Chronic Pain is a Manifestation of the Ehlers–Danlos Syndrome

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Abstract

The Ehlers–Danlos syndrome (EDS) is a group of heritable systemic disorders of onnective tissue manifesting joint hypermobility, skin extensibility and tissue fragility. Although the presence of pain has been documented in the various types of the EDS its natural history, distribution and management have not been defined. We conducted a semi–structured interview in 51 individuals affected with different types of EDS. The overwhelming majority of individuals reported chronic pain of early onset involving severaljoints and refractory to a variety of pharmacologic and physical interventions. Our data shows that chronic pain is a common manifestation of EDS.

Key Words: Ehlers–Danlos syndrome, chronic pain, heritable disorders of connective tissue, natural history, analgesics.

Introduction

The Ehlers–Danlos syndrome (EDS) is a group of heritable disorders of connective tissue characterized by varying degrees of joint hypermobility, skin extensibility, and tissue fragility [Beighton, 1993]. Pain is a frequent yet poorly characterized clinical finding in EDS [Beighton,
1993]. Nine different types of EDS have been described, each clinical type distinguished from the others depending on what system is primarily involved. Most of the types of EDS are inherited as an autosomal dominant trait, although X–linked and autosomal recessive types have been described

[Beighton, 1993]. The diagnosis of EDS is clinical. Although diagnostic criteria have been promulgated for each of the different types of EDS, it is impossible to determine the exact type of EDS in a substantial proportion of affected individuals [Beighton et al., 1988]. The variable degree of clinical expression probably accounts for the underdiagnosis of EDS and hence the lack of accurate figures of prevalence for the various types. EDS type III is the most common form of the disorder presenting with generalized joint hypermobility frequently complicated by recurrent joint dislocations [Beighton, 1993]. Affected ndividuals are often unable to ambulate because of joint instability. EDS types I and II whose cardinal manifestation are skin fragility and generalized joint hypermobility are the best recognized forms of the disorder [Beighton, 1993]. EDS type IV is an uncommon type of EDS but also one associated with the highest morbidity and reduced life xpectancy [Beighton, 1993]. EDS type IV is associated with spontaneous rupture of internal organs, i.e. arteries, intestine, uterus and to a lesser degree with skin and joint manifestations.

Although the presence of pain has been documented, its contribution to the overall morbidity associated with the disorder has never been assessed, nor has its scope and intensity been formally investigated. The impetus for the present study was provided by the findings of Lumley et al. [1994] who reported that pain significantly affected the psychosocial functioning of individuals with EDS. The present study indicates that chronic, frequently debilitating pain of early onset and diverse distribution is a constant feature in most individuals affected with different types of EDS. The presence of pain in association with the absence of a systematic approach for chronic pain management impacts dramatically on the well being of affected individuals and, as a previous study suggested, influences their social interactions.

Methods

Data were collected in semi–structured interviews with an opportunistic sampling of individuals drawn from either the University of Connecticut Heritable Disorders of Connective Tissue Clinic or attendants of the Annual Meeting of the Ehlers–Danlos National Foundation held August 15–18, 1995 in Cincinnati. Interviews were conducted

by two of us (AS in the General Clinical Research Center of the University of Connecticut Health Center in Farmington and JS in Cincinnati). The length off interviews ranged from 20 to 60 minutes and in addition to recording age, sex, and the type of EDS, three major topics were explored:

1) The experience of chronic pain was described by a series of questions concerning intensity, quality, time of onset and general progression for each location identified (modeled on the McGill–Melzack Pain Questionnaire [Melzak, 1975]).
Intensity was assessed for each location on a 10 point analogue scale with 0 = no pain and 10 = worst pain imaginable. Respondents were asked to describe the quality of each pain with adjectives. A list of adjectives such as throbbing, burning, tingling, etc. was given.

2) Functional impacts of chronic pain were elicited with a 5 item checklist (sleep, sexual functioning, social relations, physical activity, school or job functioning).

3) Strategies utilized to control pain were elicited with an eight item checklist medication, narcotics, physical therapy, heat/cold, massage, bandages/splits/braces, exercises, other).

The strategy for coding the data for purposes of descriptive analysis included categorization of specific pain locations, pain quality, coping strategies and onset periods (childhood, adolescence, adulthood).

Results

Sample Characteristics

Demographics of the sample are provided in Table 1. The majority (42/51) of those interviewed were women. The participants ranged in age from 9 to 70 years with a mean of 34, but only 6 were less than 20 years of age. For the purpose of this study we relied on patients* reports of their previously determined diagnosis. Fifteen of the participants were interviewed in Connecticut and the remainder were interviewed in Cincinnati. The patients interviewed in Connecticut had been previously evaluated by one of us
(PT). Twenty–eight (55%) of those interviewed stated that they were affected with EDS Type III. Although there are no accurate figures about the relative frequency of each EDS type the previous number reflects the distribution observed by one of us (PT) in the clinic. The remaining 23 were distributed between Types I, II, IV and Joint Hypermobility Syndrome, a phenotypically similar disorder. Two individuals were affected with a form of EDS which could not be typed.

Nature of Pain

Forty–six of the 51 individuals interviewed indicated they had chronic pain over the last 6 months or longer (Table 1). Of the adults only two (2/45) felt they were free of chronic pain.

Individuals' reports of pain locations, intensity, and course are summarized in Table 2. The mean number of pain locations for all 51 respondents was 8.0. Although individuals with EDS type IV seemed to have a substantially smaller number of painful locations as compared to individuals with EDS type I and type III, the small sample size precludes meaningful statistical analysis. The "mean intensity" rating, calculated for each individual as the mean of the intensity ratings for those locations affected, was 5.3 for the total sample and similar for all types. Forty–three (84%) individuals indicated that their pain had become worse during the course of their life (Table 2).

Respondents identified a total of 13 principal locations of their pain, ranging from 22 individuals (43%) noting elbow pain to 41 (80%) reporting pain in the shoulders at one time or another. Similar numbers of individuals reported pain in their hands (38, 75%), knees(36, 71%), and spine (34, 67%). Interestingly, almost half of the patients reported frequent headaches and a third had stomach aches. Approximately 70% of all patients reported continuous pain in their lower extremities, ankles, feet, toes, and hips. The description of pain qualities suggested a pattern of significant distress,described primarily as aching, sharp, throbbing or burning.

The locations noted and the time of onset during the life cycle for the 45 adults are shown in Figure I. Approximately 50% of individuals reported onset of pain in most locations in adulthood, although pain in shoulders, knees, ankles, feet and toes began earlier. owever, forty of the forty–five (89%) adults remembered chronic pain beginning in at least one location with onset in childhood or adolescence.

The percentages of individuals experiencing dysfunction in various areas are presented in Figure 2 . Sleep and physical activity were most frequently noted (70%) with sexual activity the least, although still substantial (45%). Only 6 respondents (11.8%) noted no dysfunction related to their pain.

Coping Strategies

Respondents identified more than 20 major strategies for coping with pain. Figure 3 shows the utilization (number who use or tried) of the 7 most frequent strategies and their efficacy for the total sample. Additional strategies less frequently noted included distraction, diet, TENS, rest, water bed and pillow, craniosacral therapy, shiatsu, energy work, smoking, and use of the Alexander Technique. These were used in less than 5% of the cases. Eighty–eight percent of the respondents had taken pain medications, and 51% had taken narcotics.

Discussion

A number of points emerge clearly from the interviews of individuals with EDS. First, and most striking, is the fact that moderate to severe pain is a common every day occurrence for essentially all of them. In addition, the pain associated with EDS starts early in life and evolves over time. The overwhelming majority of patients feel that their pain has gotten worse. Despite these observations, we were unable to find any articles reviewing

the management of pain associated with EDS.

The pain problems associated with EDS are complex and not uniform. Most patients affected with EDS have pain in several locations. The origins of these pains are probably quite variable. Some pains are likely secondary to frequent dislocations/subluxations, some from repeated soft tissue injury, or multiple surgical operations and resultant nerve injury.

Our limited sample size precludes statistical analysis of differences in pain patterns associated with various types of EDS. It appears that the number of pain locations and pain intensity are similar across the different types of EDS with the exception of individuals affected with EDS type IV who identified fewer pain locations. This could reflect the relative paucity of joint hypermobility in that EDS type.

This life–long history of discomfort has compelled many people to explore numerous coping strategies. Most patients have taken some type of medication and over half the sample have used opioids. A host of physical interventions were also used by patients with EDS. Physical therapy has been tried by many, particularly for pain in the shoulders, spine, knees, and hips. Massage, use of heat or cold, and chiropractic manipulation are frequently used in an attempt to cope more effectively with day–to–day pain associated with this condition. The need to use multiple coping strategies suggests that no one approach is uniformly successful.

More investigation is clearly necessary to study the origin of pain and the efficacy of specific intervention in these individuals. In the interim, some basic principles of pain management could be extrapolated from other chronic diseases. Certainly a pain problem list should be a part of their medical record [Portenoy, 1988]. The various types of pain that individuals with EDS experience may have different origins, different intensities, and run different courses. A detailed pain problem list will allow for a more thorough understanding and tracking of each type of pain and intervention for it. A pain assessment technique that is developmentally appropriate should be taught to the patient and used routinely [Paige and Cioffi, 1993]. From the pharmacological point of view, non–steroidal anti–inflammatory agents (NSAIDs) would appear to have a major role, especially if the pain is of inflammatory origin. It should be noted that the chronic use of these agents is frequently associated with gastrointestinal, renal, and hematologic consequences; therefore, they should be monitored if used chronically. Particular caution should be exercised in individuals affected with EDS type IV who are particularly prone to bruising and bleeding. For moderate to severe pain, an NSAID in conjunction with a weak opioid usually in a fixed combination is often used [Acute Pain Management Guideline Panel, 1992]. This approach, in chronic non–malignant pain, is considered controversial [Turk, et al. 1994]. If used however, care should be taken so that the NSAID and/or acetaminophen do not reach toxic levels in individuals who take large numbers of these pills daily. In those instances, a separate NSAID or acetaminophen can be given in onjunction with codeine or oxycodon. Opioids, either short acting or long acting, should be considered for severe pain. They should be monitored for side effects, in particular constipation, which can cause extreme discomfort. Therefore, any individual on chronic opioids should take prophylactic laxatives. A newer drug, tramadol (Ultramä), which is

an opioid analgesic may be a valuable alternative to opioids for some individuals with EDS in chronic pain because it lacks some of the side effects traditionally associated with opioids [Sunshine, 1992]. Finally, tricyclic antidepressants may be of benefit. These agents may help the patient sleep better at night and have some analgesic activity particularly against neuropathic pain. Neuropathic pain arises from nerve injury and is often opioid resistant.

Non–pharmacologic approaches, such as physical therapy and exercise may be warranted but may also be quite traumatic and stressful for this group of patients. Physical therapy taking place in water (hydrotherapy),however, may be less damaging to joints and more enjoyable. Behavioral and cognitive coping techniques may also be extremely valuable. These include hypnosis, breathing, meditation, visual imagery, and other forms of distraction.

Obvious limitations of our study are the small sample size, the over–representation of women in our sample, the potential self–selection bias and lack of a control group. These sampling issues stem from our reliance on the participants of the annual meeting of the Ehlers–Danlos National Foundation, our decision to utilize an interview approach and our inability to identify an appropriate age–matched control population. These limitations notwithstanding, our findings are congruent with our clinical experience.

In summary, our data reveals that individuals with EDS experience frequent and severe pain through much of their lives. These problems have been unrecognized previously in the published literature. Because EDS is relatively rare, no systematic study of pain in this population or its relief has been performed. Extrapolation from the literature on other diseases allows us a starting point from which to develop a clinical pain management algorithm. EDS should be considered in the differential diagnosis of chronic musculoskeletal pain. Clearly, further research is necessary to identify the most humane way to manage the devastating effects of this symptom in individuals with EDS.

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