

## PAIN IN WOMEN: THE DIMENSION OF THE PROBLEM

Maria Adele Giamberardino

Department of Medicine and Science of Aging, "G. D'Annunzio" University of Chieti - Italy

Pain is a ubiquitous phenomenon, an experience common to every individual in the course of life. Is there a need, then, to distinguish between pain in women and pain in the rest of the population? Why should we pay more effort to women's suffering, to the point of devoting a whole year of the world pain community to this theme? The answer is that women's pain has specific features and poses specific problems that require unique attention on behalf of the international community.

We are all familiar with the experience of pain as a symptom, a precious alarm system that warns us about something going wrong somewhere in our body and that helps us detect the abnormal situation threatening our well-being and possibly have it treated properly. Unfortunately, pain is not always of this "helpful" nature. In particular chronic pain lasting for months or years or a whole lifetime can lose its protective function, persist far beyond the removal of the primary insult that has generated it and become a "disease in itself". This is the type of pain that raises most of the concerns and interest of the scientific community at large, for the obvious implications in terms of difficult medical management and also personal and social direct and indirect costs (Breivik et al., 2006).

Epidemiological studies clearly show that **chronic pain is on the whole more common in women than in men**. Without underestimating the impact of typically female forms of acute pain - childbirth causes one of the most intense pains that a human being can experience - we should always remember that a number of common chronic pain conditions constitute more a women's than men's problem (Berkley and Holdcroft, 2005). Irritable Bowel Syndrome (IBS), for instance, with its recurrent crises of abdominal pain, can reach a prevalence of 23% in the general population, with two thirds of patients being women and with a female predominance also in greater symptom severity (Chang and Harris, 2007). Migraine has a prevalence of up to 25% in women vs 9% in men (Lipton and Bigal, 2005), while Temporomandibular Disorders (TMD), which reach a frequency of 10% in the general population, are twice as common in women than in men (Shinal and Fillingim, 2007). Osteoarthritis and chronic musculoskeletal pain disorders at large are also prevalent in women (Wijnhoven et al., 2006); in the latter group, Fibromyalgia Syndrome (FMS), a very disabling pain condition whose treatment is still a challenge for the medical community, is from 7 to 9 times more common in female than in male patients (Abeles et al., 2007). Not to mention recurrent/chronic pain conditions that are exclusive to the female sex, because linked to the area of the reproductive organs, such as dysmenorrhea - affecting over 50% of menstruating women -, painful endometriosis - present in up to 10% of women of childbearing age -, and chronic pelvic pain of gynecological origin, which accounts for up to 20% of consultations in gynaecology clinics (Collett et al., 1998; Proctor and Farquhar, 2006). Women are also much more frequently than men affected with multiple painful conditions at a time; there is a high level of co-morbidity, for instance, between FMS, IBS, Dysmenorrhea, Headache as well as Interstitial Cystitis - also called "painful bladder syndrome" (Caldarella et al., 2006; Parsons et al., 2007; Tietjen et al., 2007). Furthermore, when the co-existing pains originate from internal organs with partially overlapping innervation - such as the reproductive organs, gastrointestinal and urinary tracts - an enhancement of symptoms is frequently experienced, with more intense and longlasting pain as well as increased tenderness in affected areas, a phenomenon called "viscero-visceral hyperalgesia", in percentage much higher in female than male patients (Giamberardino, 2000a; Berkley, 2005).

In addition to epidemiology, another important aspect is that **women often report their pain symptoms differently from men**: awareness of these diversities is essential to avoid misdiagnosis. For example, chest pain from myocardial infarction tends to be atypical and more aspecific in women than in men (Lockyer, 2005; Albarran et al., 2007), with the atypical presentation resulting in delayed diagnosis, higher risk of complications and adverse prognosis (McSweeney et al., 2005; Jensen, 2007). As a general rule, pain expression in women is reported to be less predictive of a given disease than it is in men, with inevitable negative consequences on diagnosis and treatment. In contrast, pain in men tends to manifest with a somewhat more clear-cut profile, which is much more easily traced to a specific pathology (Giamberardino et al., 2000b).

As compared to men, **women** also have higher sensitivity to pain stimuli and **are subject to fluctuations of their pain symptoms in relation to their hormonal status**: pre-menopausal, post-menopausal, and during the different phases of the cycle in fertile years. Though the direction and extent of these fluctuations are reported to vary in the different studies, also depending on the type of pathologic pain entity considered, this hormonal-linked variability is a unique feature to take into account when dealing with women's pain (Hellstrom and Anderberg, 2003; Berkley, 2005; Aloisi and Bonifazi, 2006).

A further issue is that **the response to analgesic treatment is different in women compared to men**, which means that clinical trials devoted to test new drugs should specifically take into account the gender diversity and plan a systematic differentiated investigation in women and in men. Too often the results of trials conducted mostly in men are, instead, merely extrapolated to the women's population, with deceiving results (Fillingim and Gear, 2004; Fillingim and Ness, 2004; Graven-Nielsen and Arendt-Nielsen, 2007).

Another important aspect is that **the attitude of the Healthcare System and operators is often "negative" towards women patients in pain**. In many cases, female pain is underestimated simply because it is regarded as "normal" or "physiological", especially that originating from the reproductive area, since "if one is born a woman, one must put up with pain" (Reddish, 2006). In other circumstances, the underestimation is motivated by the conviction that mood disorders – anxiety/depression- are typical of the women and bring them to complain of pain more frequently than men, without plausible reasons. Again the example of Fibromyalgia Syndrome is demonstrative. Since this pain condition is not associated with any detectable organic alteration, but frequently co-exists with affective disturbance, and because it preferentially affects middle-aged women, it is often dismissed by physicians as "all in your mind", a psychological problem of women in this phase of life. Not surprisingly, FMS was referred to, fortunately in the past, as "Psychogenic Rheumatism" (Abeles et al., 2007).

All these elements/diversities together can explain why women's pain is too often underestimated and less accurately diagnosed and treated than in men. Since socio-cultural influences play a crucial role in a number of these diversities (Myers et al., 2003), the result is that the problem of **pain in women is often dealt with differently in different nations**.

EFIC is particularly attentive to diversities in European countries, as it feels that awareness of the national peculiarities is essential when trying to draw up common lines of political intervention in Europe aimed at increasing the well-being of women. It is with this purpose that EFIC has launched a campaign to collect information about the individual national status of women's pain throughout Europe. All chapters have been invited to submit reports on the "state of the art" of pain in women in their country, e.g., the most prevalent pain conditions, level of public/private assistance, difficulties specifically encountered in diagnosis and treatment. The collection of these reports is underway and EFIC will publish

the complete results in its website. We trust that this information will be of help to those in charge of raising awareness of the EU organizations responsible for healthcare and research funding in Europe.

Last, but certainly not least, pain in women also needs more research; **the reasons underlying differences in women's vs men's pain are multiple and complex**: in addition to the already mentioned socio-cultural influences, there are genetic, hormonal, as well as psychological factors (Fillingim, 2000; Myers et al., 2003; Bernardes et al., 2007; Buskila, 2007). Clinical and basic science studies in each of these areas are further needed to better understand the uniqueness of women's pain and consequently to better approach its management. EFIC is devoting a grant to research in the field, in this year: the grant is dedicated to former President of EFIC Professor David Niv, who so attentively looked after the needs of people in chronic pain in Europe.

The readers will find all details of EFIC initiatives in the website of the association.

We trust that a whole year devoted to female pain by the international community will strongly increase the degree of attention to this problem at all levels – individual, institutional, educational, political and scientific - an essential condition towards a better understanding and management of women's suffering.

## References

- Abeles AM, Pillinger MH, Solitar BM, Abeles M, Narrative Review: The Pathophysiology of Fibromyalgia, *Ann Int Med*, 146(2007)726-734.
- Albarran JW, Clarke BA, Crawford J, 'It was not chest pain really, I can't explain it!' An exploratory study on the nature of symptoms experienced by women during their myocardial infarction, *J Clin Nurs*, 16(2007)1292-1301.
- Aloisi AM, Bonifazi M, Sex hormones, central nervous system and pain. *Horm Behav*, 50(2006)1-7.
- Berkley KJ, A life of pelvic pain, *Physiol Behav*, 86(2005)272-280.
- Berkley KJ, Holdcroft A, Sex and gender differences in pain. In: SB McMahon, M Koltzenberg (Eds), *Wall and Melzack's Textbook of Pain* (5th ed.), Edinburgh, UK, Elsevier, 2005, pp 1181–1197.
- Bernardes SF, Keogh E, Lima ML, Bridging the gap between pain and gender research: A selective literature review, *Eur J Pain*, 2007 Oct 11 [Epub ahead of print].
- Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D, Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment, *Eur J Pain*, 10(2006)287-333.
- Buskila D, Genetics of chronic pain states, *Best Pract Res Clin Rheumatol*, 21(2007)535-547.

- Caldarella MP, Giamberardino MA, Sacco F, Affaitati G, Milano A, Lerza R, Balatsinou C, Laterza F, Pierdomenico SD, Cuccurullo F, Sensitivity disturbances in patients with irritable bowel syndrome and fibromyalgia, *Am J Gastroenterol*, 101(2006)2782-2789.
- Chang L, Harris L, Irritable Bowel Syndrome and Functional Abdominal Pain Syndromes: Clinical Features and Management. In: PJ Pasricha, WD Willis, GF Gebhart (Eds), *Chronic Abdominal and Visceral Pain*, Informa Healthcare, New York, London, 2007, pp 357-372.
- Collett BJ, Cordle CJ, Stewart CR, Jagger C, A comparative study of women with chronic pelvic pain, chronic nonpelvic pain and those with no history of pain attending general practitioners, *Br J Obstet Gynaecol*, 105(1998)87-92.
- Fillingim RB, Sex, gender, and pain: women and men really are different, *Curr Rev Pain*, 4(2000)24-30.
- Fillingim RB, Gear RW, Sex differences in opioid analgesia: clinical and experimental findings, *Eur J Pain*, 8(2004)413-425.
- Fillingim RB, Ness TJ, Sex-related hormonal influences on pain and analgesic responses, *Neurosci Biobehav Rev*, 24(2000)485-501.
- Giamberardino MA, Visceral Hyperalgesia. In: M Devor, MC Rowbotham, Z Wiesenfeld-Hallin (Eds), *Proc. 9<sup>th</sup> World Congress on Pain*, *Progr Pain Res Man*, Vol. 16, IASP Press, Seattle, 2000a, pp 523-550.
- Giamberardino MA, Sex-Related and Hormonal Modulation of Visceral Pain. In: RB Fillingim (Ed), *Sex, Gender, and Pain*, *Progr Pain Res Man*, Vol 17, IASP Press, Seattle, 2000b, pp 135-163.
- Graven-Nielsen T, Arendt-Nielsen L, Gender differences in response to pain, *Ugeskr Laeger*, 169(2007)2425-2427.
- Hellstrom B, Anderberg UM, Pain perception across the menstrual cycle phases in women with chronic pain, *Percept Mot Skills*, 96(2003)201-211.
- Jensen J, Gender differences in ischemic heart disease, *Ugeskr Laeger*, 169(2007) 2435-2437.
- Lipton RB, ME Bigal, Migraine: Epidemiology, Impact, and Risk Factors for Progression Headache, *J Head and Face Pain*, 45 (2005)3-13.
- Lockyer L, Women's interpretation of their coronary heart disease symptoms, *Eur J Cardiovasc Nurs*, 4(2005)29-35.
- McSweeney JC, Lefler LL, Crowder BF, What's wrong with me? Women's coronary heart disease diagnostic experiences, *Prog Cardiovasc Nurs*, 20(2005)48-57.
- Myers CD, Riley JL 3rd, Robinson ME, Psychosocial contributions to sex-correlated differences in pain, *Clin J Pain*, 19(2003)225-232.

- Parsons JK, Kurth K, Sant GR, Epidemiologic issues in interstitial cystitis, *Urology*, 69(2007)5-8.
- Proctor M, Farquhar C, Diagnosis and management of dysmenorrhoea, *BMJ*, 332(2006)1134-1138.
- Reddish S, Dysmenorrhea, *Aus Fam Physic*, 35(2006)842-849.
- Shinal RM, Fillingim RB, Overview of orofacial pain: epidemiology and gender differences in orofacial pain, *Dent Clin North Am*, 51(2007)1-18, v.
- Tietjen GE, Herial NA, Hardgrove J, Utley C, White L, Migraine comorbidity constellations, *Headache*, 47(2007)857-865.
- Wijnhoven HA, de Vet HC, Picavet HS, Prevalence of musculoskeletal disorders is systematically higher in women than in men, *Clin J Pain*, 22(2006)717-724.