The consensus terminology of persistent vulvar pain and vulvodynia

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INTRODUCTION
Vulvar pain is an enigma. Its etiology, pathophysiology and treatment have not yet been elucidated. This condition is presented with pain during intercourse. Around the enigma of vulvar pain, myths about its causes and treatments that have not been proved to be effective emerged. However, in 2015, an evidence based consensus terminology has been introduced (“2015 terminology”)1,2,3, with a clear definition and understanding of vulvar pain. Consequently, a new paradigm to the treatment of vulvar pain was developed making it etiology-based.

“VULVAR PAIN”, “VULVODYNIA” OR “DYSpareunia”?
For years, the International Society of Vulvovaginal Disease (ISSVD) discussed “vulvar pain”, but this is somewhat misleading. In fact, the most common and disturbing presenting symptom is introital pain during intercourse, i.e. superficial dyspareunia. Dyspareunia is one of the most common complaints associated with sexual dysfunction. Why has the ISSVD chosen to focus on “vulvar pain” and not on “Dyspareunia”? There are several reasons to this. One is an attempt of the ISSVD to broaden the terminology so that it involves pain in general and not only pain during intercourse. An additional reason may be to move away from the limited psycho-sexual connotation of dyspareunia that prevailed years ago.

THE 2015 TERMINOLOGY
The 2015 consensus terminology of “persistent vulvar pain and vulvodynia” (table 1) has been created by three international societies: the ISSVD, the International Society for The Study of Women’s Sexual Health (ISSWSH) and the International Pelvic Pain Society (IPPS). The new terminology was achieved in four steps. The first involved a terminology consensus conference with representatives of the three societies, held in April 2015. Then, an analysis of the relevant published studies was used to establish a level of evidence for each factor associated with vulvodynia. The terminology was amended based on feedback from members of the societies. Finally, each society’s board accepted the new terminology.

The final terminology was simultaneously published by three journals1,2,3.

CATEGORIES OF PERSISTENT VULVAR PAIN
The 2015 terminology divides ‘persistent vulvar pain’ into two categories: vulvar pain that is its cause is known, so that it is related to a specific disorder (e.g., inflammatory, neoplastic, infection-related, neurologic, traumatic, iatrogenic, and hormonal) and ‘vulvodynia’.

DEFINITION OF VULVODYNIA
The new definition of Vulvodynia is “vulvar pain of at least three months’ duration, without clear identifiable cause, which may have potential associated factors”.

DESCRIPTORS OF VULVODYNIA
The 2015 terminology further characterizes vulvodynia based on location (vestibulodynia, Cliterodynia, generalized, mixed), provocation (upon contact or spontaneous), temporal pattern (intermittent or constant), and onset (primary or secondary).

Of the various descriptors that are included in the 2015 terminology, the most important is its localization (localized or generalized) and relation to provocation (provoked and spontaneous) of vulvodynia. Generalized vulvodynia (formerly termed ‘essential’ or ‘dysesthetic’ vulvodynia affects the whole vulva and is usually spontaneous. It is regarded as a neuropathic pain and affects postmenopausal women mainly.

In addition, the onset of vulvodynia significantly matters to treatment outcome. LPV that has been present since the first attempt of vaginal penetration is termed primary. If LPV started after a period of pain-free intercourse it is named “secondary” LPV. Several researchers believe that primary LPV is difficult to treat than secondary.

The severity of LPV is determined by the patient’s level of pain during vaginal intercourse (dyspareunia), using the Marinoff criteria6: Level 1 – dyspareunia causes discomfort but does not prevent sexual intercourse; Level 2: dyspareunia sometimes prevents sexual intercourse; Level 3: dyspareunia completely prevents sexual intercourse. However, when intercourse is not practiced, a tampon insertion may be used to determine severity of LPV and evaluate the success of therapy.

The significance of determining severity of LPV is that the approach to treatment should be determined according to the severity of the condition, e.g. In level 1 cases, treatment should not involve surgery. In many cases there is deterioration of LPV severity with time, and LPV that was level 1 may become level 3. Less frequently, a level 3 LPV will spontaneously resolve or become a level 1 in severity. In other cases, treatment will reduce the level of sensitivity, rather than leading to a complete resolution of the pain.

FACTORS ASSOCIATED WITH VULVODYNIA
The most important innovation of the 2015 terminology is an appendix table (Table 2) with a list of potential associated factors (musculoskeletal, neuroproliferation, associated co-morbidities, psychosocial factors, etc) acknowledging that vulvodynia likely is not one disease, but several disease processes. Only few recognize the significance of that “appendix” to the consensus terminology, but these “potential associated factors” are helpful in identifying pos-
Global sensitization of nociceptive transmission.

Visceromotor responses to vaginal distension;

Activation of the hypothalamic pituitary adrenal (HPA)

Central nervous system processing;

posed:

Central nervous system involvement in vulvodynia

Neuroproliferation or hyperinnervation

An increase in the density of nerve endings in the vestibular endoderm of women with LPV as compared to controls has been repeatedly documented. These nerve endings have been shown to be nociceptors and have an increased density of the vanilloid receptor VR1. We have shown that the increased density of nerve fibers in women with LPV was 10 times greater than in non-affected women, and was associated with significant increase in the number of mast cells and degranulated mast cells within the vestibular stroma. We then demonstrated an increased subepithelial heparanase activity (degranulated from the aforementioned mast cells) in the vestibular mucosa. We further postulated that histamine, leukotrienes, and nerve growth factor – which are released from the degranulated mast cell – can cause nociceptor proliferation and sensitization. In addition, the heparanase, which can degrade the vestibular strroma, allows these activated and proliferating nociceptors to penetrate through the degraded basement membrane into the superficial mucosal epithelium of the vestibule. It has been theorized by many groups that certain genetic polymorphisms may predispose affected women with LPV to have an exaggerated inflammatory response or chronic infection, which leads to mast cell activation and subsequent nociceptor proliferation.

Central nervous system alterations as a cause of vulvodynia has been suspected. Several mechanisms have been proposed:

• Altered central nervous system processing;
• Activation of the hypothalamic pituitary adrenal (HPA) axis via chronic stress;
• Visceromotor responses to vaginal distension;
• Global sensitization of nociceptive transmission.

Central nervous system involvement in vulvodynia

Hormonal factors

A controversy exists as to whether combined oral hormonal contraceptives pills (HCP) play a role in the development of LPV. Against that association is that of the millions of women taking HCP, only a slight fraction suffers from LPV.

Indeed, three studies have failed to show an association between HCPs and vulvodynia. A case control study even showed that HCPs actually decreased the risk of vestibulodynia.

On the other hand, some women with LPV describe an improvement that with cessation of the HCP, and other studies depicted association of vestibulodynia with HCP and identified a polymorphism in the androgen receptor that significantly increased the risk of developing HCP-induced LPV in affected women.

With prolonged use of HCP, the net effect is progestogenic, so that the estrogen influence on the vestibule and vagina is reduced. This leads to diminished lubrication and decreased elasticity, causing increased friability and epithelial damage with vaginal intercourse. Later, allogynia and burning may occur.

Embryological/Congenital Factors

Vulvodynia is sometimes associated with painful bladder syndrome (interstitial cystitis) and pudendal hyperpessivity. This association dates back to the embryo development period; the vestibule develops from the urogenital sinus, which is contiguous with the allantois, which later differentiates to the urachus and the umbilicus.

Inflammatoy factors

Women with vulvodynia are more likely to have a history of allergic rashes. This may clarify the excess of mast cells, found in cases with LPV compared to controls. Mast cell produced tumor necrosis factor (TNF) which has been as-
Appendix: Potential factors associated with Vulvodynia

- Co-morbidities and other pain syndromes (e.g. painful bladder syndrome, fibromyalgia, irritable bowel syndrome, temporomandibular disorder) [Level of evidence 2]
- Genetics [Level of evidence 2]
- Hormonal factors (e.g. pharmacologically induced) [Level of evidence 2]
- Inflammation [Level of evidence 2]
- Musculoskeletal (e.g. pelvic muscle overactivity, myofascial, biomechanical) [Level of evidence 2]
- Neurologic mechanisms:
  - Central (spine, brain) [Level of evidence 2]
  - Peripheral – Neuroproliferation [Level of evidence 2]
- Psychosocial factors (e.g. mood, interpersonal, coping, role, sexual function) [Level of evidence 2]
- Structural defects (e.g. perineal descent) [Level of evidence 3]

* The factors are ranked by alphabetical order.

REFERENCES


CONCLUSION

The terminology of vulvar pain and vulvodynia was prepared by the ISSVD, ISSWSH, and IPPS. It acknowledges the complexity of the clinical presentation and pathophysiology involved in vulvar pain and vulvodynia, and incorporates data from evidence-based studies conducted during the last decade. The inclusion of factors associated with vulvodynia enables novel approach to research, diagnosis and treatment.