REVIEW

doi: 10.5455/medarh.2018.72.362-366
MED ARCH. 2018 OCT; 72(5): 362-366
RECEIVED: AUG 10, 2018 | ACCEPTED: SEP 25, 2018

The Impact of Stress on Pressure Ulcer Wound Healing Process and on the Psychophysiological Environment of the Individual Suffering from them

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ABSTRACT

Introduction: The occurrence of a pressure ulcer constitutes a major psychological and physiological burden and it has been linked with a reduced quality of life and increased stress of the individual. **Objective:** The main objective was to investigate the impact that stress has on pressure ulcer healing process and on the psychophysiological environment of the individual suffering from them. **Method:** The scientific literature was reviewed through Cinahl, Pub-med, EBSCO, Medline and Google scholar. The articles were chosen due to their direct correlation with the objective under study and their scientific relevance. **Results:** Increased stress has been demonstrated to increase the glucocorticoids levels affecting negatively the production of wound healing cytokines (IL1α, IL1β and TNFα). Matrix metalloproteases has been identified to be unregulated in occasions of increased stress in acute wounds. Stress has also been correlated with poor health behaviors that may not have a direct link on the wound healing process, although they can in part explain or enhance some of the effects of stress on wound healing. **Conclusion:** The correlation between stress and wound healing in acute wounds has been thoroughly investigated and its negative effects have been established. The presence of a pressure ulcer can have a detrimental impact on the stress level of an individual although further investigation is needed to establish the role of stress in chronic wounds such as pressure ulcers.

Keywords: stress, anxiety, pressure ulcer, pressure sores, wound healing.

1. INTRODUCTION

According to the most recent estimation the prevalence of Pressure Ulcer (PU) worldwide is 0%-72, 5% (1). PU are thought to be one of the most common and frequent issues in the elderly, immobile or individuals with serious comorbidities (1, 2, 3).

EPUAP and NPUAP (1) define PU as: Localized injury to the skin and/or underlying tissue usually over a bony prominence as a result to pressure, or pressure in combination with shear. A number of contributing factors are also associate with PUs, the significance of this factors is yet to be elucidated.

The occurrence of a PU constitutes as a major psychological and physiological burden and it has been linked with a reduced quality of life and increased stress (4, 5).

Stress can be determined as an unpleasant feeling that can be acute or chronic, having psychological and physiological effects (6). Stress occurs after a stressor appears in an individual's environment, the individuals response to the stressor lays on the appraisal of the situation, coping behavior and the resources available (6, 7). When the individual cannot adequately cope with the demands made on them, psychological, biological and behavioral changes occur (8, 9).

Stress and wound healing has been found to have a strong negative correlation. A systematic review conducted by Walburn et al. (10) found that out of 22 papers reviewed 17 showed that stress had a negative impact on WH. Individuals suffering from PU come face to face with a number of stressors such as pain (11) ulcer odour, restriction of daily activities, body image disturbances and social isolation (12). This results in an increase in stress levels to the degree potentially causing serious disturbance's to their psycho-physiological environment (13). This

assignment will focus on the mechanism and theories of stress and its physiological effects on the process of wound healing in patients with PU.

2. AIM

The aim of the review was to investigate the effect that stress has on the pressure ulcer healing process and on the psychophysiological environment of the individual.

3. METHODS

The scientific literature was reviewed between March 2017 and April 2017 through the databases Cinahl, Pubmed, EBSCO, Medline and Google scholar. The key words used were stress OR anxiety AND pressure ulcer OR pressure sores AND wound healing, 51 scientific articles where identified**.** The inclusion criteria for the articles where the existence of full text the direct correlation with the objective under study and their scientific credibility (peer review articles).

4. FINDINGS

Stress mechanism of action

For many years it has been known that stress has a negative effect of health (6). Selye (14) defined stress as a nonspecific adapting response of the body towards a threating situation. The response was described in three stages alarm, resistance and exhaustion (14). This definition was modified in 1992 by Chrousos and Gold, the term nonspecific was replaced by the hypothesis that every stressor exceeding a certain limit can cause the release of different stress hormones (2). Stress of different magnitude, time and type can initiate the adaptation response of the organism towards stress by triggering two pathways (15).

When a stressor is applied from the environment on an individual the organism sets in motion two different pathways in its effort to maintain equilibrium (7). The first mechanism is the Sympathomedulary (SAM) pathway, which begins its action by secreting catecholamines, norepinephrine and epinephrine resulting in increased blood flow to the muscles, pupil's dilation and metabolism increase, preparing the individual for the response known as fight or flight (7). SAM activation can be attributed to different stressful situation for example a speech test or lower marriage satisfaction has been found to increase epinephrine and norepinephrine secretion (16,17).

Activation of the second pathway (Hypothalamic-Pituitary-Adrenal) causes the secretion of corticotrophin, which releases hormones from the hypothalamus. The hormones stimulate the release of adrenocorticotropic (ACTH) from the anterior pituitary gland, resulting in the secretion of glucocorticoids from the adrenal gland (7). Physiological levels of cortisone are thought to be immunomodulatory and in excess levels immunosuppressive (6). A number of stressors in different situations can set in motion the HPA pathway. For example, examination stress in medical students has been showed to increase the ACTH and cortisol levels in fall semester where the examination period took place but not during the Spring break period. This suggests a difference in the activation of HPA axis between seasons and situations (18).

Extreme exercise has been found also to increase ACTH and cortisol levels in triathlon athletes of all ages (19). Aging does not seem to be a contributing factor affecting the HPA stress response (19). Marital stress (acute or chronic) also can increase ACTH and cortisol levels and has been linked with the HPA pathway (20).

Effects of stress

PU can range from superficial skin injury on stage I, to full thickness tissue loss stage IV (21). The healing process of the PU follows a three stage process: inflammation, epithelization and remodelling although varies of the stage that the PU has developed (22). In PU stage I and II, the regeneration mechanism is triggered and for stage III and IV, the PU are healed through scar formation and contraction (23). In addition the PU healing process can follow a different pathway if they become chronic. The chronic state can be described as an abnormality and is developed only after a disruption in molecular level occurs by an extrinsic or intrinsic factor. This affects the physiology of the wound, resulting in elevated levels of MMPs, GF and cytokines (24, 25). It has been proposed that stress, chronic or acute and in different situations can impair the healing procedure in humans and animals through interruption of the regulation of the wound healing cascade (15, 26, 27).

Glucocorticoids are a product of the activation of the Hypothalamic-Pituitary-Adrenal (HPA) axis, as a response to stress. This has been associated in both human and animal with impaired WH through the suppression of the immune system (28, 29). A study conducted by Detillion et al. (29) demonstrated that social isolation expressed by immobility increased cortisol levels and slowed the WH process in mice compared to socially housed group. The removal of the factor cortisol through an adrenectomy, and the treatment of the experimental group with oxytocin (a hormone released as a result to social contact) resulted in normal WH rates with normal expression of cytokines levels (29). Another study that used normally bred mice as the control group and pharmacological glucocorticoid treated mice as the intervention group, to study the effects of glucocorticoid on WH cytokines, has demonstrated significantly reduced levels of IL1α, IL1β and TNFα in the glucocorticoid treated group (30). Stress induced levels of glucocorticoids through exercise in humans participants was found to affect IL1β and TNFα but not IL6 production (28).

A strong relationship has been observed between stress and the suppression of cytokines by glucocorticoids in both humans and animals studies (31, 32). PU cannot heal if the inflammation phase is not initiated in the absence of cytokines. Cytokines help the prevention of infection, prepare damaged tissue for repair and enhance the recruitment of phagocytosis cells (31). In addition if the ability of fibroblasts and epithelia cells to remodel destroyed tissue is impaired by the depletion of cytokines, this will lead to the stagnation of the PU in the inflammatory phase (31).

Stress and the effects on Matrix Metalloproteases (MMPs) have also been examined. MMPs are a group of enzymes activated in response to TNFa, they clear debris, enable cell migration through the extracellular matrix and aid to the contraction and remodeling of the scar (33). In a group of patients undergoing an inguinal hernia repair, wound fluid was collected over the first 20-hour postoperative period to assess WH through the presence of IL1, IL6 and MMPs, stress was also measured via a pre-operative questionnaire. The results showed that greater preoperative stress correlated with lower MMP-9 levels (34). In a human study using a blister chamber wound model, the authors found a negative correlation between MMPs and cortisol levels. Stress was measured using a questionnaire and cortisol levels using blood plasma samples. The authors of the study suggested that a link reaction exist between Stress, HPA axis–glucocorticoids secretion, cytokines and MMPs activation (35).

MMPs are crucial components of the PU WH process and unregulated levels of MMPs can lead to the degradation of the ECM. As a result, the healing process may be compromised, which may cause the wound to become chronic (24). The increased stress that individuals suffer from PU is well documented in the literature, and as it was proposed, increased stress may lead to increased level of MMPs. This may not be the case in chronic wounds as raised MMPs levels are a common phenomenon especially in PU (25,36). Research focusing on the effects of stress on raised MMPs levels in chronic wounds will aid to clarify if the same mechanism of action exists as it was proposed for acute wounds or normally healing wounds.

Stress has also been correlated with poor health behaviors that may not have a direct link on the wound healing process, although they can in part explain or enhance some of the effects of stress on WH (37). Sleep is one important factor that's been found to be affected by excess stress levels (38, 39). Women that were kept awake for a forty-eight hour period had significant dysregulations of the circulating cytokines number and delayed skin barrier recovery after tape striping (40). In addition disrupted sleep patterns has been associated with reduced levels of GH (41). GH is mainly produced by the organism during sleep and has the ability to stimulate monocyte migration, enhance macrophage activation and amplify bacterial cleansing (15, 42). The assumption can be made that if increased stress exists in patients with PU and stress levels affect sleep patterns, then GH and cytokines regulation may be deregulated, affecting the healing process.

Another important health behaviour that seems to be affected by increased stress levels is the nutritional intake (43). PU healing is highly dependent on the individuals nutritional status, Vitamins A, C, E, zinc, protein and fatty acids are all essential factors of the healing process (44). In a phenomenological study by Beitz and Goldberg (45) it is reported that a differentiation exists between the opinions of the participants for example, some felt that their appetite was unchanged and others that had deteriorated. Negative mood has also been associated with increased food intake and consummation of 'comfort food' (43). Further research on the effects of stress on nutritional intake and eating behavior is needed as a systematic examination could help to clarify the relationship between this factor and WH (43).

Stressors and pressure ulcers

PU have a significant impact on the quality of life and on the psychophysiological environment of the individual suffering from them (4). Individuals suffering from PU were found to have lower scores on the HRQoL tool, suggesting that the presence of an ulcer lead to a poorer quality of life (4). Clark (46) proposed that this is due to factors such as pain, social exclusion, malodour, reduced mobility and alternations in body image.

Pain has been reported in a number of studies as a significant issue for individuals with PU. In a qualitative study by Fox (47), pain was described by the majority of the participants as an overwhelming feature of living with a PU. In the same study it was reported that pain had an impact on their sleep and on other aspects of their daily lives (47). Pain and immobility has also been reported to have a strong lead in a study by Hopkins et al. (12) . Participants reported that PU caused more pain when they were trying to mobilise than when they were immobile, and preferred to stay as still as possible to limit the effects of pain (12).

PU are open wounds that disrupt the continuum of the skin causing alteration to its normal morphology (47). Harding-Okimoto (48) described that the individuals that she interviewed suffering from PU had negative body image perception. In a study investigating the effects of PU on the quality of life, female participants reported that the presence of the wound made them lose their femininity, in contrast the male participants did not report any issues (47).Generally, women are more likely to report body alternation as significant burden than men (49). This mainly can be attributed to the fact that women are more likely to report psychological issues and symptoms than men (50).

Increased exudate and odour was found to have a significant impact on the lives of people suffering from PU (51). Patients described the smell of the ulcer as the worst part and that the heavy leakage that sometimes came out of the dressings was restricting them from socializing and made them feeling embarrassed (12, 47).

As discussed, the negative impact of PU include a lack of socialization of the individual and their ability to undertake daily activities, the exudate and the odour of the PU and the feeling of pain when moving. Overall this can lead to increased anxiety, fatigue and distress, having a detrimental effect on the psychological wellbeing of the individual (11).

5. CONCLUSION

PU have a significant impact on the psycho-physiological environment of the individual resulting in increased anxiety and stress levels. This is mainly attributed to factors such as pain, social exclusion, malodour, reduced mobility and body image alternation

It has been proposed that stress, chronic or acute, can impair the healing process through the interruption of the regulation of the WH cascade, mainly by the activa-

tion of the HPA axis and the effect on the immune system. In addition it has been proposed that stress has an influence on negative health behaviours, such as sleep and nutrition, which have a pivotal role in the WH process

The effect of stress on the WH process is widely investigated and has turned the interest of the scientists away from what stress can cause, to how the eradication of stress and its effects, through coping mechanism, can improve WH outcomes. On the contrary, the field of the effect of stress in chronic wounds is an unmapped area and further research needs to be conducted to investigate if a link exists and if the same mechanism applies as acute wounds and stress.

- **Authors' contributions:** C.C, A.V, A.K, S.E, S.P, F.A, M.P, Z.P gave substantial contributions to the conception or design of the work in acquisition, analysis, or interpretation of data for the work. Each author had a part in article preparing for drafting or revising it critically for important intellectual content, and all authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **Conflicts of interest:** There are no conflicts of interest.
- **Financial support and sponsorship:** None.

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