Itch in Patients with Acute Heart Failure

Małgorzata PONIKOWSKA[1], Jan BIEGUS[2,3], Robert ZYMLINSKI[2,3] and Jacek C. SZEPIETOWSKI[1]
[1]Department of Dermatology, Venereology and Allergology, and [2]Department of Heart Diseases Wrocław Medical University, ul. T. Chałubińskiego 1, PL-50-368 Wrocław, and [3]Department of Cardiology, Centre for Heart Disease, 4th Military Hospital, Wroclaw, Poland. E-mail: gosiaponikowska@gmail.com
Accepted Apr 2, 2019; E-published Apr 2, 2019

Itch is a common and distressing symptom occurring not only in dermatological conditions but also in chronic systemic diseases (1). In heart failure (HF) – which is a complex clinical syndrome – underlying pathophysiologies, course of the disease, coexisting comorbidities and medications – all tend to predispose patients to developing itch (2–5). Only a few studies investigated the occurrence of itch in HF, reporting a wide prevalence ranging from 10–40% (2–5). However, these studies used inconsistent definitions and different tools for itch evaluation, and included heterogeneous HF populations (2–5). Therefore, we set-up the prospective study among patients with acute HF, using standardized methods for itch assessment in order to investigate the prevalence of itch and explore the potential underlying causes.

METHODS

Study population

The study population consisted of patients hospitalized with a diagnosis of acute HF (Heart Failure, as assessed by NYHA class III and IV on admission), prospectively included into the registry that runs in our institution. Inclusion criteria were: age ≥18 years; acute HF as the primary cause for hospitalization (6); patient's written agreement to participate. Exclusion criteria for this analysis included: mental status changes preventing the patient from performing a detailed assessment of itch (see below); known severe renal or liver disease; history of chronic dermatological disease. After inclusion, detailed information on demographics, clinical history, comorbidities, previous therapies and physical findings was recorded. Standard laboratory assessment was performed using methods applied in our laboratory. The local ethics committee approved the protocol (consent No KB-406/2015) and all subjects gave written informed consent.

Evaluation of itch

Itch assessment was performed in all patients once they were clinically stable and before hospital discharge using the following instruments: the visual analogue scale (VAS), numerical rating scale (NRS), and the 4-item Itch Questionnaire (7–10). Patients were asked to assess itch during the last 3 days. Various clinical features of itch, including exact location, quality and descriptors and the most common factors responsible for its aggravation or alleviation, were assessed (10). Dermatology Life Quality Index (DLQI) was applied to assess the impairment in quality of life, related to itch (11).

Statistical analysis

Continuous variables with a normal distribution were presented as means ± standard deviation (SD), variables with skewed distribution as medians with upper/lower quartiles, categorized variables as numbers and percentages. The statistical significance of the differences between groups was assessed using: *t*-test, Mann-Whitney *U*-test or Chi^2 test, where appropriate. The associations between variables were tested using univariable and multivariable logistic regression models. The $p<0.05$ was considered statistically significant. Statistical analyses were performed using the STATISTICA 12 (StatSoft, Inc, Tulsa, OK. 74104, USA).

RESULTS

Of 84 patients enrolled, 63 (75%) were men, with the mean age of 66 ± 13 years. Baseline clinical and laboratory characteristics of the study population are presented in Table SI[1].

Fourteen patients reported history of itch (prevalence 17%): in 11 patients (79%) itch occurred during the last 3 days, whereas 3 (21%) reported a history of itch before the current hospital admission. We found the following characteristics in patients reporting itch: more severe HF symptoms on admission, need for inotropic drugs during the hospital stay, more frequent use of the novel oral anticoagulants before admission, higher serum bilirubin level ($p<0.05$ in all comparisons) (Table SI[1]).

Characteristic of itch

In the majority ($n=10$, 71%) of patients itch was limited to a certain skin area, mostly lower and upper limbs ($n=7$, 50%). Four (29%) patients reported itch of the lower legs and feet, which coincided with bilateral oedema. Six patients (43%) experienced itch on a daily basis, 7 (50%) reported it as appearing a few times per week, 1 (7%) few times per month. Most frequently patients described itch-related sensations as tingling ($n=7$, 50%), tweaking ($n=4$, 29%), burning ($n=3$, 21%) or stinging ($n=2$, 14%). Itch was reported as being predominantly annoying ($n=9$, 64%) or burdensome ($n=7$, 50%). Itch was responsible for problems with falling asleep in 6 (43%) patients (none reported use of hypnotics). We did not observe any specific factors responsible for either aggravation or alleviation of itch: only 2 (14%) patients linked itch exacerbation with sweating and hot water; 3 (21%) its alleviation with cold water. None of the patients have ever received any specific therapy for this symptom.

The mean ± SD severity of itch measured with VAS was 4.4 ± 2.8 points (mild–moderate in 10 (71%), severe

[1]https://doi.org/10.2340/00015555-3187

doi: 10.2340/00015555-3187
Acta Derm Venereol 2019; 99: 679–680

in 4 (29%) patients). Using NRS the mean ± SD severity of itch was 4.2 ± 2.9 points (mild–moderate in all). Using 4-item Itch Questionnaire, mean ± SD severity of itch was 8.6 ± 3.6 points. Itch severity evaluated with NRS and VAS was perfectly interrelated ($r = 0.99$, $p < 0.0001$), but did not correlate with severity assessed with the 4-item Itch Questionnaire ($p > 0.05$ for both correlations). An impairment in the quality of life related to itch, assessed with DLQI, revealed the mean ± SD of 3.4 ± 1.5 points.

Treatment with angiotensin converting enzyme (ACE) inhibitor was related to the higher values of NRS and VAS ($p < 0.05$) and that 4-item Itch Questionnaire scores was inversely related to NYHA class on admission (those with NYHA class III had higher values vs NYHA class IV). All others correlations were not significant.

DISCUSSION

These are the new findings of our study: itch was a moderately common symptom reported by patients with acute HF (prevalence of 17% in our population); those who reported itch had more severe HF symptoms on admission, worse in-hospital course, higher bilirubin level and more frequent use of novel oral anticoagulants; itch was of mild–moderate intensity, limited to certain skin areas; there were no consistent factors responsible for alleviation/aggravation of this sensation.

To the best our knowledge, this is the first prospective study, investigating specifically the prevalence of itch among patients with acute HF, in whom we obtained detailed characteristics and applied a comprehensive, validated methodology to characterize itch. The prevalence of itch in our population is lower than that recently reported by other authors (2–5), however, they all studied patients with stable chronic HF, and either did not specifically study itch but rather symptom-burden in HF (5) or used only a posted questionnaire to assess itch (2).

Older age, comorbidities such as chronic kidney disease (CKD), liver dysfunction or diabetes mellitus – can all contribute to the development of itch in HF (1, 12, 13). In our study we observed neither age nor CKD being related to the higher prevalence of itch. It may be explained by relatively young patients and mild–moderate severity of CKD in our population, whereas CKD-related itch mainly affects those at the advanced/dialysis-stage of the disease (13). Patients who reported itch had elevated bilirubin level, but did not differ in liver enzymes (AST, ALT) or albumin levels, which may confirm cholestatic origin of this sensation in acute HF.

Some of the cardiovascular medications used in HF patients – such as ACE inhibitors, angiotensin receptor blockers or statins are known to cause itching (14), while loop diuretics, administered transdermally, inhibit histamine-induced itching (15). Interestingly, in our study, only the use of novel oral anticoagulants was more frequent in patients reporting itch; we are not aware of any previous studies reporting such an association.

Itch severity was reported as mild–moderate, there was no specific factor responsible for its alleviation/aggravation and itch intensity did not correlate with impairment in the quality of life. As HF patients suffer from multiple symptoms and have an already poor quality of life, itch itself may not have a relevant clinical impact.

In summary, our prospective study, on patients with acute HF, found itch as a moderately frequent symptom, which can be associated with HF severity, medications and comorbidities. To date, prevalence of itch in HF was not widely addressed in the literature and our material presents the complexity of this issue, therefore the results should be treated with caution.

REFERENCES

1. Weisshaar E, Szepietowski JC, Darsow U, Misery L, Wallengren J, Mettang T et al. European guideline on chronic pruritus. Acta Derm Venereol 2012; 92: 563–581.
2. Niklasson O, Boman K, Stenberg B.The prevalence and characteristics of pruritus in patients with heart failure. Br J Dermatol 2015; 172: 1541–1546.
3. Zambroski CH, Moser DK, Bhat G, Ziegler C. Impact of symptom prevalence and symptom burden on quality of life in patients with heart failure. Eur J Cardiovasc Nurs 2005; 4: 198–206.
4. Nordgren L, Sorensen S. Symptoms experienced in the last six months of life in patients with end-stage heart failure. Eur J Cardiovasc Nurs 2003; 2: 213–217.
5. Bekelman DB, Havranek EP, Becker DM et al. Symptoms, depression, and quality of life in patients with heart failure. J Card Fail 2007; 8: 643–648.
6. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Eur J Heart Fail 2016; 18: 891–975.
7. Reich A, Heisig M, Phan NQ, Taneda K, Takamori K, Takeuchi S, et al. Visual analogue scale: evaluation of the instrument for the assessment of itch. Acta Derm Venereol 2012; 92: 497–501.
8. Phan NQ. Assessment of itch intensity: prospective study on validity and reliability of the visual analogue scale, numerical rating scale and verbal rating scale in 471 patients with chronic itch. Acta Derm Venereol 2012; 92: 502–507.
9. Reich A, Mędrek K, Szepietowski J. Four-item itch questionnaire – validation of questionnaire. Przegl Dermatol 2012; 99: 600–604.
10. Matusiak L, Szczech J, Kaaz K et al. Clinical characteristics of itch and pain in patients with hidradenitis suppurativa. Acta Derm Venereol 2018; 98: 191–194.
11. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) – a simple practical measure for routine clinical use. Clin Exp Dermatol 1994; 19: 210–216.
12. Yalçin B, Tamer E, Toy GG, Oztaş P, Hayran M, Alli N. The prevalence of skin diseases in the elderly: analysis of 4099 geriatric patients. Int J Dermatol 2006; 45: 672–676.
13. Combs SA, Teixeira JP, Germain MJ. Pruritus in Kidney Disease. Semin Nephrol 2015; 35: 383–391.
14. Reich A, Ständer S, Szepietowski JC. Drug-induced pruritus: a review. Acta Derm Venereol 2009; 89: 236–244.
15. Willis EF, Clough GF, Church MK. Investigation into the mechanisms by which nedocromil sodium, frusemide and bumetanide inhibit the histamine-induced itch and flare response in human skin in vivo. Clin Exp Allergy 2004; 34: 450–455.