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SHORT REPORT

Human Factors Validation of a Wearable, On-Body Infusor for Subcutaneous Administration of Furosemide

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Purpose: Furoscix® (subcutaneous furosemide) is administered using a wearable On-Body Infusor (OBI) and is approved for the treatment of congestion associated with heart failure (HF). The purpose of this study was to assess the safe and effective use of the OBI and Instructions for Use (IFU) by patients with HF, caregivers, and healthcare practitioners (HCPs).

Methods: Sixty participants (patients, n=30; caregivers, n=15; HCPs, n=15) were evaluated on completion of OBI use tasks and IFU knowledge tasks in a simulated use environment. Fifteen of the patients received OBI/IFU training before evaluation.

Results: Overall, 893/900 (99.2%) use tasks and 2211/2220 (99.6%) knowledge tasks were completed successfully, without differences due to training. The most common (n=6) use error was failure to wipe skin or cartridge tip with an alcohol wipe. Errors were due to forgetfulness/misinterpretation rather than IFU clarity.

Conclusion: The subcutaneous furosemide OBI can be safely and effectively used by patients, caregivers, and HCPs, regardless of training.

Keywords: heart failure, furosemide, subcutaneous furosemide, on-body infusor, human factors

Introduction

The prevalence of heart failure (HF) continues to increase and was estimated to affect 64.3 million adults globally in 2017 and 6.2 million adults in the United States in 2018.[1,2] Likewise, mortality attributed to HF continues to increase in younger and older adults.[3,4] Hospitalizations, including repeat hospitalizations, are the primary driver of costs attributed to HF and are projected to increase to $53 billion in the United States by 2030.[5–7] Thus, HF is a substantial burden on patients and the healthcare system.

Decongestive therapy with an oral loop diuretic such as furosemide is recommended for patients with HF and volume overload.[8] However, the high variability in furosemide absorption makes dose optimization challenging, particularly during volume overload when absorption is already low, which may result in decreased efficacy.[9,10] Intravenous loop diuretics may achieve adequate decongestion but require hospitalization or an infusion center visit,[11] resulting in patient inconvenience, greater costs, and potential delays in therapy. Subcutaneous administration of furosemide intended for intravenous use has been shown to be effective in patients with severe HF; however, approximately 25% of patients develop skin toxicity, including infusion site reactions, likely as a result of the alkaline (pH, ~9.0) formulation.[12,13]

Furoscix® (subcutaneous furosemide) is a novel, buffered formulation (pH, 7.4) intended to minimize skin toxicity, has bioequivalence to intravenous furosemide, and is approved in the United States for the treatment of congestion due to fluid overload in patients with chronic HF.[14,15] Furoscix® (subcutaneous furosemide) is self-administered by the patient subcutaneously over 5 hours using a wearable On-Body Infusor (OBI). Several features of the OBI design make its operation simple and easy for users, such as the illustrated step-by-step Instructions for Use (IFU), the prefilled medication cartridge, simple adherence

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to the body, a covered needle for prevention of accidental sticks, a single button press for activation, and clear feedback from a blinking light at the start and end of dosing. In a prospective case control study, patients with worsening congestion due to HF who self-administered subcutaneous furosemide using the OBI had reduced mean 30-day HF-related healthcare costs compared with matched hospitalized controls.[16] This study evaluated the safe and effective use of the OBI and IFU by the intended users: patients with HF, their caregivers, and healthcare practitioners (HCPs).

Materials and Methods

Study Design and Participant Selection

The objectives of this validation study were to demonstrate that the intended user population (patients with HF, their caregivers, and HCPs) could safely and effectively use the OBI and IFU and that performance of critical tasks would not result in patterns of preventable use errors, harm to the patient/user, or compromised medical care. Study evaluations were performed in one day in a test room that simulated home and healthcare environments that included a table and chairs and access to the necessary materials, including the OBI and packaging, prefilled cartridge, IFU, alcohol wipes, manikin, skin simulation injection pad, laptop with video streaming, gloves (HCPs only), hand sanitizer, and sharps container. Evaluation sessions were audio/video recorded. Study personnel were a receptionist, moderator, a trainer to provide instruction on OBI use, a data logger, and an audio-video technician.

The study enrolled patients with HF, caregivers, and HCPs. Participants were recruited by phone, email, and social media, and were screened to represent the intended user groups and varied in sex, injection experience, age, occupation, race, and highest education level. Eligible participants were patients aged >35 years with diagnosed HF, caregivers of patients with HF aged >18 years, and HCPs aged >18 years. The ability to read and fluently speak English was required. Participants were excluded if hand or visual impairment prohibited unaided OBI use or if unable to hear.

On-Body Infusor Preparation and Use

The OBI is a wearable infusion system designed to deliver subcutaneous furosemide (80 mg per 10 mL) in a single dose over 5 hours (Appendix 1). The OBI was accompanied by the IFU, which includes stepwise instructions and graphic illustrations (Appendix 2). For assessment of OBI use, caregivers and HCPs applied the OBI to a skin simulation injection pad that was strapped to a provided manikin, whereas patients applied the OBI to a skin simulation injection pad that was strapped to themselves. As detailed in the IFU, use of the OBI included washing hands, checking and loading the OBI with the prefilled cartridge, preparing the application site, applying the OBI to the skin simulation injection pad, starting the infusion, and removing and disposing of the OBI. Each participant was responsible for monitoring and responding to alarms (ie, beeping or blinking light) that indicate malfunction or premature removal (Appendix 1).

Human Factors Validation Methods

Study participants were evaluated on the ability to successfully complete 52 OBI performance measures, which included 15 OBI use tasks performed without assistance and 37 knowledge, identification, and IFU reading comprehension tasks. Some OBI use tasks were classified as critical tasks, defined by the United States Food and Drug Administration (US FDA) as those that, if performed incorrectly or not performed, could cause harm or result in compromised care. Participant performance and behavior were assessed and recorded. Participants were asked to provide subjective feedback about the OBI and IFU.

One-half of the enrolled patients received training 24 hours before OBI use tasks were performed. The training was representative of what would have been provided in the healthcare setting and included an introduction to the OBI, time to review the IFU, a verbal walkthrough of OBI operation, and a verbal walkthrough of troubleshooting alarms. The caregivers, HCPs, and the other one-half of patients did not receive OBI use training but were allotted time to independently review, as desired, the OBI and IFU before starting the OBI use tasks.

Participant success, error, close calls, significant difficulties, and deviations from the IFU were recorded. Successful OBI use was defined as any task where the participant performed the correct procedure without making any preventable use errors that could result in injury to the patient or user or prevent administration of the full infusion. Overall, performance success was achieved when the user accomplished delivery of the full dose.

Statistical Analysis

Participant task data were summarized descriptively as the number and proportion of patients successfully completing a task. Subjective feedback was recorded narratively.

Results

Study Population

Sixty participants were enrolled and completed the study, including 30 patients with HF, 15 caregivers, and 15 HCPs. Of the 30 patients, 15 were trained on OBI use and 15 were untrained. All caregivers and HCPs were untrained. The median (range) age was 57 years (39−80) for patients, 49 years (34−75) for caregivers, and 37 years (33−64) for HCPs (Supplemental Table 1). Twenty-four of 30 (80%) patients were male, 7 of 15 (47%) caregivers were male, and 3 of 15 (20%) HCPs were male. Hearing impairment and hand and visual impairment not prohibitive of OBI use were more common among patients than among caregivers (43.3% vs 15.4%); HCPs did not have impairments (Supplemental Table 1). The mean (SD) duration of HF among patients was 4.6 years (5.2).

Validation of on-Body Infusor Use by the Intended User Population

Performance of OBI Use Tasks

Each of the 60 participants were evaluated on performance of 15 OBI use tasks related to preparation, application, and administration of medication. In total, 893 of 900 (99.2%) OBI use tasks were successfully completed (Table 1). There was one critical OBI use task error, which was by a trained patient who did not successfully start medication delivery using the blue start button. The patient attributed the error to distraction in the simulated environment rather than the design of the OBI or IFU clarity. The patient subsequently performed the task successfully without assistance.

Table 1 Evaluation of OBI Use Tasks

	Patients with HF		Untrained Caregivers (n=15)	Untrained HCPs (n=15)	Total (N=60)
	Trained (n=15)	Untrained (n=15)			
Completed OBI use task, n (%)	222/225 (98.7)	222/225 (98.7)	224/225 (99.6)	225/225 (100.0)	893/900 (99.2)
Critical use task	194/195 (99.5)	195/195 (100.0)	195/195 (100.0)	195/195 (100.0)	779/780 (99.9)
Remove OBI and prefilled cartridge from packaging	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Fully open cartridge holder	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Load prefilled cartridge	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Close cartridge holder	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Apply OBI to body	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Start medication delivery	14/15 (93.3)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	59/60 (98.3)
Allow medication to deliver	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Respond to OBI alarm[a]	60/60 (100.0)	60/60 (100.0)	60/60 (100.0)	60/60 (100.0)	240/240 (100.0)
Remove OBI from body	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Dispose of used OBI	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Non-critical use task	28/30 (93.3)	27/30 (90.0)	29/30 (96.7)	30/30 (100.0)	114/120 (95.0)
Clean tip (small end) of prefilled cartridge with alcohol wipe	14/15 (93.3)	14/15 (93.3)	14/15 (93.3)	15/15 (100.0)	57/60 (95.0)
Prepare application site	14/15 (93.3)	13/15 (86.7)	15/15 (100.0)	15/15 (100.0)	57/60 (95.0)

Notes: [a]Included four distinct critical use task measures: (1) notices alarm; (2) identifies alarm; (3) correctly responds to alarm; and (4) removes and disposes of on-body infusor.
Abbreviations: OBI, on-body infusor; HCP, healthcare practitioner; HF, heart failure.

There were six non-critical OBI use errors (Table 1). Three participants (trained patient, n=1; untrained patient, n=1; untrained caregiver, n=1) failed to clean the cartridge tip with an alcohol wipe before insertion into the OBI. The three participants attributed the errors to forgetfulness and indicated that the IFU clearly communicated the need to perform the task and that amendment of the IFU would not have prevented the errors. In addition, three participants (trained patient, n=1; untrained patient, n=2) did not clean the simulated skin application site with an alcohol wipe before applying the OBI. The three patients attributed the errors to forgetting to perform the task. The three patients indicated that the IFU clearly communicated the need to perform the task and that amendment of the IFU would not have prevented the error.

Performance of Knowledge, Identification, and Reading Comprehension Tasks

Each of the 60 participants were evaluated on 37 knowledge, identification, and reading comprehension tasks. In total, 2211 of 2220 (99.6%) of the knowledge, identification, and reading comprehension tasks were successfully completed (Table 2). Thirty-one of the 37 tasks were successfully completed by 100% of participants.

Three errors occurred during the knowledge tasks, where participants were asked to answer the following knowledge-based questions: identify the need to wash hands before use (trained patient, n=1; untrained HCP, n=1) and select application site (untrained caregiver, n=1). The remaining six errors occurred during the IFU reading comprehension questions: locate warning statements and other critical statements in the IFU (trained patient, n=2; untrained patient, n=1); comprehension of using only subcutaneous furosemide medication with the OBI (trained patient, n=1; untrained patient, n=1); and dispose of the used OBI (trained patient, n=1). The locating information errors were failure by two trained patients to locate the Important Information section of the IFU and a failure by an untrained patient to locate

Table 2 Evaluation of OBI Knowledge, Identification, and Reading Comprehension Tasks

	Patients with HF		Untrained Caregivers (n=15)	Untrained HCPs (n=15)	Total (N=60)
	Trained (n=15)	Untrained (n=15)			
Completed tasks, n (%)	550/555 (99.1)	553/555 (99.6)	554/555 (99.8)	554/55 (99.8)	2211/2220 (99.6)
Wash hands	14/15 (93.3)	15/15 (100.0)	15/15 (100.0)	14/15 (93.3)	58/60 (96.7)
Check expiration date[a]	45/45 (100.0)	45/45 (100.0)	45/45 (100.0)	45/45 (100.0)	180/180 (100.0)
Remove OBI and prefilled cartridge from packaging	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Inspect product for damage[a]	30/30 (100.0)	30/30 (100.0)	30/30 (100.0)	30/30 (100.0)	120/120 (100.0)
Inspect liquid medication[a]	30/30 (100.0)	30/30 (100.0)	30/30 (100.0)	30/30 (100.0)	120/120 (100.0)
Use only furosemide with OBI	14/15 (93.3)	14/15 (93.3)	15/15 (100.0)	15/15 (100.0)	58/60 (96.7)
Fully open cartridge holder	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Select application site[a]	60/60 (100.0)	60/60 (100.0)	59/60 (98.3)	60/60 (100.0)	239/240 (99.6)
Prepare application site[a]	45/45 (100.0)	45/45 (100.0)	45/45 (100.0)	45/45 (100.0)	180/180 (100.0)
Start medication delivery	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Allow medication to deliver[a]	135/135 (100.0)	135/135 (100.0)	135/135 (100.0)	135/135 (100.0)	540/540 (100.0)
Treat the infusion site, if needed	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Dispose of used OBI[a]	44/45 (97.8)	45/45 (100.0)	45/45 (100.0)	45/45 (100.0)	179/180 (99.4)
Emergency stop of infusion	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)	60/60 (100.0)
Locate information in the IFU[a]	58/60 (96.7)	59/60 (98.3)	60/60 (100.0)	60/60 (100.0)	237/240 (98.8)

Note: [a]Task included multiple task measures.
Abbreviations: OBI, on-body infusor; HCP, healthcare practitioner; HF, heart failure; IFU, instructions for use.

information on what to check on the OBI and prefilled cartridge before use. The participants attributed the errors to inattentiveness and did not suggest any changes to the IFU.

Subjective Feedback

During the subjective feedback portion that followed the OBI use tasks, all 60 participants correctly felt that they had successfully performed the steps needed to deliver the medication and that IFU provided adequate guidance through the process. Seven participants subjectively reported difficulty with OBI use tasks. A trained patient reported initially having difficulty identifying the OBI alarm but overcame the difficulty by referring to the IFU. A trained patient initially expressed having some initial confusion starting the infusion but referred to the IFU and successfully started the infusion. An untrained caregiver reported initially having difficulty in knowing how to keep the adhesive liner on the device but then successfully performed these tasks. The caregiver stated that the IFU adequately explained the procedures. One participant reported difficulty knowing when the infusion was complete but successfully identified when the infusion ended. Three participants reported some difficulty removing the OBI, but no signs of difficulty were observed by study personnel.

Participants generally provided positive feedback regarding the IFU. Only one participant (a trained patient) reported difficulty understanding the IFU. The patient initially expressed having difficulty because he skipped some steps in the IFU when setting up and starting the OBI. However, the patient then communicated that the IFU was clear and informative.

Discussion

Heart failure is incurable and therefore requires lifelong management, with the goals of controlling worsening symptoms, reducing hospitalizations, and maintaining survival.[17] Because symptom control is one of the primary causes of hospitalization among patients with congestion, the availability of a self-administered subcutaneous loop diuretic is a welcomed approach for the outpatient control of fluid overload.[11,15] On-body delivery devices such as the OBI allow patients with a variety of conditions to easily and reliably self-administer a large volume (up to 10 mL) of medication without visiting a hospital or infusion center, resulting in improved patient quality of life, satisfaction, empowerment and autonomy, adherence to treatment, and time savings, as well as reductions in hospitalizations and treatment costs.[17–24] In the prospective FREEDOM-HF study, patients who presented to the emergency department with worsening congestion due to HF and then received subcutaneous furosemide at home using the OBI had reduced mean 30-day HF-related healthcare costs compared with matched hospitalized controls.[16]

In this human factors validation study, the subcutaneous furosemide OBI was safely and effectively used by patients with HF, their caregivers, and HCPs. Both trained and untrained participants successfully prepared and used the OBI, with 99.2% of OBI use tasks successfully completed and 99.6% of knowledge, identification, and reading comprehension tasks successfully completed. No patterns of preventable use errors were identified. The relatively few use errors encountered by participants were attributed to distraction or forgetfulness, and participants indicated that the IFU clearly communicated the tasks, steps, and information. These data suggest that the simplistic design of the OBI, along with the IFU that is easily comprehended, will allow the intended user population to be successful in consistently delivering the recommended dosage of subcutaneous furosemide in an outpatient setting.

This study was strengthened by the diversity of the enrolled population, which included participants with a broad range of education from high school through professional education. Regardless of educational background, untrained participants used the OBI as successfully as trained participants. A potential limitation of this study was the relatively small sample size; however, the enrollment of 60 participants met the US FDA recommendation of 15 per user group for a human factors validation study.[25]

Conclusion

In conclusion, the subcutaneous furosemide OBI has the potential to provide a safe, convenient, and easily used option for patients with HF, their caregivers, and HCPs. The subcutaneous furosemide OBI is a viable option for the outpatient management of congestion in patients with HF when responsiveness to oral diuretics is reduced and hospitalization is not indicated.

Abbreviations

HCPs, healthcare practitioners; HR, heart failure; IFU, instructions for use; OBI, On-Body Infusor; SD, standard deviation; US FDA, United States Food and Drug Administration.

Ethics Approval and Informed Consent

The study protocol (IAA-1928) received institutional review board approval (Salus IRB, Austin, TX) before any procedures or assessments were initiated. As this was a simulated use environment study conducted using a skin simulation injection pad, it was determined to involve no more than minimal risk and qualified for expedited review in accordance with 21 CFR 56.110 and 45 CFR 46.110, under research Category 7.

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Disclosure

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