resection of the prostate. *Scand J Urol Nephrol* 1987; **21**: 177–84

2 Ayus JC, Arieff AI. Glycine-induced hypo-osmolar hyponatremia. *Arch Intern Med* 1997; **157**: 223–6

3 Ayus JC, Krothapalli RK, Arieff AI. Treatment of symptomatic hyponatremia and its relation to brain damage. *N Engl J Med* 1987; **317**: 1190–5

4 Baba T, Shibata Y, Ogata K, *et al.* Isotonic hyponatremia and cerebrospinal fluid sodium during and after transurethral resection of the prostate. *J Anesth* 1995; **9**: 135–41

5 Baggish MS, Brill AIO, Rosenweig B, Barbot JE, Indman PD. Fatal acute glycine and sorbitol toxicity during operative hysteroscopy. *J Gynecol Surg* 1993; **9**: 137–43

6 Baillo AM, Gassol JM, Redorta JP, Castro MN, Giménez NM. Physiopathology and surgical treatment of extravasated peritoneal fluid after transurethral resection. *Eur Urol* 1984; **10**: 183–6

7 Balzarro M, Ficarra V, Bartoloni A, Tallarigo C, Malossini G. The pathophysiology, diagnosis and therapy of the transurethral resection of the prostate syndrome. *Urol Int* 2001; **66**: 121–6

8 Beal JL, Freysz M, Berthelon G, D'Athis P, Briet S, Wilkening M. Consequences of fluid absorption during transurethral resection of the prostate using distilled water or glycine 1.5 per cent. *Can J Anaesth* 1989; **36**: 278–82

9 Bergström J, Hultman E, Roch-Norlund AE. Lactic acid accumulation in connection with fructose infusion. *Acta Med Scand* 1968; **184**: 359–64

10 Bernstein GT, Loughlin KR, Gittes RF. The physiologic basis of the TUR syndrome. *J Surg Res* 1989; **46**: 135–41

11 Butt AD, Wright IG, Elk RJ. Hypo-osmolar intravascular volume overload during anaesthesia for transurethral prostatectomy. A report of 2 cases. *S Afr Med J* 1985; **67**: 1059–61

12 Byard RW, Harrison R, Wells R, Gilbert JD. Glycine toxicity and unexpected intra-operative death. *J Forensic Sci* 2001; **46**: 1244–6

13 Chassard D, Berrada, K, Tournadre JP, Boulétreau P. Calcium homeostasis during i.v. infusion of 1.5% glycine in anaesthetized pigs. *Br J Anaesth* 1996; **77**: 271–3

14 Chow MYH, Tan SSW. A case of fluid embolism from transcervical endometrial resection. *Ann Acad Med Singapore* 1997; **26**: 497–9

15 Chui PT, Short T, Leung AKL, Tan PE, Oh TE. Systemic absorption of glycine irrigation solution during endometrial ablation by transcervical endometrial resection. *Med J Aust* 1992; **157**: 667–9

16 Coppinger SWV, Lewis CA, Milroy EJG. A method of measuring fluid balance during transurethral resection of the prostate. *Br J Urol* 1995; **76**: 66–72

17 Crowley K, Clarkson K, Hannon V, McShane A, Kelly DG. Diuretics after transurethral prostatectomy: a double-blind controlled trial comparing frusemide and mannitol. *Br J Anaesth* 1990; **65**: 337–41

18 Desmond J. Serum osmolality and plasma electrolytes in patients who develop dilutional hyponatremia during transurethral resection. *Can J Surg* 1970; **13**: 116–21

19 Dimberg M, Norlén H, Höglund N, Allgén L-G. Absorption of irrigating fluid during percutaneous transrenal lithotripsy. *Scand J Urol Nephrol* 1993; **27**: 463–7

20 Dorotta I, Basali A, Ritchey M, O'Hara JF, Sprung J. Transurethral resection syndrome after bladder perforation. *Anesth Analg* 2003; **97**: 1536–8

21 Drinker HR, Shields T, Grayhack JT, Laughlin L. Simulated transurethral resection in the dog: early signs and optimal treatment. *J Urol* 1963; **89**: 595–602

22 Ekengren J, Zhang W, Hahn RG. Effects of bladder capacity and height of fluid bag on the intravesical pressure during transurethral resection of the prostate. *Eur Urol* 1995; **27**: 26–30

23 Evans JWH, Singer M, Coppinger SWV, Macartney N, Walker JM, Milroy EJG. Cardiovascular performance and core temperature during transurethral prostatectomy. *J Urol* 1994; **152**: 2025–9

24 Gehring H, Nahm W, Zimmermann K, Fornara P, Ocklitz E, Schmucker P. Irrigating fluid absorption during percutaneous nephrolithotripsy. *Acta Anaesthesiol Scand* 1999; **43**: 316–21

25 Ghanem AN, Ward JP. Osmotic and metabolic sequelae of volumetric overload in relation to the TUR syndrome. *Br J Urol* 1990; **66**: 71–8

26 Goel CM, Badenoch DF, Fowler CG, Blandy LP, Tiptaft RC. Transurethral resection syndrome. A prospective study. *Eur Urol* 1992; **21**: 15–7

27 Goldenberg M, Zolti M, Bider D, Etchin A, Ben-Ami Sela, Seidman DS. The effect of intracervical vasopressin on the systemic absorption of glycine during hysteroscopic endometrial ablation. *Obstet Gynecol* 1996; **87**: 1025–9

28 Goldenberg M, Zolti M, Seidman DS, Bider D, Mashiach S, Etchin A. Transient blood oxygenation desaturation, hypercapnia, and coagulopathy after operative hysteroscopy with glycine used as the distending medium. *Am J Obstet Gynecol* 1994; **170**: 25–9

29 Grove JJ, Shinaman RC, Drover DR. Noncardiogenic pulmonary edema and venous air embolus as complications of operative hysteroscopy. *J Clin Anesth* 2004; **16**: 48–50

30 Grundy PL, Budd DWG, England R. A randomized controlled trial evaluating the risk of sterile water as an irrigating fluid during transurethral electrovaporization of the prostate. *Br J Urol* 1997; **890**: 894–7

31 Hahn RG. Ethanol monitoring of irrigating fluid absorption in transurethral prostatic surgery. *Anesthesiology* 1988; **68**: 867–73

32 Hahn RG. Hallucination and visual disturbances during transurethral prostatic resection. *Intensive Care Med* 1988; **14**: 668–71

33 Hahn RG. Serum amino acid patterns and toxicity symptoms following the absorption of irrigant containing glycine in transurethral prostatic surgery. *Acta Anaesthesiol Scand* 1988; **32**: 493–501

34 Hahn RG. Early detection of the TUR syndrome by marking the irrigating fluid with 1% ethanol. *Acta Anaesthesiol Scand* 1989; **33**: 146–51

35 Hahn RG. Fluid and electrolyte dynamics during development of the TURP syndrome. *Br J Urol* 1990; **66**: 79–84

36 Hahn RG. Dose-dependent half-life of glycine. *Urol Res* 1993; **21**: 289–91

37 Hahn RG. Transurethral resection syndrome from extravascular absorption of irrigating fluid. *Scand J Urol Nephrol* 1993; **27**: 387–94

38 Hahn RG. Transurethral resection syndrome after transurethral resection of bladder tumours. *Can J Anaesth* 1995; **42**: 69–72

39 Hahn RG. Ethanol monitoring of irrigating fluid absorption (review). *Eur J Anaesthesiol* 1996; **13**: 102–15

40 Hahn RG. The use of ethanol to monitor fluid absorption in transurethral resection of the prostate (review). *Scand J Urol Nephrol* 1999; **33**: 277–83

41 Hahn RG. Intravesical pressure during fluid absorption in transurethral resection of the prostate. *Scand J Urol Nephrol* 2000; **34**: 102–8

42 Hahn RG. Natriuresis and "dilutional" hyponatremia after infusion of glycine 1.5%. *J Clin Anesth* 2001; **13**: 167–74

43 Hahn RG. Smoking increases the risk of large-scale fluid absorption during transurethral prostatic resection. *J Urol* 2001; **166**: 162–5

44 Hahn R, Andersson T, Sikk M. Eye symptoms, visual evoked potentials and EEG during intravenous infusion of glycine. *Acta Anaesthesiol Scand* 1995; **39**: 214–9

45 Hahn R, Berlin T, Lewenhaupt A. Irrigating fluid absorption and blood loss during transurethral resection of the prostate studied by a regular interval monitoring (RIM) method. *Scand J Urol Nephrol* 1988; **22**: 23–30

46 Hahn RG, Drobin D, Ståhle L. Volume kinetics of Ringer's solution in female volunteers. *Br J Anaesth* 1997; **78**: 144–8

47 Hahn RG, Ekengren J. Absorption of irrigating fluid and height of the fluid bag during transurethral resection of the prostate. *Br J Urol* 1993; **72**: 80–3

48 Hahn RG, Ekengren J. Patterns of irrigating fluid absorption during transurethral resection of the prostate as indicated by ethanol. *J Urol* 1993; **149**: 502–6

49 Hahn R, Essén P. ECG and cardiac enzymes after glycine absorption in transurethral prostatic resection. *Acta Anaesthesiol Scand* 1994; **38**: 550–6

50 Hahn RG, Nennesmo I, Rajs J, Sundelin B, Wroblevski R, Zhang W. Morphological and X-ray microanalytical changes in mammalian tissue after overhydration with irrigating fluids. *Eur Urol* 1996; **29**: 355–61

51 Hahn RG, Nilsson A, Ståhle L. Distribution and elimination of the solute and water components of urological irrigating fluids. *Scand J Urol Nephrol* 1999; **33**: 35–41

52 Hahn RG, Olsson J, Sótonyi P, Rajs J. Rupture of the myocardial histoskeleton and its relation to sudden death after overhydration with glycine 1.5% in the mouse. *APMIS* 2000; **108**: 487–95
53 Hahn RG, Sandfeldt L. Blood ammonia levels after intravenous infusion of glycine with and without ethanol. *Scand J Urol Nephrol* 1999; **33**: 222–7
54 Hahn RG, Sandfeldt L, Nyman CR. Double-blind randomized study of symptoms associated with absorption of glycine 1.5% or mannitol 3% during transurethral resection of the prostate. *J Urol* 1998; **160**: 397–401
55 Hahn RG, Shemais H, Essén P. Glycine 1.0% versus glycine 1.5% as irrigating fluid during transurethral resection of the prostate. *Br J Urol* 1997; **79**: 394–400
56 Hahn RG, Stalberg HP, Gustafsson SA. Intravenous infusion of irrigating fluids containing glycine or mannitol with and without ethanol. *J Urol* 1989; **142**: 1102–5
57 Hahn RG, Zhang W, Rajs J. Pathology of the heart after overhydration with glycine solution in the mouse. *APMIS* 1996; **104**: 915–20
58 Hawe JA, Chien PFW, Martin D, Phillips AG, Garry R. The validity of continuous automated fluid monitoring during endometrial surgery: luxury or necessity? *Br J Obstet Gynecol* 1998; **105**: 797–801
59 Heidler H. Frequency and causes of fluid absorption: a comparison of three techniques for resection of the prostate under continuous pressure monitoring. *Br J Urol* 1999; **83**: 619–22
60 Henderson DJ, Middleton RG. Coma from hyponatraemia following transurethral resection of the prostate. *Urology* 1980; **XV**: 267–71
61 Hjertberg H, Jorfeldt L, Schelin S. Use of ethanol as a marker substance to increase patient safety during transurethral prostatic resection. *Urology* 1991; **38**: 423–8
62 Hjertberg H, Pettersson B. The use of a bladder pressure warning device during transurethral prostatic resection decreases absorption of irrigating fluid. *Br J Urol* 1992; **69**: 56–60
63 Hoekstra PT, Kahnoski R, McCamish MA, Bergen W, Heetderks DR. Transurethral prostatic resection syndrome—a new perspective: encephalopathy with associated hyperammonaemia. *J Urol* 1983; **130**: 704–7
64 Horgan KJ, Ottaviano YL, Watson AJ. Acute renal failure due to mannitol intoxication. *Am J Nephrol* 1989; **9**: 106–9
65 Hubert J, Cormier L, Gerbaud PF, Guillemin F, Pertek JP, Mangin P. Computer-controlled monitoring of bladder pressure in the prevention of 'TUR syndrome': a randomized study of 53 cases. *Br J Urol* 1996; **78**: 228–33
66 Hultén J, Bengtsson M, Engberg A, Hjertberg H, Svedberg J. The pressure in the prostatic fossa and fluid absorption. *Scand J Urol Nephrol* 1984; **82** (Suppl): 33–43
67 Hultén JO, Sundström GS. Extravascular absorption of irrigating fluid during TURP. The role of transmural bladder pressure as the driving pressure gradient. *Br J Urol* 1990; **65**: 39–42
68 Hultén JO, Tran VT, Pettersson G. The control of haemolysis during transurethral resection of the prostate when water is used for irrigation: monitoring absorption by the ethanol method. *BJU Int* 2000; **86**: 989–92
69 Ichai C, Cialis JF, Roussel LJ, *et al.* Intravascular absorption of glycine irrigating solution during shoulder arthroscopy: a case report and follow-up study. *Anesthesiology* 1996; **85**: 1481–5
70 Inman RD, Hussain Z, Elves AWS, Hallworth MJ, Jones PW, Coppinger SWV. A comparison of 1.5% glycine and 2.7% sorbitol–0.5% mannitol irrigants during transurethral prostate resection. *J Urol* 2001; **166**: 2216–20
71 Istre O. Transcervical resection of the endometrium and fibroids: the outcome of 412 operations performed over 5 years. *Acta Obstet Gynecol Scand* 1996; **75**: 567–74
72 Istre O, Bjoennes J, Naess R, Hornbaek K, Forman A. Postoperative cerebral oedema after transcervical endometrial resection and uterine irrigation with 1.5% glycine. *Lancet* 1994; **344**: 1187–9
73 Jansen FW, Vredevoogd CB, Ulzen KV, Hermans J, Trimbos JB, Trimbos-Kemper TCM. Complications of hysteroscopy: a prospective, multicenter study. *Obstet Gynecol* 2000; **96**: 266–70
74 Konrad C, Gerber HR, Schuepfer G, Schmucki O. Transurethral resection syndrome: effect of the introduction into clinical practice of a new method for monitoring fluid absorption. *J Clin Anesth* 1998; **10**: 360–5
75 Logie JRC, Keenan RA, Whiting PH, Steyn JH. Fluid absorption during transurethral prostatectomy. *Br J Urol* 1980; **52**: 526–8
76 Maatman TJ, Musselman P, Kwak YS, Resnick MI. Effect of glycine on retroperitoneal and intraperitoneal organs in the rat model. *Prostate* 1991; **19**: 323–8
77 Madsen PO, Naber KG. The importance of the pressure in the prostatic fossa and absorption of irrigating fluid during transurethral resection of the prostate. *J Urol* 1973; **109**: 446–52
78 Maluf NSR, Boren JS, Brandes GE. Absorption of irrigating solution and associated changes upon transurethral electroresection of the prostate. *J Urol* 1956; **75**: 824–36
79 Mantha S, Rao SM, Singh AK, Mohandas S, Prakash Rao BS, Joshi N. Visual evoked potentials and visual acuity after transurethral resection of the prostate. *Anaesthesia* 1991; **46**: 491–3
80 Marshall V. Renal failure after prostatectomy due to intravascular haemolysis. *Aust N Z J Surg* 1962; **32**: 123–7
81 Memon A, Buchholz N-P, Salahuddin S. Water as an irrigant in transurethral resection of the prostate: a cost-effective alternative. *Arch Ital Urol Androl* 1999; **LXXI**: 131–4
82 Mizutani AR, Parker J, Katz J, Schmidt J. Visual disturbances, serum glycine levels and transurethral resection of the prostate. *J Urol* 1990; **144**: 697–9
83 Nilsson A, Hahn RG. Mental status after transurethral resection of the prostate. *Eur Urol* 1994; **26**: 1–5
84 Nilsson A, Randmaa I, Hahn RG. Haemodynamic effects of irrigating fluids studied by Doppler ultrasonography in volunteers. *Br J Urol* 1996; **77**: 541–6
85 Norlén H, Allgén LG, Wicksell B. Mannitol concentrations in blood plasma in connection with transurethral resection of the prostate using mannitol solution as an irrigating fluid. *Scand J Urol Nephrol* 1986; **20**: 119–26
86 Norlén H, Dimberg M, Allgén L-G, Vinnars E. Water and electrolytes in muscle tissue and free amino acids in muscle and plasma in connection with transurethral resection of the prostate. II. Isotonic 2.2% glycine solution as an irirgating fluid. *Scand J Urol Nephrol* 1990; **24**: 95–101
87 Norris HT, Aasheim GM, Sherrard DJ, Tremann JA. Symptomatology, pathophysiology and treatment of the transurethral resection of the prostate syndrome. *Br J Urol* 1973; **45**: 420–7
88 Olsson J, Berglund L, Hahn RG. Irrigating fluid absorption from the intact uterus. *Br J Obstet Gynaecol* 1996; **103**: 558–61
89 Olsson J, Hahn RG. Ethanol monitoring of irrigating fluid absorption in transcervical resection of the endometrium. *Acta Anaesthesiol Scand* 1995; **39**: 252–8
90 Olsson J, Hahn RG. Simulated intraperitoneal absorption of irrigating fluid. *Acta Obstet Gynecol Scand* 1995; **74**: 707–13
91 Olsson J, Hahn RG. Survival after high-dose intravenous infusion of irrigating fluids in the mouse. *Urology* 1996; **47**: 689–92

92 Olsson J, Nilsson A, Hahn RG. Symptoms of the transurethral resection syndrome using glycine as the irrigant. *J Urol* 1995; **154**: 123–8

93 Olsson J, Hahn RG. Glycine toxicity after high-dose intravenous infusion of glycine 1.5% in the mouse. *Br J Anaesth* 1999; **82**: 250–4

94 Olsson J, Rentzhog L, Hjertberg H, Hahn RG. Reliability of clinical assessment of fluid absorption in transurethral prostatic resection. *Eur Urol* 1993; **24**: 262–6

95 Olsson J, Sandfeldt L, Hahn RG. Survival after high-dose intraperitoneal infusion of glycine solution in the mouse. *Scand J Urol Nephrol* 1997; **31**: 119–21

96 Osborn DE, Rao PN, Greene MJ, Barnard RJ. Fluid absorption during transurethral resection. *Br Med J* 1980; **281**: 1549–50

97 Périer C, Frey J, Auboyer C, *et al.* Accumulation of glycolic acid and glyoxilic acid in serum in cases of transient hyperglycinemia after transurethral surgery. *Clin Chem* 1988; **34**: 1471–3

98 Périer C, Mahul P, Molliex S, Auboyer C, Frey J. Progressive changes in glycine and glycine derivatives in plasma and cerebrospinal fluid after transurethral prostatic resection. *Clin Chem* 1990; **26**: 2152–3

99 Peters KR, Muir J, Wingard DW. Intraocular pressure after transurethral prostatic surgery. *Anesthesiology* 1981; **55**: 327–9

100 Radal M, Jonville Bera AP, Leisner C, Haillot O, Autret-Leca E. Effets indésirables des solutions d'irrigation glycollées. *Thérapie* 1999; **54**: 233–6

101 Reuter M, Reuter HJ. Prevention of irrigant absorption during TURP: continuous low-pressure irrigation. *Int Urol Nephrol* 1978; **10**: 293–300

102 Rothenberg DM, Berns AS, Ivankovich AD. Isotonic hyponatremia following transurethral prostate resection. *J Clin Anesth* 1990; **2**: 48–53

103 Salmela L, Aromaa U, Lehtonen L, Peura P, Olkkola KT. The effect of prostatic capsule perforation on the absorption of irrigating fluid during transurethral resection. *Br J Urol* 1993; **72**: 599–60

104 Sandfeldt L, Hahn RG. Comparison of urological irrigating fluids containing glycine and mannitol in volunteers. *Prostate* 1999; **41**: 89–98

105 Sandfeldt L, Riddez L, Rajs J, Ewaldsson C-A, Piros D, Hahn RG. High-dose intravenous infusion of urological irrigating fluids containing glycine and mannitol in the pig. *J Surg Res* 2001; **95**: 114–25

106 Schulte MJ, Lenz W. Fatal sorbitol infusion in patient with fructose-sorbitol intolerance. *Lancet* 1977; **2**; 188

107 Sharma D, Harvey AB. Does intraprostatic vasopressin prevent the transurethral resection syndrome? *BJU Int* 2000; **86**: 223–6

108 Shipstone DP, Inman RD, Beacock CJM, Coppinger SWV. Validation of the ethanol breath test and on-table weighing to measure irrigating fluid absorption during transurethral prostatectomy. *BJU Int* 2002; **90**: 872–5

109 Siddiqui MA, Berns JS, Baime MJ. Glycine irrigant absorption syndrome following cystoscopy. *Clin Nephrol* 1996; **45**: 365–6

110 Singer M, Patel M, Webb A, Bullen C. Management of the transurethral prostate resection syndrome: time for reappraisal? *Crit Care Med* 1990; **18**: 1479–80

111 Sohn MH, Vogt C, Heinen G, Erkens M, Nordmeyer N, Jakse G. Fluid absorption and circulating endotoxins during transurethral resection of the prostate. *Br J Urol* 1993; **72**: 605–10

112 Stalberg HP, Hahn RG, Hjelmqvist H, Ullman J, Rundgren M. Haemodynamics and fluid balance after intravenous infusion of 1.5% glycine in sheep. *Acta Anaesthesiol Scand* 1993; **37**: 281–7

113 Steffensen AJ, Hahn RG. Fluid absorption and the long-term outcome after transcervical resection of the endometrium. *Acta Obstet Gynaecol Scand* 1998; **77**: 863–8

114 Tuzin-Fin P, Guenard Y, Maurette P. Atypical signs of glycine absorption following transurethral resection of the prostate: two case reports. *Eur J Anaesthesiol* 1997; **14**: 471–4

115 Tauzin-Fin P, Krol-Houdek MC, Saumtally S, Muscagotty J-M. Intoxication par la glycine après chirurgie rénale par voie percutanée. *Can J Anaesth* 1993; **40**: 866–9

116 Tauzin-Fin P, Sanz L, Houdek MC, Saumtally S, Muscagorry JM. Coma lors d'une résection endoscopique de prostata. *Ann Fr Anesth Réanim* 1991; **10**: 486–9

117 van Renen RG, Reymann U. Comparison of the effect of two heights of glycine irrigation solution on serum sodium and osmolality during transurethral resection of the prostate. *Aust N Z J Surg* 1997; **67**: 874–7

118 Verilli RA, Uhlman RC, Viek NF, Hunsicker WC. The hypotensive effect of a prostatic extract. *J Urol* 1962; **87**: 184–6

119 Wakim KG. The pathophysiologic basis for the clinical manifestations and complications of transurethral prostatic resection. *J Urol* 1971; **106**: 719–28

120 Wang JM-L, Creel DJ, Wong KC. Transurethral resection of the prostate, serum glycine levels, and ocular evoked potentials. *Anesthesiology* 1989; **70**: 36–41

121 Weis N, Jörgensen PE, Bruun E. "TUR syndrome" after transurethral resection of the prostate using suprapubic drainage. *Int Urol Nephrol* 1987; **19**: 165–9

122 Wilkes NJ, Woolf R, Mutch M, *et al.* The effects of balanced versus saline-based hetastarch and crystalloid solutions on acid–base and electrolyte status and gastric mucosal perfusion in elderly surgical patients. *Anesth Analg* 2001; **93**: 811–16

123 Williams EL, Hildebrand KL, McCormick SA, Bedel MJ. The effect of intravenous lactated Ringer's solution versus 0.9% sodium chloride solution on serum osmolality in human volunteers. *Anesth Analg* 1999; **88**: 999–1003

124 Windsor A, French GWG, Sear JW, Foëx P, Millett SV, Howell SJ. Silent myocardial ischaemia in patients undergoing transurethral prostatectomy. *Anaesthesia* 1996; **51**: 728–32

125 Woods HF, Albert KGMM. Dangers of intravenous fructose. *Lancet* 1972; **2**: 1354–7

126 Wright N, Seggie J. Glycine toxicokinetics: vitreous fluid concentration and visual impairment. *Clin Invest Med* 1992; **15**: 159–62

127 Yende S, Wunderink R. An 87-year-old man with hypotension and confusion after cystoscopy. *Chest* 1999; **115**: 1449–51

128 Zhang W, Andersson B, Hahn RG. Effect of irrigating fluids and prostatic tissue extracts on isolated cardiomyocytes. *Urology* 1995; **46**: 821–4

129 Zhang W, Hahn RG. "Double toxicity" of glycine solution in the mouse. *Br J Urol* 1996; **77**: 203–6