

INTRAVENOUS UREA IN GLAUCOMA*

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HYPERTONIC solutions have been used to reduce the intra-ocular pressure in glaucoma since Cantonnet (1904) first used hypertonic salt solution. The effect of different substances was extensively studied by Hertel (1914), who administered many different solutions, including urea, to rabbits, and measured the resulting fall in intra-ocular pressure. Substances used in clinical practice include sucrose, dextrose, and sorbitol, which act by increasing the osmotic pressure of the blood; hence it is their concentration in molecules and not their weight in grammes that is significant. The disadvantages of sucrose are that it has a large molecular weight so that large amounts of it have to be given to exert sufficient osmotic pressure, and that it is also nephrotoxic and diffuses rapidly in the tissues. Dextrose and saline also diffuse in the tissues too rapidly to produce an effect of sufficient duration so that a rebound of intra-ocular pressure quickly occurs. The efficiency of sorbitol is doubtful and it is also said to be nephrotoxic. Bellows, Puntney, and Cowen (1938) found its effect to be greatest 24 hours after administration, which could not have been due to its osmotic effect.

Urea has been used as a diuretic in cases of oedema and also for reducing the intracranial pressure from various causes (Stubbs and Pennybacker, 1960). The need for an osmotic agent for reducing intra-ocular pressure has been much less since the introduction of carbonic anhydrase inhibitory drugs, but a few patients become resistant or intolerant to these drugs. Urea can be used to reduce the pressure before operation on glaucomatous eyes. The dangers of operating on eyes in which the intra-ocular pressure is raised include haemorrhage, prolapse of iris, lens, and vitreous, and expulsive haemorrhage. It obviates the need for a posterior sclerotomy when operating on cases of malignant glaucoma, before cyclodialysis and injection of air into the anterior chamber.

Technique

The urea† is used as a 30 per cent. solution in 10 per cent. invert sugar, which reduces the tendency to haemolysis. The urea solution is freshly

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prepared and the solvent must be warmed before adding the urea as the dissolution is an endothermic reaction. The patient is catheterized using an indwelling catheter and placed on continuous drainage. There is a very rapid diuresis and the patient may become very distressed if not catheterized before starting to administer the urea solution as an intravenous drip. The solution is allowed to run in at approximately 30 to 40 drops per minute, so that the total dose is between 1 and 1.5 g. urea per kg. body weight, and the administration lasts for about one hour. After half-an-hour the ocular tension is usually soft and the operation can be performed. An expendable intravenous drip outfit is supplied with the preparation used in these cases.

In this short series the urea was administered only to patients who were resistant or intolerant to Diamox, and it was always given immediately before the operation.

Case Reports

Case 1, a man aged 73, was first seen on May 5, 1960, when he had had an acute attack of glaucoma for 3 weeks in the left eye. The right eye was normal but had a very narrow angle in the anterior chamber. The visual acuity in the left eye was reduced to hand movements and the tension was 70 mm. Hg (Schiötz).

He was treated with eserine drops and Diamox by injection and tablet. The ocular tension fell to 28 mm. Hg the following day, but the next day rose to 35 mm. Hg; it stayed at that level for 2 days and then rose to 55 and even to 70 mm. Hg in spite of Diamox 500 mg. 6-hourly. An intravenous urea drip was started and within 90 minutes the tension had fallen to 20 mm. Hg (Fig. 1, opposite).

A left iris inclusion was performed without difficulty and the patient made an uneventful recovery.

Case 2, a man aged 75, was seen on June 17, 1960, with an acute attack of glaucoma in the left eye, which had lasted for 3 weeks. The right eye was normal apart from a very shallow anterior chamber. In the left eye the ocular tension was 60 mm. Hg (Schiötz) and there was extensive iris atrophy. The patient was treated with Diamox tablets and eserine drops and the tension fell gradually over the next 3 days to 20 mm. Hg. At this stage the Diamox tablets were discontinued, but this was followed by a rise in tension to 50 mm. Hg, and this high pressure was not controlled by re-commencing the Diamox. On the next day an intravenous urea drip was started and the pressure fell to 20 mm. Hg. within 45 minutes (Fig. 2, opposite).

A left iris inclusion was performed and no difficulty was experienced apart from some operative hyphaema. At present there is a good draining bleb and the tension is normal.

Case 3, a woman aged 64, was deaf and blind with bilateral corneal opacities. In September, 1959, a lamellar corneal graft was performed on the right eye. In June, 1960, a cataract extraction was proposed, the patient was prepared for operation by cocainization of the right eye and administration of gutt. Phenylephrine 10 per cent. The operation had to be postponed however as the patient was very restless and unco-operative. The following day she vomited and complained of pain in the right eye and the intra-ocular pressure was found to have risen to 45 mm. Hg (Schiötz). She was treated with eserine drops and Diamox tablets and the tension fell to 32 mm. Hg, but she later vomited copiously and became very drowsy and dehydrated. The pressure rose to 45 mm. Hg but fell to 28 mm. Hg on the morning of the operation. As this was

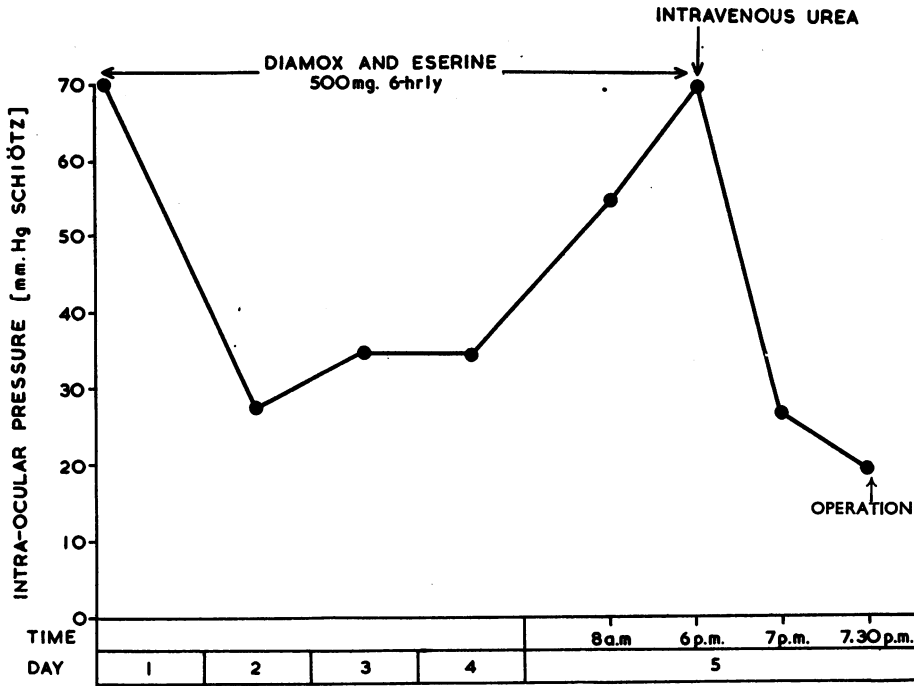


FIG. 1.—Progress in Case 1.

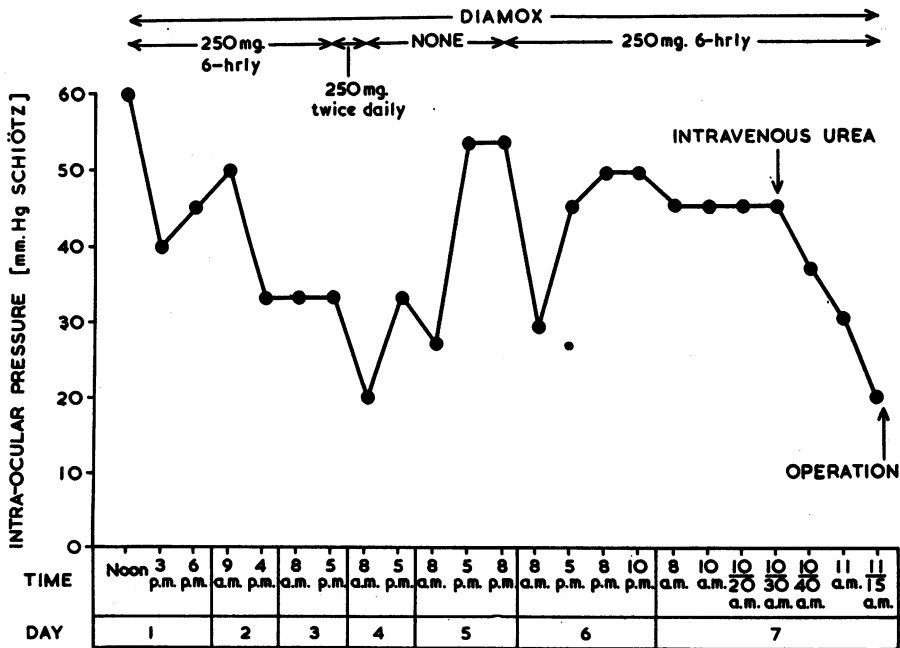


FIG. 2.—Progress in Case 2.

such a complicated case it was decided to reduce the pressure even further and an intravenous urea drip was started (Fig. 3). The intra-ocular pressure became unrecordable after 75 minutes, and as the lens had become dislocated an intracapsular cataract extraction was performed with a vectis. No difficulty was experienced in making the cataract section in spite of the soft eye, but the post-operative condition of the eye is poor.

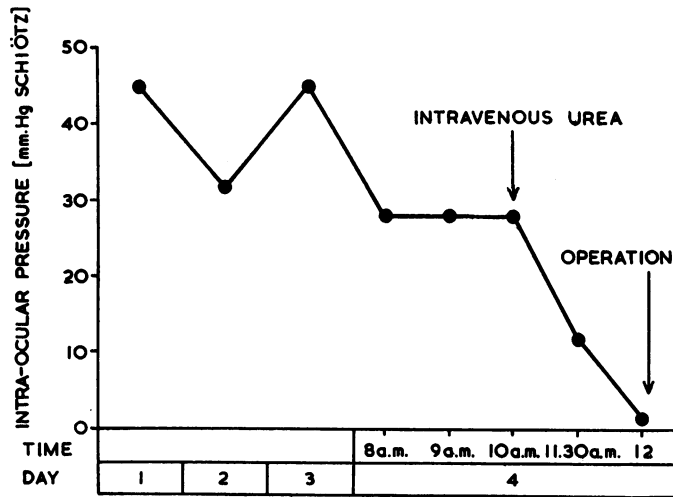


FIG. 3.—Progress in Case 3.

The effect of other carbonic anhydrase inhibitors was not tested on these patients. None of these patients experienced any untoward after-effects from the administration of the urea.

Discussion

Intravenous urea is a potent drug for reducing the intra-ocular pressure. It is believed to act by its osmotic effect, as urea does not diffuse freely into the anterior chamber and the concentration in the aqueous humour is less than that in plasma. The rate of transfer of urea into the aqueous humour is slow. It has been suggested that the diuretic effect of the urea causing relative dehydration produces the fall in pressure (Bunge, Danforth, and Settlege, 1957), but Javid and Anderson (1959) showed by experiments on a nephrectomized cat that it was the change in the osmotic pressure of the blood that caused the fall in intracranial pressure and the behaviour of the intra-ocular pressure is probably analogous. de Roeth (1954) has shown that the facility of aqueous outflow remains constant during the administration of sorbitol; hence the reduction in pressure must be due to a reduction in aqueous inflow.

Urea has been shown to be more effective in reducing the intra-ocular pressure than the other substances that have been tried (Galín, Aizawa, and

McLean, 1959a). It is non-toxic and rapidly excreted, and because of its very low molecular weight small amounts exert a relatively great osmotic effect. The clinical state of uraemia is almost certainly caused not by the retention of urea but by other factors, including the failure of other renal functions such as the regulation of the acid-base balance, the production of renin causing hypertension, the maintenance of body water, and electrolyte control. The use of urea is not recommended in the presence of renal failure, although its use in such cases has not been attended by harmful effects.

Toxic reactions to urea are rare. Rigors have been reported but these may occur during any intravenous infusion and may not have been related to the urea. The vein into which the solution is passing may become inflamed, which may be due to the hypertonicity of the solution. Stubbs and Pennybacker (1960) found that bleeding was increased in the early stages of operations on the brain after administration of intravenous urea. In one of our cases there was troublesome bleeding, but this may have been due to the congested state of the eye before operation. Urea has been administered orally but its application has been limited by its unpalatability (Galín and others, 1959b). Duke-Elder (1926) showed that saline and dextrose were more effective when given intravenously than orally.

Summary

Intravenous urea administered to three patients who were resistant to Diamox therapy was followed by an immediate reduction in the intra-ocular pressure.

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