What are the characteristics of the inflammatory components of PVD? A systematic review.

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Provoked vestibulodynia (PVD) is characterised by pain at the vulval vestibule on touch and attempted entry to the vagina[1]. It was previously thought to be a purely inflammatory condition, originally bearing the name vulval vestibulitis. However, recent studies have revealed other pathological processes like nerve proliferation[2] and pelvic floor muscle dysfunction[3], prompting a change in name to one that does not implicate solely inflammation. Nevertheless, inflammation plays a major role in the development of PVD[4]. The nature of this role remains unclear, and the characteristics of the inflammatory process are poorly defined.

OBJECTIVE

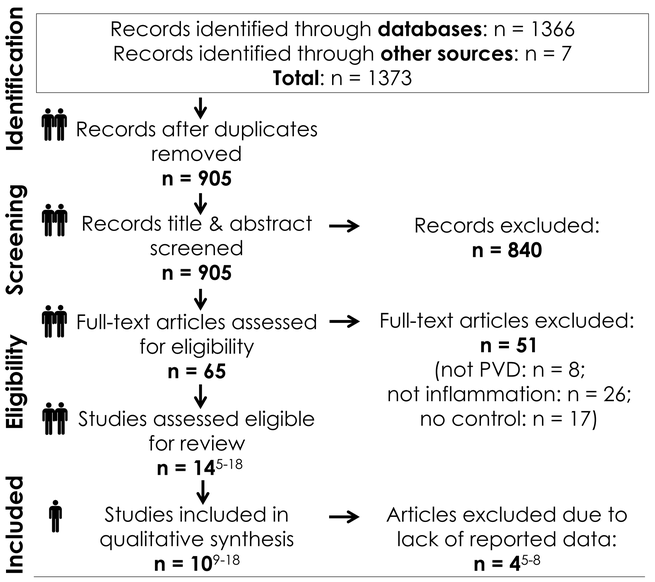
To synthesise and evaluate all available evidence investigating whether PVD is associated with a specific inflammatory profile at both a local and a systemic level.

METHODS

Comprehensive searches were conducted in nine electronic databases and reference lists from published reviews on PVD. Two independent investigators screened titles and abstracts, extracted data and evaluated risk of bias. Studies were sub-grouped according to whether the sample was sourced at the vulval vestibule or elsewhere.

RESULTS

14 articles were included. Full data were not available for four studies[5-8], so they were excluded. Ten studies that investigated inflammation in women with PVD in a quantitative[9-15,17] and/or a semi-quantitative[13,13,16-18] manner were included.



RISK OF BIAS ASSESSMENT

The methodological quality of included studies was assessed using a modified version of The Cochrane Collaboration's tool for assessing risk of bias. The quality of studies was generally low, and the design of studies was varied. Many aspects tested in the tool were not mentioned in the studies, leading to a high proportion of 'unclear' marks. Particularly, the blinding of those taking the samples and analysing the samples was not reported, and analyses of data were not entirely provided. The majority of studies did not assess participants for confounding diagnoses.

DATA SYNTHESIS

The inflammatory properties investigated across studies varied greatly. Table1 outlines the findings from the 10 studies included; studies that support an increase, decrease, or no difference in particular inflammatory properties are listed. Shaded boxes indicate the expected result of studies if PVD is a pro-inflammatory condition.

	PVD > CONTROLS	CONTROLS > PVD	NO DIFFERENCE
Blood samples			
IFNa			Gerber et al. (2009)
IFNϒ			Gerber et al. (2009)
NK Cells		Masterson et al. (1996)	
MHC			Masterson et al. (1996)
Tissue samples			
TNFa		Eva et al. (2007)	Foster & Hasday (1997)
IL-1β	Foster &Hasday (1997)		Eva et al. (2007) Foster & Hasday (1997)*
IL-1a		Eva et al. (2007)	Eva et al. (2007)^
Mast cell count	Goetsch et al. (2010) Bornstein et al. (2004) Chaim et al. (1996) Korcheva & Morgan (2008)		Halperin et al. (2005)
Non-specific inflammation	Goetsch et al. (2010) Bornstein et al. (2004) Korcheva & Morgan (2008)		Halperin et al. (2005) Slone et al. (1999)

^measured using different methods, therefore may appear conflicting
*measured in different areas, therefore may appear conflicting

The only systemic difference between controls and women with PVD were levels of Natural Killer (NK) Cells[10]. Interestingly, levels of NK Cells were lower in women with PVD. In local tissue samples, levels of TNFa and IL-1a were decreased[11] in women with PVD, suggesting an anti-inflammatory state in these women. Conversely, women with PVD expressed higher levels of local IL-1β[12]. It is important to note that these local findings were also negated by other studies which found no difference between women with PVD and healthy women. The majority of studies agree there is local mast cell proliferation[13-16] and non-specific inflammation[13,14,16]; however, most studies do not define 'non-specific inflammation', making it difficult to compare studies.

CONCLUSION

There is limited and contradictory evidence regarding the characteristics of the inflammatory profile in PVD. Studies varied greatly in design, methodology, and quality; most data were also reported semi-quantitatively, rendering meta-analysis impossible. Further rigorous, standardised studies are required in order to characterise and quantify the inflammatory profile in women with PVD.

Refs: [1] Freidrich (1987) *J Reprod Med*; [2] Westrom & Willen (1998) *Obstet Gynecol*; [3] Reissing et al. (2005) *J Psychosom Obst Gyn*; [4] Gerber, Witkin, & Stucki (2008) *J Med & Life*; [5] Foster et al. (2007) *Am J Obstet Gynecol*; [6] Tympanidis, Terenghi, & Dowd (2003) *Brit J Dermatol*; [7] Lundqvist et al. (1997) *Acta Derm-Venereol*; [8] Chadha et al. (1998) *In J Gynecol Pathol*; [9] Gerber et al. (2002) *Am J Obstet Gynecol*; [10] Masterson, Galask, & Ballas (1996) *J Reprod Med*; [11] Eva et al. (2007) *J Reprod Med*; [12] Foster &Hasday (1997) *Obstet Gynecol*; [13] Goetsch et al. (2010) *Am J Obstet Gynecol*; [14] Bornstein, Goldschmid, & Sabo (2004) *Gynecol Obstet Inves*; [15] Chaim et al. (1996) *Eur J Obstet Gyn R B*; [16] Korcheva & Morgan (2008) *USCAP*; [17] Halperin et al. (2005) *Gynecol Obstet Inves*; [18] Slone et al. (1999) *In J Gynecol Pathol*

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PVD = provoked vestibulodynia; IFN = interferon; NK = natural killer; MHC = major histocompatibility complex; TNF = tumor necrosis factor; IL = interleukin