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Increases in Psychological Stress Precede Flares of Rosacea: A Prospective Study

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Abstract

Objective: Psychological stress is thought to exacerbate symptoms of rosacea. However, this view is based largely on cross-sectional surveys and retrospective clinical reports. Thus, the aim of this study was to determine prospectively whether psychological stress precedes increases in symptom severity in patients with rosacea.

Method: Twelve women and four men aged between 35 and 70 years who had been diagnosed with rosacea by a general practitioner or dermatologist filled out a rosacea symptom checklist and rated psychological stress daily for up to two months (mean ± SD, 59 ± 14 days). Each day, they recorded the presence of papules and pustules and rated the average intensity of facial redness, stinging or burning, and psychological stress between 0 ("none") and 10 ("extreme").

Results: In 12 of the 16 patients, higher levels of stress were associated with more severe symptoms. This association was similar in summer and winter, and in medicated and un-medicated patients. In the group as a whole, stress ratings increased the day before facial flushing increased, and remained high when symptoms were severe. In addition, stress ratings were higher when stinging was severe than when stinging was mild.

Conclusion: These findings support the view that psychological stress exacerbates symptoms of rosacea. Further studies are required to determine whether a surge of cutaneous blood flow associated with stress-linked flushing aggravates inflammation in vulnerable facial vessels, or whether stress hormones such as corticotropin releasing factor activate cutaneous mast cells which, in turn, release vasoactive and pro-inflammatory mediators into the skin. Neurogenic inflammation (characterized by stinging pain) might further intensify the inflammatory process when symptoms are severe, so that symptoms and distress escalate in a vicious circle. If so, psychological treatments such as cognitive-behavioural therapy might not only help to alleviate symptom-related distress but could also decrease the frequency and/or intensity of rosacea flares.

Keywords: Rosacea; Psychological stress; Symptom severity; Facial flushing; Facial stinging; Papules and pustules; Prospective study

Introduction

Rosacea results from an inflammatory disorder that provokes persistent flushing and stinging of the cheeks, nose, chin or forehead. The flushing is often associated with acne-like facial papules or pustules, prominent facial capillaries, swollen sebaceous glands, skin thickening and ocular discomfort [1-4].

Symptoms appear to be aggravated by a wide spectrum of factors (e.g., alcohol and hot beverages, irritants such as soaps and creams, physical activity, extremes of heat or cold, strong winds or sunlight) [5,6], possibly due to an inflammatory response that triggers an increase in blood flow through vulnerable facial vessels [7]. Psychological stress may also evoke flares of rosacea, but this belief is founded on cross-sectional surveys and retrospective clinical reports that could be influenced by expectancy effects and/or recall biases [6,8]. In a recent population-based case-control study, having an affective disorder did not increase the risk of developing rosacea in subsequent years [9]. Furthermore, in a cross-sectional study that compared patients with rosacea or psoriasis to healthy controls, rosacea was not associated with personality traits that increased vulnerability to stress [10].

Nevertheless, psychological stress might exacerbate symptoms of rosacea in the short-term [8]. To explore this, we examined the association between symptoms of rosacea and psychological stress, tracked daily for 1-2 months. It was hypothesized that increases in psychological stress would precede increases in symptom severity.

Methods

Participants

Twelve women and four men aged between 35 and 70 years who had been diagnosed with rosacea by a general practitioner or dermatologist were recruited via community newspaper advertisements, dermatology practices, radio interviews, an internet forum for rosacea sufferers and university classes.

Procedures

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the

1964 Helsinki declaration and its later amendments. Each participant provided their informed consent for the procedures, which were approved by the University Human Research Ethics Committee.

Participants recorded symptoms daily for up to 67 days in a structured diary developed by the authors. At four weeks, participants were reminded to return completed forms and to continue to fill out the diary. Each day, they were asked to record the presence of papules and pustules and the average intensity of stinging or burning and facial redness (i.e., flushing) by circling a number between 0 and 10 on numerical rating scales where 0 corresponded to "none", 1-4 to grades of "mild", 5-8 to grades of "moderate", and 9-10 to "extreme". To standardize ratings of facial redness, photographs illustrating no facial redness, and mild, moderate and extreme redness were included in the diary. Participants were also asked to rate the average level of stress they had experienced that day between 0 (none) and 10 (extreme) on a numerical rating scale using the descriptors listed above. Missing entries (less than 1% of the entire data set) were replaced by the mean of values recorded on the day before and the day after the missing entry.

Statistical approach

First, the association between stress and symptom ratings was investigated with Spearman's rank-order correlation coefficient for each participant. Next, to determine whether increases in psychological stress preceded increases in symptom severity, the median intensity of each symptom was identified for each participant. Mean scores for psychological stress were then calculated for: (i) days when the symptom score fell below the median symptom intensity, excluding the "prodrome" (i.e., the day before the increase in symptom severity); (ii) the "prodrome"; (iii) the first day that the symptom was severe; and (iv) the remainder of days when the symptom was severe. To ensure that these scores were representative, ratings on four or more days were required for each category. Differences in stress ratings across the four categories were investigated using Friedman's two-way analysis of variance by ranks for related samples. If the main effect was statistically significant, the "prodrome" was compared with each other category in planned contrasts, to determine whether increases in stress preceded increases in symptom severity. The criterion of statistical significance was $p<0.05$. Except where otherwise indicated, results are reported as the mean ± standard deviation.

Results

The diary was filled out for 59 ± 14 days (range 32 to 67 days) (Table 1). Flushing was reported on 90 ± 16% of days, stinging on 76 ± 7% of days, and papules and pustules on 50 ± 12% of days.

	Duration of rosacea	Recording period	Days with Symptoms (%)			Symptom Intensity on Days with Symptoms (± S.D.)			Association with stress (Spearman's rho)[4]		
Sex, Age	(years)	(days)	Flushing	Stinging	P/P	Flushing	Stinging	P/P	Flushing	Stinging	P/P
F, 37	10	67[2]	84	60	10	2.7 ± 1.0	2.6 ± 1.5	1.7 ± 0.8	**0.31**	**0.31**	0.09
F, 53	2	32[2]	100	44	0	1.4 ± 0.5	1.2 ± 0.6	-	**0.45**	**0.47**	
F, 38	2	67[2]	100	57	75	6.3 ± 1.2	2.8 ± 1.1	2.4 ± 1.7	0.13	-.01	0.06
F, 51	15	67[2]	76	52	19	4.2 ± 1.3	3.2 ± 1.0	3.5 ± 1.3	**0.38**	**0.29**	-.03
F, 43	13[1]	67[2]	100	79	100	5.2 ± 1.1	3.7 ± 1.7	4.8 ± 1.4	-.09	-.27	0.10
M, 69	6[1]	65[2]	70	11	5	4.0 ± 1.7	2.0 ± 0.6	1.0 ± 0	**0.26**	-.03	-.03
M, 69	1[1]	32[2]	100	88	100	3.7 ± 2.1	2.7 ± 1.7	3.4 ± 2.0	**0.74**	**0.58**	**0.67**
F, 37	6[1]	67[2]	100	93	99	5.5 ± 0.8	2.9 ± 1.1	4.6 ± 1.3	**0.26**	-.20	**0.50**
F, 38	10	66[3]	100	100	0	5.6 ± 1.3	4.7 ± 1.1	-	**0.27**	0.24	
F, 56	16	67[3]	43	42	12	2.3 ± 0.8	1.6 ± 0.8	1.1 ± 0.4	**0.76**	**0.74**	**0.40**
F, 68	1	67[3]	88	99	0	3.4 ± 1.1	4.8 ± 1.5	-	**0.48**	**0.43**	
F, 44	2	67[3]	100	100	100	1.5 ± 0.7	1.3 ± 0.7	1.4 ± 0.8	-.20	-.04	-.17
M, 70	1[1]	40[3]	100	100	93	1.7 ± 0.8	1.5 ± 0.7	1.6 ± 0.8	**0.37**	**0.35**	0.22
F, 35	8[1]	67[3]	84	84	81	2.9 ± 1.1	3.0 ± 1.2	3.0 ± 1.0	**0.57**	**0.58**	**0.48**
F, 58	8[1]	35[3]	97	100	100	2.9 ± 0.7	2.4 ± 0.7	2.6 ± 1.1	**-.35**	-.10	0.12
M, 68	2[1]	67[3]	100	100	0	2.1 ± 0.6	2.4 ± 0.6	-	**0.56**	**0.53**	

Table 1: Association between the intensity of rosacea symptoms and psychological stress for each of the 16 participants (P/P: papules and/or pustules. [1]Currently being treated with antibiotics and/or topical agents. [2]Symptoms recorded during summer. [3]Symptoms recorded during winter. [4]Spearman's rho was statistically significant for numbers highlighted in bold ($p<0.05$)).

Eight of the 16 participants filled out the diary during Australian summer months (January to March) and the other eight during Australian winter months (June to August). Symptoms and stress ratings were similar in both of these groups.

Half of the participants used antibiotics and/or topical medications to treat their symptoms. When averaged over the entire recording period, intensity ratings for papules and pustules were greater in medicated than un-medicated participants (2.4 ± 1.8 *versus* 0.5 ± 0.7 on the 0-10 scale of symptom intensity, Mann-Whitney U test, p=0.038), suggesting that drug treatment did not fully suppress symptoms when medication was required. However, all other ratings were similar in the medicated and un-medicated groups.

Stress ratings were associated directly with symptom severity in 12 of 16 participants (Table 1). These associations were similar during summer and winter and in medicated and un-medicated patients, and were unrelated to age, sex or the duration of rosacea.

Psychological stress increased significantly the day before flushing intensified (the "prodrome" in Figure 1) and remained high when flushing was severe (difference across the four categories, Friedman's test, p=0.002). In addition, stress ratings were greater on days when stinging was severe than when stinging was mild (Friedman's test, p=0.024) (Figure 1). A similar trend for papules and pustules did not achieve statistical significance.

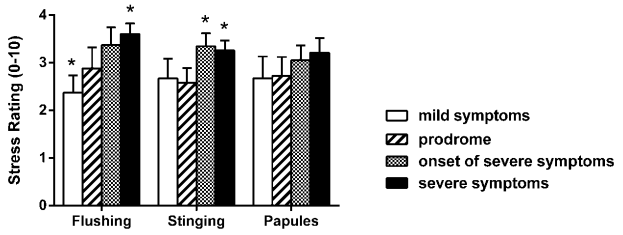

Figure 1: Changes in psychological stress (± standard error) associated with increases in the intensity of flushing, stinging or papules and pustules. * Significantly different from the "prodrome" (Wilcoxon's matched-paired signed-ranks test, $p \leq 0.05$).

Discussion

In early cross-sectional studies of patients with rosacea, patients testified that excitement or worry brought on hot flushes, and reported that emotional stress intensified the severity of rosacea symptoms [11,12]. Similarly, in our prospective study, symptoms of rosacea were associated with psychological stress in the majority of patients. In addition, stress ratings increased the day before an increase in facial flushing, and increases in stress coincided with the onset of severe bouts of stinging. Together, the findings suggest an association between emotional distress and symptoms of rosacea.

Active sympathetic vasodilatation drives increases in facial blood flow during physical and psychological stress [13]. This response begins sooner and is associated with greater increases in sympathetic activity in the supraorbital nerve of rosacea sufferers than controls [14]. Skin biopsies from patients with rosacea are characterized by signs of marked vasodilatation, dermal lymphatic failure, inflammatory cell infiltrate, and mast cell and fibroblast accumulation [7,15]. Hence, sun exposure or some other physical trigger, together with impairment of the innate immune system [16,17], might damage lymphatic drainage vessels and, in turn, trigger papule formation and the growth of aberrant cutaneous blood vessels [7]. Under these conditions, a surge of cutaneous blood flow associated with stress-linked flushing could intensify inflammation in these vulnerable vessels. In addition, stress hormones such as corticotropin releasing factor might activate cutaneous mast cells which, in turn, release vasoactive and pro-inflammatory mediators into the skin [18]. Neurogenic inflammation (characterized by stinging pain) could further exacerbate the inflammatory process when symptoms are severe [19,7].

Once the flare is underway, symptoms and distress may escalate in a vicious circle [8,6,20]. This reciprocal relationship could account for moderate to strong associations between psychological stress and symptom severity in the majority of our patients. The association was stronger for flushing and stinging than for papules and pustules, possibly because papules and pustules generally were rated as mild or non-existent.

Several caveats apply to our findings. In particular, patients who believed that their disorder was exacerbated by stress might have been over-represented, because participants were self-selected. Our sample was small and heterogeneous in terms of age, duration of rosacea and types of treatment. We could find no clear relationship between the patients' demographic characteristics or medication status and the association between stress and symptom ratings (Table 1). In addition, the association was similar in patients studied during summer and winter. Nevertheless, it is possible that anti-inflammatory agents masked this association in some cases. To encourage participation, ratings of symptom severity and stress were based on individual items rather than validated scales. Thus, stress ratings might not have covered the full domain of the construct being measured; even so, rating a single item is useful in clinical practice to detect clinically significant distress [21]. Finally, "third variable" effects might have influenced both psychological distress and symptom ratings.

Controlled experimental trials are now required to investigate the link identified here between psychological stress and rosacea flares. If this link is confirmed, psychological treatments such as cognitive-behavioural therapy might not only help to alleviate symptom-related distress [20-23] but could also decrease the frequency and/or intensity of episodes of rosacea.

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