Intraosseous infusion into the skull: potential application for the management of hydrocephalus

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Object. Hydrocephalus results from abnormal cerebrospinal fluid (CSF) volumes or flow patterns. The absorption of CSF is determined largely by pressures within veins and venous sinuses in the head and adjacent to the spine. Most surgical solutions for hydrocephalus involve diversion of excess CSF into alternative absorption sites, and most of these solutions are still suboptimal. The focus of this work has been to recreate more normal CSF absorption into the dural venous sinuses without having to directly access the superior sagittal sinus (SSS).

Methods. Intraosseous skull infusion for the purpose of accessing the SSS and the systemic venous system was tested by experimental skull infusions of tracer fluids into living large animals (14 adult pigs). Compared with control injections into an ear vein, infusions into the skull through specially designed infusion devices had similar systemic absorption characteristics. This suggested that intraosseous skull infusion in a living large animal was successful in gaining access to the SSS and systemic venous system.

Conclusions. This study constitutes the first demonstration of the success of intraosseous skull infusion in gaining rapid access to the systemic venous system and it thus opens the possibility of using this strategy for diversion of CSF back into the intracranial venous system for the treatment of hydrocephalus.

Key Words • hydrocephalus • cerebrospinal fluid absorption • intraosseous infusion • diploic veins • pig • pediatric neurosurgery

The brain and spinal cord are supported and cushioned inside the osseous confines of the skull and spinal column by CSF. Produced continually by the choroid plexus, CSF flows from the ventricular system of the brain to circulate around the central nervous system, removing metabolic wastes, maintaining the extracellular fluid microenvironment, and moderating changes in intracranial pulsatility and volume. Hydrocephalus results from the obstruction to normal CSF circulation that can occur within the ventricular system (noncommunicating hydrocephalus) or along the pathway of CSF flow to the site of CSF absorption (communicating hydrocephalus). Hydrocephalus is the most common disorder treated by pediatric neurosurgeons and surgical solutions have been used for this condition for more than 50 years. Nevertheless, even the best surgical solutions continue to be associated with frequent complications.8

The current management of hydrocephalus often involves the diversion of CSF from the cerebral ventricles to some distant site for absorption—most commonly the peritoneal cavity. Various valves have been developed to regulate flow and prevent siphoning and overdrainage. However, no single shunt system or valve is effective for all patients.

Our goal has been to recreate natural CSF circulation pathways utilizing the inherent wisdom of the venous system of the head and neck for managing the absorption of CSF through all changes in body size and position. The complex dynamics of CSF physiology are not particularly relevant to the design or implementation of most simple CSF shunt systems. Bulk flow of CSF into the venous system and the cranial venous sinuses probably plays a significant role in normal circulation. The idea of CSF diversion into this venous system of the head and neck is not new. Payr attempted shunting of CSF directly from the ventricular system to the SSS in 1907 without success.2 Since then, there have been numerous further attempts—none yet successful enough to change the practice or philosophy of CSF diversion. However, indirect vascular access by intraosseous infusion through the skull to the SSS has not been previously studied.

Intraosseous infusions into other osseous structures, such as the tibia or sternum, are widely used for fluid resuscitation and the delivery of medication.6,15,23,29 However, the ability of the skull to absorb fluids into the systemic circulation has never before been demonstrated. The richly vascular skull contains numerous emissary and diploic veins that drain freely into the SSS and systemic venous system (Johnston et al., unpublished data). It may be possible to in-

Abbreviations used in this paper: CSF = cerebrospinal fluid; FITC = fluorescein isothiocyanate; SSS = superior sagittal sinus.
fuse fluids into this diploic space and thereby gain access to the general circulation; this may then provide an alternative site for the diversion of CSF in the treatment of hydrocephalus.

**Materials and Methods**

To study the absorption of fluids in a dynamic state, 14 cross-bred (Lendrace-Yorkshire) adult pigs, each weighing 40 to 56 kg, were sedated using ketamine (20 mg/kg) and atropine (0.05 mg/kg) by intramuscular injection and maintained under general anesthesia using 2 to 3% isofluorane for the duration of the terminal experimental study. All aspects of the study were approved by the Health Sciences Animal Policy and Welfare Committee at the University of Alberta. The experimental paradigm is illustrated in Fig. 1.

An indwelling central venous catheter was placed by cutdown into the left or right femoral vein in all animals to allow frequent serum sampling of infused tracers. Heparinized saline (1,000 IU/L) was infused through the femoral line to prevent venous thrombosis prior to sampling. A three-way stopcock with a Vacutainer connection (Becton, Dickinson and Co.) was used to allow frequent blood sampling. The intraosseous infusion device was placed into the skull by direct surgical exposure using a midsagittal linear incision through the scalp and the subcutaneous tissues to the periosteum. The periosteum was reflected until the cranial sutures could be identified over the flat parietal surface of the skull. All animals had infusion devices placed just lateral to the SSS near the coronal sutures. Infusions of tracer substances were carried out either by hand injection or, later, by infusion pump with an intracranial pressure monitor in place.

The infusion sites were removed postmortem and then freshly bisected using an ultra–high-pressure waterjet with a 1/10,000-in diameter at 52,000 psi with a traverse speed of 3 in per minute. The use of a waterjet to obtain sections allowed us to avoid mechanical disruption of the osseous architecture and thus allowed detailed examination of the infusion site using scanning electron microscopy.

**Tracer Injection**

To study the response to injected dextrose, 20 ml of 50% dextrose solution was injected into the skull through the intraosseous infusion device in six experimental animals and into the ear vein in a control animal. Serum glucose was measured from the femoral vein every 15 seconds from time zero for the first 2 minutes, then every 30 seconds thereafter to follow the systemic response to this injection of dextrose.

A second tracer, FITC-labeled dextran (average molecular weight 70 kD) was injected through the intraosseous infusion device in eight experimental animals and the ear vein in the control animal. Serum samples were taken from the femoral vein every 15 seconds from time zero for the first 2 minutes, then every 30 seconds thereafter for fluorescence measurement.

**Infusion Devices**

Specific intraosseous infusion devices suitable for skull infusion were developed. Two designs were used in this study. First, a cannulated screw-type infusion device (length 12 mm, external diameter 5 mm, internal diameter 3 mm) with eight side holes and a single end hole was used for the glucose injection studies (Fig. 2A). A 13/64-in drill bit was used with a hand-twist drill to create a 15-mm-deep bur hole through the outer table into the diploic space of the skull. This hole was then tapped by hand prior to placement of the screw-type infusion device. A silicone gasket was used to improve the seal at the interface between the infusion device and skull.

Subsequently, an infusion cap device (aperture 5 mm), secured to the skull using six Bioplate screws (Codman, Johnson and Johnson) was used for FITC-dextran infusion (Fig. 2B). Using the same 13/64-in drill bit and hand-twist drill, a 10-mm-deep bur hole was created through the outer table of the skull into the calvarial diploë. No tapping was required to secure the infusion cap device. Care was taken to ensure that air was not entrained into the vascular diploë by continuously irrigating through and around the device while securing it in place.

**Results**

The time required for the injection of 20 ml of 50% dex-

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**Fig. 1.** Schematic representation of the experimental paradigm. Tracers were injected into the porcine calvarial diploë through the infusion device. Delivery into the systemic circulation was confirmed by serial blood samples taken from the femoral vein.
trose into the experimental animals ranged from 16 to 86 seconds, with an average delivery time of 43 seconds. In contrast, the control animal received 20 ml of 50% dextrose in 26 seconds into the ear vein. The baseline serum glucose levels, measured at time zero, ranged from 31 to 90 mg/dl in the six experimental animals (mean 64.2 mg/dl). The baseline serum glucose level in the control animal was 36 mg/dl.

Even with the relatively slow delivery of dextrose through the intraosseous infusion device, an elevation was observed in the serum glucose level within 45 seconds (Fig. 3 upper). This finding is remarkable in light of the fact that the average delivery time was 43 seconds, implying that the dextrose was rapidly absorbed and distributed to the central circulation. The control animal received 20 ml of 50% dextrose in 26 seconds into the ear vein and demonstrated a more dramatic elevation of the serum glucose level by 45 seconds, with the peak occurring within 75 seconds.

Due to the variability in infusion times with the large volume of 50% dextrose solution, as well as the variability of baseline serum glucose levels, FITC-dextran was used to study the rate of systemic absorption. Only 2 ml of FITC-dextran was injected to measure uptake of the fluorescence marker compared with 20 ml of 50% dextrose. Delivery time in eight experimental animals averaged 7.7 seconds, whereas the delivery time in the control animal was 6 seconds (Fig. 3 lower). The rapid uptake demonstrates that fluid injected into the skull is absorbed into the general circulation as quickly as when delivered directly through the ear vein into the venous system. Serum fluorescence was measured based on the estimated blood volume of each of the experimental animals and the control animal.

Various techniques including bone curettage and high- and low-speed drilling were used to prepare the bur holes prior to infusion. After the infusion studies were completed, the section of calvaria was removed and stored in 10% formalin. The skull was cut into sections using a high-pressure waterjet to allow detailed inspection of the surface and depth of the bur hole. Scanning electron microscopy was used to study the anatomic disruption of the bone by the different drilling techniques (Fig. 4). Hand-twist drilling seemed to preserve the native architecture of the bone to the greatest degree. As the holes were drilled into the skull, bleeding was most active with slow drilling using a sharp bit. Curetting...
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Discussion

The ability of the medullary space of long bones to absorb fluids into the general circulation is well known. Results of studies have demonstrated that fluids and medications delivered through intraosseous lines reach the central circulation as quickly as those delivered through central and peripheral venous lines. Results of long-term studies have shown no adverse effect on the structure or histological characteristics of bones used for intraosseous infusion. The complication rate of intraosseous infusion is extremely low, and most complications have been reported following infusions of hypertonic fluids.

Intraosseous infusions are commonly used in infants and children when there is a delay or difficulty obtaining vascular access. The most common sites for intraosseous infusions are the proximal tibia and distal femur, though other sites have also been used with success. McCarthy challenged the notion that intraosseous infusion requires a marrow or medullary space by successfully injecting fluids into the calcaneus. The human skull does not have a medullary space, but it does have hematopoietic potential and is richly vascular. Although the underlying brain makes the skull a high-risk site, the vascularity of the skull should be ideal for intraosseous infusion of fluid.

Tocantins and O’Neill demonstrated that the intraosseous pressure is similar to the venous pressure of the veins draining the bone. In the case of the skull, the draining veins are primarily the dural venous sinuses and internal jugular vein. If the resistance to infusion is dictated by the pressure in the SSS, diverting CSF into the calvarial diploë could potentially recreate some of the natural dynamics of CSF drainage.

Fig. 4. Scanning electron micrographs of the porcine skull. The natural architecture of the skull in cross-section is demonstrated (A). Bur holes prepared using a hand-twist drill and then bone curette (B) or prepared using a high-speed drill (C) led to osseous disruption and smearing. Using the hand-twist drill alone preserved the natural trabecular appearance of the diploë (D).
To measure the physiological absorption of fluids injected into the calvarial diploë, we used both dextrose and FITC-dextran. The 50% dextrose solution is readily available and easy to administer, and serial serum glucose levels are simple to measure. However, there was variability in the baseline serum glucose levels of the animals despite care in planning the studies for the same time each day. Also, the insulin response to glucose loads in pigs necessitated large-volume injections in order to document changes in serum glucose levels. Although this strategy was successful, the inconsistency in the resistance to infusion led to variability in the delivery time of the 50% dextrose and therefore in the rate of rise of serum glucose levels. For these reasons, FITC-dextran was used as an alternative tracer. Using a dextran carrier with an average molecular weight of 70 kD, the fluorescein remains intravascular and can be measured easily using a fluorometer. This advantage allowed for the administration of a small volume of FITC-dextran, thereby standardizing the delivery time and allowing a more accurate comparison between intraosseous infusion and direct intravenous injection. Using the FITC-dextran technique, we confirmed rapid access to the systemic circulation by intraosseous injection into the skull diploic space.

The venous system of the head and neck is naturally designed to control the rate of CSF absorption. The dynamics of the neck veins (jugular venous pressure) are affected by changes in body position. The neck veins in turn determine some of the dynamics of CSF absorption and CSF pressure regulation. Using the calvarial diploë for indirect access to the sagittal sinus could recreate some of the natural dynamics for CSF flow and resorption.

Conclusions

To our knowledge, this is the first study in which the absorptive capacity of the calvarial diploë has been demonstrated in a living system.

Achieving access to the SSS indirectly through the diploic spaces of the skull may provide another option for the management of hydrocephalus. Use of an intraosseous infusion device to deliver CSF indirectly into the sagittal sinus may create a more natural pathway for CSF absorption and utilize the inherent wisdom of the venous system of the head and neck.

Diverting CSF back into a known CSF absorptive site by intraosseous skull infusion may eventually provide another alternative in the management of hydrocephalus.

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References

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