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Effects of Intravenously Administered Hypertonic Urea Solution*

By


With 3 Figures

Introduction

In the past 30 years, neurological and neurosurgical clinics have made frequent use of intravenously administered hypertonic urea solutions to lower intracranial pressure. Many papers have been published on this subject (e.g. Javid and Settlage, 1956; Javid, 19581, 1961; Stubbs and Pennybacker, 1960; Langfitt, 1961; Beks and v. d. Kuy, 1962; Nemetschek-Gansler, Loew and Plogsties, 1964). Administration of such solutions is believed to increase the osmolarity in the blood, thus dehydrating the tissues, and particularly the brain. It is believed that the brain in particular is dehydrated as a result of the activity of the blood-brain barrier. Also, urea is believed to diffuse more slowly to the central nervous system than other intravenously injected hypertonic solutions, e.g. sodium chloride, glucose, mannitol and sorbitol.

Some effects of intravenously administered hypertonic urea solutions were studied in 12 patients with increased intracranial pressure caused by an expanding process, who during a craniotomy received a hypertonic urea solution of the following composition:

urea "pro analyse" ............................................................... 300 g
sterile invert sugar solution (50 g/100 ml) ...................... 200 ml
sterile propylene glycol with, per 100 ml: 6,5 g methylparaben 7 ml
3,5 g propylparaben

NaOH 4 N up to pH 7,0
sterile pyrogen-free water up to 1000 ml.

The solution was prepared without heating lest the urea should be decomposed. After dissolving, the pH of the fluid was adjusted to 7 with

* This study was supported by a grant from the Netherlands Organization for the Advancement of Pure Research (Nederlandse Organisatie voor Zuivervetenschappelijk Onderzoek, Z. W. O.).

Acta Neurochirurgica, Vol. XIII, Fasc. 1
the aid of NaOH. The solution was then submitted to aseptic bacterial filtration (Seitz bacterial filter). The paraben mixture was added as preservative (v. d. Kay and Huizinga, 1961). The patients received 1 g urea per kg body weight.

**Method and Material**

In this group of 12 patients, the following preoperative serum values were determined: K, Na, Cl, urea, Ca, PO₄, glucose, total protein, haemoglobin, haematocrit and osmolarity. Four of these patients, moreover, were submitted to determinations of Ca, glucose, urea, total protein and osmolarity in the cerebrospinal fluid (C. S. F.).

After opening the cranium, the surgeon obtained biopsy specimens from the temporal muscle and from the cerebral cortex in the vicinity of the pathological tissue, for tissue analysis. The urea solution was then administered intravenously, evenly distributed over 20 minutes (1 g/kg body weight). After this the abovementioned substances in the serum and the C. S. F. were again determined; the urine production over this period was measured, and the quantity of urea excreted in the urine during this period was determined.

Muscle and cerebral tissue specimens were again excised and analysed. The entire procedure was repeated before the dura mater was closed, about 3 hours after starting the operation. After another 3 hours (i.e. 6 hours after starting the operation), the abovementioned determinations in serum and C. S. F. were repeated.

Sodium and potassium determinations were made with the aid of a flame photometer; the chloride was determined coulometrically; the urea by the method of Chaney and Marbach; the calcium titrimetrically with complexon; the phosphate according to Taussky and Shorr; the glucose according to Hagedorn and Jensen; the total protein by the biuret method; the Hb value by the Hi-CN method; and the osmolarity by the freezing-point lowering method.

**Results**

Like Mason and Rauj (1961) and Gilboe and Javid (1963) we found that administration of urea solution is not followed by any distinct changes in serum Na, K and Cl values (Table 1).

Table 1. Serum concentrations at different times (before and after a hypertonic urea solution had been given intravenously)

<table>
<thead>
<tr>
<th></th>
<th>osmolality m osm</th>
<th>urea mg/100 ml</th>
<th>total protein g/100 ml</th>
<th>Ca mg/100 ml</th>
<th>PO₄ mg/100 ml</th>
<th>K mEq/l</th>
<th>Na mEq/l</th>
<th>Cl mEq/l</th>
<th>creatinine mg/100 ml</th>
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<tr>
<td>1 before urea infusion</td>
<td>292</td>
<td>23.3</td>
<td>7.1</td>
<td>10.0</td>
<td>3.3</td>
<td>4.1</td>
<td>141</td>
<td>97.0</td>
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<tr>
<td>at the end of urea</td>
<td>324</td>
<td>111.7</td>
<td>5.9</td>
<td>9.3</td>
<td>4.4</td>
<td>4.2</td>
<td>141</td>
<td>94.0</td>
<td></td>
</tr>
<tr>
<td>infusion</td>
<td>308</td>
<td>80.3</td>
<td>6.5</td>
<td>11.1</td>
<td>5.7</td>
<td>4.1</td>
<td>141</td>
<td>93.0</td>
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<td>3 hours after the</td>
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