Progressive Changes in the Concentrations of Phenol and Glycerine in the Human Subarachnoid Space

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In a previous study we found that concentrations of pure ethyl alcohol deposited in the human and canine subarachnoid spaces would decline to levels innocuous to nerve tissue within 15-20 minutes of instillation if the amount instilled did not exceed 1 ml. In the present study we determined the changes in concentration of a phenol–glycerine solution in the human subarachnoid space.

METHODS

Twelve subarachnoid blocks with a 7 per cent (w/v) phenol solution in glycerine were achieved in ten patients who had intractable abdominal pain. The patients were placed in a ventrally flexed, 45-degree laterospine position in which the segments to be blocked were brought to the lowest point. Following subarachnoid puncture, 0.3 ml per segment (total 0.6–0.9 ml) of the phenol solution was instilled at a rate of 0.01 ml/sec. At scheduled times following instillation cerebrospinal fluid (CSF) samples, 10–30 μl, were withdrawn into 50-μl microsyringes via the same spinal needle.

Analyses of CSF for phenol and glycerine contents were carried out by gas chromatography, using a gas chromatographic unit with a hydrogen-flame ionization detector (GC-3BF, Shimazu, Kyoto, Japan). The chromatographic column, a glass tube 260 cm long and 3.0 mm ID, was packed with 60/80 mesh polymer, Shimazu Tenax GC. The flow rates of the carrier gases, nitrogen and hydrogen, were 100 and 70 ml/min, respectively. Column, oven and detector temperatures were 195, 300 and 300 C, respectively. The internal standard used was 1.0 per cent m-cresol. The areas under the peaks for phenol and glycerine were integrated by a digital integrator (TR 2215A, Takeda Riken, Tokyo, Japan) incorporated in the gas chromatographic unit. Under these conditions the reproducibility was within 3.7 per cent for phenol and 2.6 per cent for glycerine.

RESULTS

In six patients concentration changes of phenol and glycerine were observed together (fig. 1). The changes in concentrations of phenol alone in the 12 subarachnoid blocks were very similar to the curve shown in figure 1. Within the observation period both phenol and glycerine decreased in patterns consisting of three separate exponential curves. At 0 time (extrapolated from the first phase) the concentration of phenol was about 30 per cent and that of glycerine about 40 per cent, respectively, of the original concentrations. The curve for phenol bends at about 15 and 50 min. At 15 min the mean phenol concentration was 0.1 per cent (7 × 0.015).

DISCUSSION

The patterns of changes in subarachnoid concentrations of phenol and glycerine are somewhat different from those observed with local anesthetics and ethyl alcohol. The initial rapid decrease and the subsequent slower decline are common to all these substances, but phenol and glycerine present a third phase of still slower decrease.

The primary mechanism of the initial rapid decay manifested by phenol is probably uptake by neural tissue. The phenol concentration at 0 time was about 30 per cent of the original concentration, similar to the figures found for local anesthetics (28 per
cent\textsuperscript{2} and ethyl alcohol (25.6 per cent,\textsuperscript{1} 25 per cent\textsuperscript{3}).

The second phase may have reflected mainly mechanisms such as vascular absorption, washout by CSF, dilution by vascular pulsation,\textsuperscript{2} etc. The third phase probably resulted from the presence of the solvent glycerine, which is less miscible with the CSF, since the slopes of the third phase for phenol and glycerine are almost identical.

Glycerine is used as a hyperbaric solvent to maintain a high concentration of phenol at the target segments and to govern the rate of release of phenol into CSF.\textsuperscript{4} The rapidity of the initial decrease in glycerine, however, indicates that this effect of glycerine is not marked. At 0 time it was about 40 per cent of the original concentration, and it declined to only 3 per cent at 15 minutes, rapidly becoming a dilute watery solution.

The similarity of the slopes of the first phase for phenol and glycerine implies that uptake of phenol by neural tissue is little affected by the presence of glycerine. Phenol block, therefore, is more likely to be achieved by phenol that is taken up by the nerve fibers during the very short initial period of the first phase, rather than by phenol gradually released from a mass of glycerine deposited locally.

The above-described assumption may serve to explain the regular ineffectiveness of phenol block in cases in which anesthesia fails to develop immediately (2-3 min) after the instillation. It also emphasizes the critical importance of precise patient positioning at the time of instillation and the futility of efforts to alter the area of effect by positional change after instillation.

Nathan and associates,\textsuperscript{5,6} in their histologic study in man and the cat, found that 5-8 per cent phenol solutions in glycerine affected the nerve fibers almost exclusively, sparing the root ganglia and the spinal cord. They, however, failed to demonstrate a selective destructive action of phenol on the small "pain-carrying" fibers. Nathan and Sears\textsuperscript{4} also found, in cat spinal nerve roots in situ and in vitro, that the action potential of A\textalpha{} fibers (depressed by 20 per cent) recovered completely when the time of contact with 0.1 per cent phenol in water was within 3 min, whereas that of C fibers (depressed to null) recovered only partially.

They thus proposed two categories of action of phenol, local anesthetic and destructive, the former category being selective and the latter nonselective. Which category predominates depends on the concentration of phenol and the length of its contact with nerve fibers.

Clinically, the recommended periods of absolute patient immobility after instillation of phenol–glycerine range from 15\textsuperscript{2} to 60 min.\textsuperscript{6} In the present study the mean concentration of phenol 15 min after instillation was 0.1 per cent and that of glycerine, 3 per cent. The phenol–glycerine solution at this time, therefore, is almost isobaric with CSF (specific gravity of 3 per cent glycerine in water at 37\textdegree{}C is 0.9979). Since the phenol concentration would undergo a rapid fall at a new site, it seems unlikely that even small fibers would sustain irreversible damage, even if the CSF were displaced in toto by positional change at this time.
Pancuronium and the Patient with Myasthenia Gravis

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Pancuronium, a nondepolarizing neuromuscular blocking agent, has recently been made available for general clinical usage in the United States. Patients with myasthenia gravis should be “sensitive” to pancuronium. To test this hypothesis we evaluated the neuromuscular blocking effects of pancuronium in two myasthenic patients undergoing thymectomy.

METHODS

An 8-year-old boy and a 21-year-old man, with myasthenia gravis of 4 and 6 months’ duration, respectively, were studied. Written consent was obtained for each study. All anticholinesterase therapy was discontinued 8 hours prior to operation. Premedication consisted of atropine sulfate, 0.3 and 0.4 mg, im, respectively, one hour prior to induction of anesthesia. Following topical nasopharygeal anesthesia with 2 percent tetracaine and transtracheal block with 4 percent lidocaine, a nasotracheal tube was passed into the trachea with the patient awake. Anesthesia was then induced with sodium thiopental and maintained with 70 percent nitrous oxide and meperidine, iv. Esophageal temperature was maintained between 35 and 36.5°C. Controlled ventilation kept $P_{\text{a}}$CO$_2$ between 36 and 40 torr for the duration of the study. Neuromuscular transmission was studied by supramaximal stimulation of the ulnar nerve at the wrist with a Wellcome peripheral nerve stimulator, and thumb adduction was measured with a force-displacement transducer and recorded on a Brush recorder.

A dilute solution of pancuronium bromide containing 0.01 mg/ml was infused at a rate of 1 ml/min until twitch height was reduced to 50 percent of control. When twitch height had recovered to 60 percent of control, additional pancuronium was administered to reduce twitch height to 5 percent of control (95 percent twitch depression) and the infusion of pancuronium then stopped. When twitch height had recovered to 10 percent of control, 2.5 mg neostigmine and 1 mg atropine were administered iv.

RESULTS

Infusion of pancuronium, 0.1 mg/m² BSA, or 0.0033 mg/kg in Patient 1 and 0.0025 mg/kg in Patient 2, over a 10-minute period, reduced twitch height to 50 percent of

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Received from the Department of Anesthesiology, University of Arizona College of Medicine, Tucson, Arizona 85724. Accepted for publication November 16, 1974.

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