Review Article

Management of Pain in Autosomal Dominant Polycystic Kidney Disease and Anatomy of Renal Innervation

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Abbreviations and Acronyms

ADPKD = autosomal dominant polycystic kidney disease

LCD = laparoscopic cyst decortication

SCS = spinal cord stimulation

TAE = transcatheter arterial embolization

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Purpose: Chronic pain is a prominent feature of autosomal dominant polycystic kidney disease that is difficult to treat and manage, often resulting in a decrease in quality of life. Understanding the underlying anatomy of renal innervation and the various etiologies of pain that occur in autosomal dominant polycystic kidney disease can help guide proper treatments to manage pain. Reviewing previously studied treatments for pain in autosomal dominant polycystic kidney disease can help characterize treatment in a stepwise fashion.

Materials and Methods: We performed a literature search of the etiology and management of pain in autosomal dominant polycystic kidney disease and the anatomy of renal innervation using PubMed® and Embase® from January 1985 to April 2014 with limitations to human studies and English language.

Results: Pain occurs in the majority of patients with autosomal dominant polycystic kidney disease due to renal, hepatic and mechanical origins. Patients may experience different types of pain which can make it difficult to clinically confirm its etiology. An anatomical and histological evaluation of the complex renal innervation helps in understanding the mechanisms that can lead to renal pain. Understanding the complex nature of renal innervation is essential for surgeons to perform renal denervation. The management of pain in autosomal dominant polycystic kidney disease should be approached in a stepwise fashion. Acute causes of renal pain must first be ruled out due to the high incidence in autosomal dominant polycystic kidney disease. For chronic pain, nonopioid analgesics and conservative interventions can be used first, before opioid analgesics are considered. If pain continues there are surgical interventions such as renal cyst decortication, renal denervation and nephrectomy that can target pain produced by renal or hepatic cysts.

Conclusions: Chronic pain in patients with autosomal dominant polycystic kidney disease is often refractory to conservative, medical and other noninvasive treatments. There are effective surgical procedures that can be performed when more conservative treatments fail. Laparoscopic cyst decortication has been well studied and results in the relief of chronic renal pain in the majority of patients. In addition, renal denervation has been used successfully and could be performed concurrently with cyst decortication. Nephrectomy should be reserved for patients with intractable pain and renal failure when other modalities have failed.

Key Words: anatomy; innervation; kidney; pain management; polycystic kidney, autosomal dominant

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AUTOSOMAL dominant polycystic kidney disease is relatively common, with a worldwide prevalence of 1:400 to 1:1,000.[1] Pain is a prominent feature of all types of polycystic kidney disease, affecting more than 60% of patients, and is most commonly located in the flank, followed by the back and abdomen.[1,2] Pain is often present early in the disease process and is the most common symptom that leads to a diagnosis of the disease.[3] The hardships of living with chronic pain can prevent patients with ADPKD from performing physical and social activities, which detrimentally affects their quality of life.[4] The difficulty of pain management is demonstrated by many patients, with up to 39% being somewhat or completely dissatisfied with pain treatment because they are physically unable to do what they would like.[5] A better understanding of the etiology of pain that occurs in ADPKD in addition to the underlying anatomy can help guide treatment.

MATERIALS AND METHODS

We performed a literature search of the etiology and management of pain in ADPKD using PubMed and Embase from January 1985 to April 2014 with limitations to human studies and English language. Search terms included pain management, chronic pain, treatment, therapy, polycystic kidney, autosomal dominant, cyst, hepatic, liver, kidney and renal. References of the studies found were reviewed. Further searches were performed using MEDLINE® and Embase for each relevant treatment of ADPKD identified, with additional search terms including analgesics, Alexander technique, tolvaptan, opioids, aspiration, celiac plexus, splanchnic nerves, splanchnicectomy, block, ablation, spinal cord stimulation, sclerotherapy, decortication, laparoscopic, marsupialization, denervation, percutaneous, sympathectomy, nephrectomy, transplant and transcatheter arterial embolization.

A comprehensive review of the literature identified 140 studies involving the presentation of pain and symptomatic treatment in ADPKD. Of these studies 30 were selected for this review based on appropriate study design, followup duration, number of patients and method of measuring pain control. The literature selected consisted of systematic reviews, randomized controlled trials, cross-sectional studies, retrospective case series and case reports.

A literature search was also performed to better delineate the anatomy and histology of renal innervation using PubMed and Embase with limitations to English language. Search terms included anatomy, histology, renal, kidney, nerve, innervation, splanchnic, celiac, sympathetic, autonomic, sensory and afferent. References of the studies found were reviewed and textbooks were consulted for additional information. Overall 54 articles of anatomy and histology were reviewed, and 17 were included based on the number of samples in the study, the method of histopathological sectioning and the presence of afferent neural tissue.

RESULTS

Chronic Renal Pain

Renal cysts can lead to pain in the back, abdomen and flank region. Patients with ADPKD often experience multiple types of pain, which can be described as dull, an uncomfortable fullness, stabbing and cramping.[3] Chronic pain due to cyst formation may also present as persistent discomfort localized to a small area that is aggravated by standing or walking.[6] Many patients also experience sudden onset of pain while performing physical activities.[4] Renal mechanosensory nerves, which respond to changes in pressure, and renal chemosensory nerves, which respond to ischemia or alterations of the renal interstitial fluid, have been identified in the kidney.[7] Cystic compression of the renal capsule and parenchyma can lead to transmission of pain through afferent sensory nerve fibers around the renal vasculature, in the corticomedullary connective tissue and in the renal pelvic region.[8] Pain is not related to kidney size early in the disease process (estimated glomerular filtration rate greater than 60 ml/minute/1.73 m^2) unless the kidneys are extremely large, with a height adjusted kidney volume greater than 1,000 ml/m.[5] Pain presentation based on cyst size can be variable, as some patients with smaller cysts can experience severe pain while others with larger cysts remain pain-free.[6] Renal pain in ADPKD can present in various ways, making it difficult to clinically confirm its etiology. Clinical findings often need to be correlated to diagnostic images to confirm the source of the pain.

Mechanical Back Pain

Cystic enlargement of kidneys can lead to lumbar lordosis and an asymmetrical cystic enlargement of the kidneys can cause postural changes of the spine. These mechanisms can lead to stress and degeneration of the spine, resulting in mechanical back pain. Cystic enlargement of the liver can cause mechanical back pain through this same mechanism. An observation was made that patients with ADPKD have lumbodorsal muscle hypertrophy, serving as further evidence of the mechanical changes that can occur in patients with ADPKD.[6]

Abdominal Fullness and Early Satiety

The feeling of abdominal fullness can occur due to cystic expansion of the kidney or liver and is present in 20% of patients with ADPKD.[5] Compression on the stomach and duodenum can result in decreased appetite and abdominal fullness, leading to a risk of malnutrition.[5,6]

Chronic Liver Pain

Hepatic cysts in ADPKD can be identified with magnetic resonance imaging in up to 94% of