

Domiciliary application of CryoCuff in severe haemophilia: qualitative questionnaire and clinical audit

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Abstract. The acute management of haemophilic bleeding episodes in the home setting is based on the concept of immediate factor replacement therapy and the PRICE regime – an acronym representing the concepts of Protection, Rest, Ice, Compression and Elevation [1,2]. Integral to this regime is the application of cold therapy, and yet little is known regarding the safe periods of application, or the relative safety of cryotherapy devices such as the CryoCuff™ when used in the home setting by patients suffering from severe haemophilia and related bleeding disorders. This study examines the subjective patient response to the application of the CryoCuff™ device in the home setting in terms of the effect on pain, joint swelling and the return to 'pre-bleed status' of the knee, ankle or elbow in patients with severe haemophilia A/B or type III von Willebrand's disease (VWD) immediately following haemarthrosis, and any potential adverse effects related to the device or recommended duration of application as stated in the PRICE guideline (Fig. 1). Twelve patients, either with severe haemophilia A/B or with VWD were recruited and asked to use the CryoCuff™ device as part of the PRICE regime

immediately following the onset of knee-, ankle- or elbow bleeds for the next one year. Each subject was then sent a qualitative questionnaire to determine subjective responses to the device. All patients reported that the application protocol was easy to follow, they were able to apply the device as per the PRICE regime and they were able to tolerate it for the recommended period. Whereas, all the patients felt that the device had a significant impact on alleviation of pain and return to pre-bleed status, 78% of the patients felt that the device led to a significant reduction in swelling around the affected joint. There was no conclusive evidence that the device resulted in any reduction in the amount of factor used to treat the acute bleeding episode, however, no patients reported any perceived delay in achieving haemostasis or required extra factor replacement therapy consequent to the usage of the device. No other adverse effects were reported by participants in this study.

Keywords: haemophilia, haemarthrosis, haemostasis, cryotherapy, cryocuff, PRICE, physiotherapy, rehabilitation

Introduction

The aim of this research was to provide evidence for the safety and usefulness of the CryoCuff™ device (DJO Inc., Vista, CA) in the management of acute haemarthroses when applied in the home setting, and to determine whether the application protocol for this device is reasonable and achievable for patients with severe forms of haemophilic bleeding disorders.

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The CryoCuff™ device has long been advocated as a useful intervention in reducing joint pain and swelling in orthopaedic and musculoskeletal physiotherapy settings, particularly following joint replacement surgery [3]; however, the CryoCuff™ has not been widely utilized by patients suffering from haemophilia. Given the relatively minimal adverse effects of this device when used in postsurgical cases, there is a strong theoretical argument for the efficacy of this device when managing the musculoskeletal aspects of haemophilia, and in particular acute haemarthroses.

Minimizing the extent of bleeding around a hinge joint such as the knee, ankle or elbow using cold therapy as part of the PRICE regime may be a useful intervention in reducing the pain and immobility related to haemarthroses, and may help the affected joint to return to its 'pre-bleed' status faster.

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PATIENT CRYOCUFF QUESTIONNAIRE

1) How satisfied were you with the information provided to you at the start of the study?

Very Satisfied
 Somewhat Satisfied
 Undecided
 Somewhat Dissatisfied
 Very Dissatisfied
 Other:

2) Did you find the instructions easy to follow when applying the cryocuff?

Yes
 No

3) Were you, generally, able to apply the cryocuff immediately following the onset of bleeding at the knee, ankle or elbow?

Yes
 No

4) Were you, generally, able to apply the cryocuff for the recommended time (10–15 min, not exceeding 20 min)?

Yes
 No

5) Do you think the cryocuff was useful in reducing the pain around the joint compared to when it is not used?

Strongly Disagree
 Disagree
 Undecided
 Agree
 Strongly Agree

6) Did you notice less swelling around the joint following application of the Cryocuff device?

Strongly Disagree
 Disagree
 Undecided
 Agree
 Strongly Agree

7) Do you think the cryocuff helped the joint return to its 'pre-bleed' status faster than if you had not used the device?

Strongly Disagree
 Disagree
 Undecided
 Agree
 Strongly Agree

8) Did you feel, overall, that you used less Factor to treat bleeds at the knee, ankle and elbow relative to when you were not using the cryocuff?

Strongly Disagree
 Disagree
 Undecided
 Agree
 Strongly Agree

9) Did you notice any adverse effects from using the Cryocuff?

10) Did you require any extra Factor replacement as a result of using the cryocuff?

Yes
 No

11) Do you feel, overall, that the Cryocuff device has been beneficial in the management of your bleeding episodes?

Strongly Disagree
 Disagree
 Undecided
 Agree
 Strongly Agree

12) Do you have any suggestions on how the instructions or protocol may be improved for future patients?

Fig. 1. Continued.

Fig. 1. The qualitative participant questionnaire, given following 1 year of unsupervised use in the home setting immediately following the onset of the symptoms of haemarthroses.

Although there is anecdotal evidence for the potential benefit of cold therapy in both inpatient orthopaedic settings and outpatient sports injury clinics [3,4] – the exact effects and the most effective mode or frequency of application is unknown [3]. Relatively little is known regarding the safety of the recommended application duration of cold therapy, the impact on joint pain or swelling, the return of the affected joint to its 'pre-bleed' status or the possible adverse effects of devices such as the CryoCuff™ when used in the home setting without the supervision of a haemophilia clinician.

This study examines the patient's response to the application of the CryoCuff™ device following acute knee-, ankle- or elbow bleeding episodes following use of the device for 1 year, and the

perceived benefit compared with non-use of such a device. Consideration is also given to the impact on the patient's 'return to pre-bleed status', a major factor in the patient's perceived ability to return to work and maintain normal daily function. Consideration is also given to the possible adverse effects noted as a result of using the device. These may include any perceived delay in haemostasis, any increase in the amount of factor replacement therapy required to control bleeding at the joint, or any other difficulties that may arise from following the PRICE guidelines, the CryoCuff™ application protocol or the recommended duration of application.

Materials and methods

The CryoCuff™ device consists of a 'Cooler Barrel' containing ice and water, connected via a pipe to knee, ankle or elbow-shaped cuffs, which wrap

around the affected joint allowing cold therapy and compression to be applied to the site of intra-articular bleeding. It is designed to allow application by an individual, and uses a one-way pressure valve-gravity system to fill and drain the cuffs, which are fastened with elasticized Velcro straps. The cuffs used with this device have the advantage of minimizing the risk of ice burns that can be associated with direct application of cold to the skin.

All recruited participants remained under the long-term management of the Centre for Haemostasis and Thrombosis at St Thomas' Hospital, London for the duration of this study. This single-centre method was used in order to allow close monitoring of all subjects by the author and each participant's respective haematologist.

Twelve patients diagnosed with severe haemophilia A/B or type III von Willebrand's Disease were identified and recruited for this study. Male and female patients, including those with pre-existing autoimmune inhibitors were also included. Participants were identified by the severity of their bleeding disorder, a history of recent significant knee-, ankle- or elbow bleeding in the year prior to commencement of the trial, and by an age range of 5–45 years. This upper age limit was imposed to minimize the presence of age-related osteoarthritic arthropathies and the subsequent joint effusions that could mimic some of the symptoms of haemarthroses.

Patients with mild or moderate haemophilia or patients who had not suffered knee-, ankle- or elbow-bleeds in the previous year were excluded, as were those who had previous orthopaedic interventions to these joints, patients with chronic hypertrophic synovitis, or patients with any other neurological or systemic medical disorders that may have affected haemostasis or musculoskeletal function. Subjects were able to withdraw from the study at any time, and were to be withdrawn by the Principal Investigator if any adverse effects resulting from application were noted by the participant during the study period.

Potential participants were approached by the specialist physiotherapist and were given a comprehensive information pack and teaching session for application of the CryoCuff™, and were asked to take a few days to consider involvement in the trial before signing informed consent documents.

Participants were then asked to take the device home, and apply it immediately (or as near as possible to the onset of a bleeding episode at the knee, ankle or elbow), as part of the PRICE regime. Participants were asked to report any adverse effects

related to using the device immediately, and were also managed with regular outpatient physiotherapy and haematology reviews to ensure that all aspects of care were being attended to.

The cold therapy protocol, as stated in the PRICE regime, involves application of the CryoCuff™ for short periods during the day, repeated regularly. The recommended application period of 15 min, not exceeding 20 min, repeated every 1–2 h as tolerated was deemed to be a safe period for this study, based on anecdotal evidence from supervised application in the Centre for Haemostasis and Thrombosis at St Thomas' Hospital. Following use of the CryoCuff™ device for 1 year, each patient was then sent a qualitative questionnaire to determine the perceived benefit or any previously unreported adverse reactions to the device. A copy of the qualitative questionnaire can be found in Fig. 1.

All patient information documents, consent forms, the application protocol and PRICE regime documents were approved prior to commencement of this research by NHS COREC and the Guy's and St Thomas' NHS Foundation Trust Research and Development Committee. The full PRICE regime can be seen in Fig. 2.

Results

A response rate of 75% was achieved in this study, without the withdrawal of any of the patients from the study prior to completion on account of adverse

P	Protection. Reduce weight bearing or stress on the affected joint or muscle by using crutches or other supports. You may need to avoid putting weight on the affected side completely for the first 24–48 h.
R	Rest. The affected area should initially be rested completely. This allows the swelling to go down (which usually happens in around 48 h) and prevents further bleeding. The injured area should not be forced into any position, but instead rested in the most comfortable position possible.
I	Ice. Ice helps to reduce swelling, prevent further bleeding and eases pain. Use your 'CryoCuff™' immediately upon feeling the onset of bleeding symptoms. Cold therapy should be applied to the affected area 'little and often', for around 10–15 minutes every two hours or so. Do not apply for more than 20 min at a time and never place ice directly on the skin as it can burn.
C	Compression. Due to the increased volume of fluid, the more swollen an injury becomes, the more pain you will feel. Compression reduces swelling, and therefore pain. Your physiotherapist will provide you with an elasticised bandage or pad and will make sure it fits correctly, as additional damage can be caused where the bandage is too tight. Try not to allow wrinkles in the bandage and remove it at night.
E	Elevation (raising). This helps to reduce swelling and relieve pain by increasing the blood flow away from the injured area. The injured area should be raised above the level of your heart. When you elevate your leg, remove the compression stocking to allow normal, healthy circulation. Elevate 'little and often', for around 20 min at a time.

Fig. 2. The PRICE regime: the home management programme devised for patients to apply immediately upon the onset of symptoms, given alongside the application protocol for the CryoCuff™ device upon commencing the trial.

reactions to the use of the device. No participants were withdrawn from this trial on account of the development of new autoimmune inhibitors or any other significant co-morbidities during the trial period.

Patients were initially questioned regarding the quality of the pretrial teaching and instruction in using the device. Eight of the nine responding participants stated that they were 'very satisfied' with the CryoCuff™ application teaching prior to commencing the study, with one respondent stating that they were 'somewhat satisfied'. When asked if the written instructions and PRICE guidelines given at the start of the study were easy to follow in the home setting, following the onset of a bleed, all subjects responded positively. All subjects felt they were able to apply the device as per the PRICE protocol, and all subjects stated that they were able to tolerate the CryoCuff™ device for the recommended period.

When asked whether the participants thought that the CryoCuff™ was a useful device in reducing the pain around the joint, compared with when it had not been used previously, all subjects either agreed or strongly agreed that the device had a positive impact on pain reduction following haemarthrosis.

Participants were then asked whether they noticed less swelling around the affected joint following application of the CryoCuff™ device, with 22% of respondents stating that they were unsure. A much larger proportion (78% of subjects) either agreed or strongly agreed that the device significantly reduced the swelling associated with haemarthrosis. All but one respondent (who was undecided on this issue) felt that the CryoCuff™ helped to return the joint to its 'pre-bleed' status faster than when they had previously not used the device; however, the impact on factor usage was unclear.

While no patients reported any perceived delay in haemostasis or required extra doses of factor replacement therapy to control the haemarthrosis, most patients (56%) were undecided following 1 year of application as to whether the CryoCuff™ reduced the need for factor replacement therapy following a hinge joint bleed. Whereas, 22% of respondents felt they needed less factor replacement to treat the joint bleed, another 22% of respondents felt that they used the same quantity.

In the reporting of serious adverse events following application of the device, no respondent reported any increase in pain, swelling or hypomobility. One subject reported that the skin could occasionally become irritable on account of contact with the elasticized Velcro cuff fasteners, while one patient

stated that the affected joint felt heavier once the cuff was applied and filled with icy water.

When asked to assess the overall perceived benefit in the management of knee-, ankle- or elbow haemarthroses, all patients either agreed or strongly agreed that the CryoCuff™ was beneficial to them compared with the year prior to the study when it had not been used. One subject went on to suggest that smaller cuffs for very young children may be useful, while another suggested that the CryoCuff™ could possibly be applied for longer than the 15 min recommended in the PRICE guidelines. One patient also highlighted the point that although the CryoCuff™ was a very useful tool in the management of haemarthroses, they did not feel it was a substitute for factor replacement therapy.

Discussion

The historical physiotherapeutic management of acute haemarthroses using cold therapy is an anecdotally well-established component of a successful treatment regime; however, evidence for the length of time of application, or safety of different types of cold therapy device is scarce. It is important therefore to try and gain insight into the possible benefits or harm that may be caused by a device such as the CryoCuff™ when applied to acute haemarthroses at the knees, ankles or elbows, and test whether there are any perceived adverse effects related to the recommended duration of application as stated in the PRICE regime.

In terms of participant response, the perceived benefit of this device in improving the domiciliary management of knee-, ankle- or elbow acute haemarthroses was very encouraging. Although the sample size was small in this study, a response rate of 75% is a relatively high number, given that this was a qualitative questionnaire.

Compared with when the device was not used, all patients felt that pain decreased significantly, and most felt that there was a significant reduction in swelling and a faster return to a 'pre-bleed' status when using the device. This has significant ramifications for a patient's perceived ability to return to work, and may therefore have significant financial implications for patients suffering from haemophilia.

No increase in pain or swelling, or any perceived delay with respect to haemostasis were reported, and no respondent reported any increase in required factor use as a result of using the CryoCuff™. Theoretically, the reduced pain and swelling around the joint when cold therapy is applied from the earliest onset of bleeding symptoms or injury may

lead to reduced exposure of the surrounding soft tissues or articular surfaces to blood by its vasoconstrictive effect. This in turn may speed up the resolution of haemarthrosis, or may reduce the overall exposure of the articular surfaces, thereby reducing blood-induced joint damage. Further research in this area is required, particularly where it involves more objective analysis of the effects of cold therapy on acute haemarthroses using thermal imaging or Doppler scanning. Further research on larger subject populations is also required, in order to determine whether there is a significant overall impact on factor usage following hinge-joint haemarthroses over a year of application compared with the previous year's data. This would ideally be suited to younger adult populations prior to the onset of age-related degenerative joint disease, as this type of research also requires very accurate record keeping, particularly with regards to differentiation between haemarthroses and other sources of joint pain and effusion such as degenerative or osteoarthritic pathology.

Clearly correcting for all variables in this type of research can be extremely difficult, particularly where results are subject to patient compliance or where there may be other clinical factors, for example where patients develop autoimmune inhibitors over the course of the study period, or where patients confuse the symptoms of Chronic Haemophilic Arthropathy or joint effusions related to degenerative changes with haemarthroses. The focus of this research has therefore been kept relatively narrow, in terms of a simple qualitative questionnaire, in part on account of difficulties in correcting for these and other variables.

Although there may be inherent bias in this study, in terms of recruitment from a single source, the low statistical power afforded by a small study group and the lower level of evidence applied to a qualitative questionnaire, the patient's perceived response after a year of application can still give a valuable insight into the benefit, and, more importantly, the safety of this device. It is reasonable to assume that even in this small subject population, given the severity of bleeding disorder and the length of the monitoring period that significant adverse reactions to the CryoCuff™ would have been reported by participants.

Crucially, all patients reported that the PRICE guidelines and the application protocol used in the home setting (given to them at the start of the trial) was easy to follow, was realistic and achievable in the presence of an acute haemarthrosis, and that there were no adverse reactions to the recommended

application period of 15 min (not exceeding 20 min). This therefore gives musculoskeletal clinicians working in haemophilia cases, a clear baseline to work from, with scope for improved advice regarding cold therapy or the PRICE regime based on further research.

Conclusion

The CryoCuff™ is a safe device for the application of cold therapy to haemarthroses affecting hinge joints such as the knees, ankles or elbows, and can significantly reduce perceived pain associated with joint bleeding. There is a strong indication that joint swelling and return to pre-bleed status are improved, however there is no evidence that this device allows for reduced factor therapy in response to haemarthroses.

No adverse effects were noted as a result of a recommended 15-min application, and there was no reported requirement for extra factor use as a result of delayed haemostasis following its use. This device can be used safely in the home setting, with instruction, without the need for supervision by a haemophilia clinician.

The PRICE regime is a useful guideline that can be easily followed in the home setting and appears to be realistic for patients suffering from severe haemophilic bleeding disorders. It is hoped that this regime will form the basis for further research and more objective data regarding the possible risks or benefits of cold application in the home setting can be assessed in the haemophilia population.

Disclosures

The author stated that he has no interests which might be perceived as posing a conflict or bias.

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