

Tissue changes induced by the absorption of formocresol from pulpotomy sites in dogs

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Abstract

Formocresol applied to vital pulp tissue is absorbed systemically and distributed throughout the body. The sites of injury and the systemic effects of the intravenous administration of high doses of formocresol have been determined. The purpose of this project was to determine whether cellular injury could be detected following formocresol application to vital pulp tissue.

Five dogs were anesthetized and pulpotomies performed on selected incisors and canines. Formocresol-moistened cotton pellets were applied to 16 pulpotomized teeth in one dog, to 4 pulpotomized teeth in a second dog, and to 1 in a third dog. The formocresol pellets were left in place for five minutes. One dog received 16 pulpotomies without formocresol application and served as an anesthesia control. After six hours, and prior to sacrificing, sections of kidney, liver, lung, and heart tissues were removed from each animal and prepared for histological evaluation. The dog which received 16 formocresol pulpotomies displayed histological findings suggestive of early tissue injury to the kidney and liver. The heart and lung tissue from that dog and all tissues from the other animals were essentially unremarkable.

A formocresol pulpotomy is currently the recommended treatment for carious pulp exposures in vital primary teeth.¹⁻³ In spite of its popularity, the use of formocresol as a pulpotomy agent remains controversial. Recent clinical studies raise questions as to its effectiveness as a pulpotomy agent.⁴⁻⁸

In addition to the clinical response, the biological effects of formocresol must be considered. The recommended composition for formocresol is 19% formaldehyde and 35% cresol in a glycerin and water base.⁹ Formocresol is toxic to living tissue; numerous studies have investigated the mutagenic and carcinogenic effects of formaldehyde and a federal panel in 1980 concluded that it was prudent to regard formaldehyde as posing a carcinogenic threat to humans.¹⁰⁻¹³

Formocresol applied to vital pulp tissue is absorbed readily into the systemic circulation and distributed throughout the body.¹⁴ A portion of the absorbed formocresol is metabolized and excreted by the kidney and lungs.^{14,15} The remaining formocresol is tissue bound with the liver, kidney, and lungs—the predominate sites of tissue binding.^{14,15}

The systemic toxic reaction to high doses of intravenously administered formocresol is characterized by changes in blood and urinary enzymes as well as histological evidence of injury to the kidney, liver, and lungs.^{16,17} Histological evidence of injury to the kidney and liver appeared to be the most significant feature of animal response to high doses of systemically administered formocresol.^{16,17}

Since the probable sites of injury from absorbed formocresol have been identified, the purpose of this project was to determine whether cellular injury could be detected following formocresol application to vital pulp tissue.

Methods and Materials

Five young, healthy, mongrel dogs weighing from 20 to 25 kg were anesthetized with pentobarbital and intubated with a cuffed endotracheal tube.

Pulpotomies were performed on maxillary and mandibular permanent incisors and canines. Access was obtained with a #699 carbide fissure bur in a high-speed handpiece using a water spray. The coronal pulp tissue was amputated with a #4 round bur. After amputation of the coronal pulp tissue, pulpal hemorrhage was controlled by applying pressure with dry cotton pellets. A cotton pellet was moistened with formocresol containing 19% formaldehyde and 35% cresol, then blotted in gauze to remove the excess formocresol. A fresh formocresol cotton pellet was prepared in the same manner for each pulpotomy site. The formocresol cotton pellet was applied to the pulp tissue and allowed to remain in contact with the pulp for five minutes and then removed.

Dog 1 received 16 pulpotomies on the maxillary and mandibular incisors and canines. Formocresol pellets were applied to each pulpotomy site. Dog 2 received 4 pulpotomies, 1 on each canine tooth, and a formocresol pellet was applied to each pulpotomy site. Dog 3 received 1 pulpotomy, on a maxillary canine, and a formocresol pellet was applied. Dog 4 received 16 pulpotomies to the maxillary and mandibular incisors and canines. No formocresol was applied to these pulpotomy sites. Dog 4 served as an anesthesia and pulpotomy control. Dog 5 received no pulpotomy treatment and served as an anesthesia control.

The animals were maintained under anesthesia for six hours following completion of the pulpotomy procedures. After six hours, and prior to sacrificing, sections of the kidney, liver, lung, and heart tissues were removed from each animal. The tissue specimens were placed in 10% neutral buffered formalin and processed for hematoxylin and eosin staining and histological evaluation. The microscopic sections were evaluated by a pathologist without knowledge as to the dog or the treatment employed.

Results

The kidney and liver of Dog 1, which received 16 formocresol pulpotomies, demonstrated histological changes suggestive of tissue injury. The heart and lung tissue from Dog 1 and all tissues from the other experimental animals were essentially unremarkable.

The glomeruli in the kidney from Dog 1 demonstrated a decrease in the width of Bowman's space and the glomerular tufts appear terse due to fluid retention (Figure 1).

The kidney tubules from Dog 1 displayed evidence of cloudy swelling and hydropic change in the convoluted tubules (Figure 2). The liver tissue from Dog 1 shows evidence of cloudy swelling and cellular edema (Figure 3).

Discussion

Histological examination of the kidney and liver tissue from the dog which received 16 formocresol pulpotomies demonstrates evidence of early tissue changes. In the kidney tissue, the decrease in width of Bowman's space

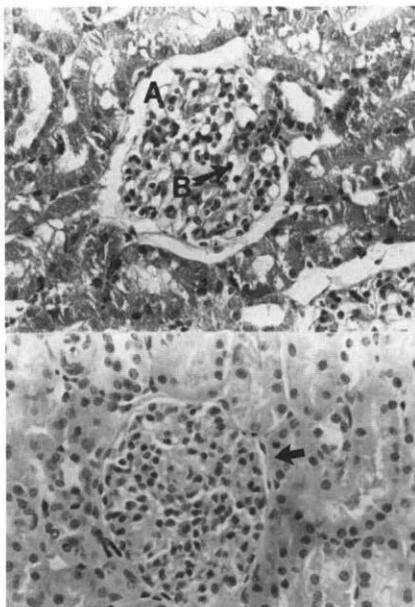


Figure 1. Top: Normal dog kidney cortex showing the glomerular apparatus. Note the clearly demarcated urinary space (A) of Bowman's capsule and the presence of the capillaries (B) in the glomerular tuft (380x). Bottom: Kidney cortex from a formocresol-treated dog showing an edematous glomerular apparatus. Note that the urinary space (arrow) of Bowman's capsule is almost obliterated and the glomerular capillaries not as prominent because of the edema of the glomerular tuft (called terseness by pathologists) and the increased cellularity due to retained leukocytes (380x).

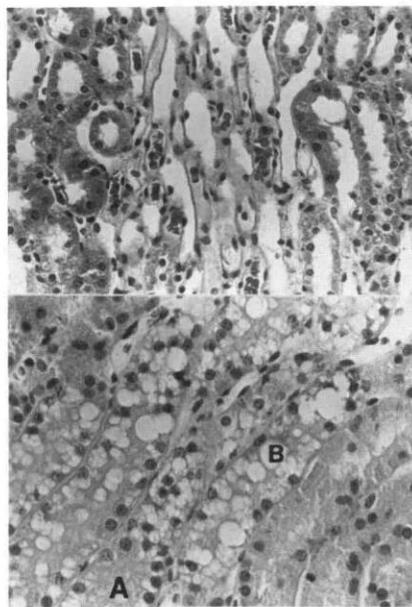


Figure 2. Top: Normal dog kidney medulla showing the patency of the descending and ascending tubular structures. Note the clarity of the cell definition and outline (380x). Bottom: The kidney medulla from a formocresol-treated dog showing a fuzzy outline of some tubular cells (A), called cloudy swelling, and a soap bubble appearance of other tubular cells (B) called hydropic change. Both of these morphological changes denote the occurrence of moderate cell injury (380x).

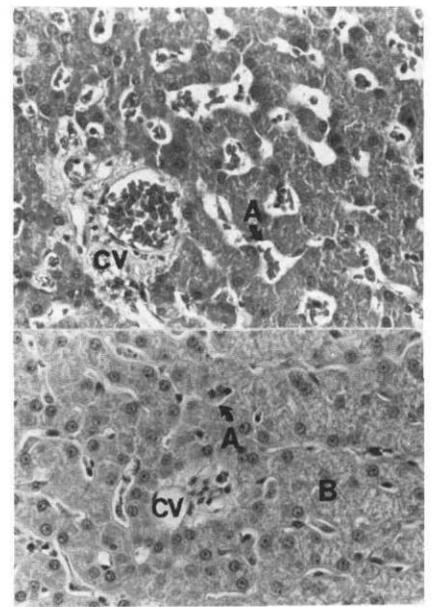


Figure 3. Top: Normal dog liver. The sinusoids (A) around a central vein (CV) display normal width and contain retained RBCs. Note the uniform staining quality of the liver parenchymal cells in the normal state (430x). Bottom: Liver section from a formocresol-treated dog. The width of the sinusoids is decreased (A) because of edema and swelling of the liver cells. The cells around the central vein (CV) exhibit a patchy staining quality called cloudy swelling (B). This denotes cell injury (430x).

appears to be the result of edema of the glomerular tuft. The cloudy swelling and hydropic changes in the convoluted tubules of the kidney appears to be early in onset since there is little or no inflammatory response. The lack of normal-appearing sinusoids in the liver suggests cellular edema. Collectively these histological findings can be called hydropic changes and are indicative of early cellular injury. Sufficient formocresol apparently was absorbed from the 16 pulpotomy sites in Dog 1 to induce early signs of tissue injury. No similar changes were noted in the animals receiving fewer formocresol pulpotomies, or in the anesthesia controls.

The intravenous administration of high doses of formocresol has been shown to produce injury to the kidney and liver.^{16,17} The findings of this study suggest that full-strength formocresol absorbed from multiple pulpotomy sites may initiate tissue injury in the kidney and liver of an experimental animal. A longitudinal study is needed to determine whether the injured kidney and liver cells would recover. However, one would expect cellular recovery to occur since there is no evidence of the onset of an inflammatory reaction. No direct clinical implications regarding the toxicity of absorbed formocresol should be made from the results of this study. Sixteen formocresol pulpotomies on a small dog represents a considerably higher exposure to systemic formocresol than would occur when performing one or two pulpotomies on a child.

Further studies should be undertaken to determine precisely the quantity of formocresol absorption required to initiate evidence of cellular injury, and to determine whether dilute concentrations of formocresol will initiate cellular changes.

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