Telemedicine and telerehabilitation: current and forthcoming applications in haemophilia

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Abstract

In persons with haemophilia (PWH), the importance of comprehensive disease management to prevent bleeding, joint damage and secondary diseases has been well established. However, because haemophilia is a chronic disease, intervention programmes carried out for prolonged periods of time may create problems of patient adherence. Driven by continuous technological innovation, telemedicine is being increasingly proposed as a way to provide PWH with a range of services designed to improve their health, saving the time and cost involved in going to the treatment centre, and increasing therapeutic adherence. The aim of this article is to identify and discuss the tools available for the management of PWH by means of telemedicine and information technology. Video conferences are helpful to obtain a rapid evaluation at a distance of the occurrence and severity of bleeding episodes by the personnel of the treatment centre. Cell phones and associated applications (apps) help to improve the regular implementation of replacement therapy and monitor any ensuing adverse effect. Portable sensors help to improve lifestyle and to monitor the degree of physical activity through the fulfilment of a given number of daily walking steps and other physical activities. In the context of telerehabilitation, exergames have the potential to improve the musculoskeletal function of PWH by exploiting the recreational features of videogames. Thus, telemedicine and its multiple applications may be useful in the management of haemophilia, especially for patients living far from specialised centres. However, since this is a recent and rapidly evolving field, published studies are few and have, so far, involved only a limited number of cases. Therefore, additional evidence needs to be obtained by means of accrual of cumulative data from multiple centres specialised in haemophilia.

Keywords: haemophilia, telemedicine, telerehabilitation, peer support, physiotherapy, exercise, therapy adherence.

Introduction

In chronic diseases, adherence to therapeutic programmes, and particularly to rehabilitation and exercise programmes carried out in the context of healthcare structures, is notoriously low. For example, about 50% of patients with a very frequent ailment such as chronic obstructive pulmonary disease (COPD) refuse to take part in rehabilitation programmes, and 30-50% of them abandon them before completion[1-3]. Moreover, only about one-fifth of patients with heart failure (a very common disease, especially in older people) choose to participate in rehabilitation programmes, although their beneficial effects have been well documented[4-7]. Data available for osteoarticular pathologies are similarly unsastifactory in terms of acceptability and compliance.

The main causes of this situation are:

- logistical problems, such as difficult transportation to and from the treatment centre, especially for patients with physical disabilities and those living in remote areas; time spent at healthcare facilities to perform the prescribed rehabilitation activities, with the related loss of working days and school attendance; and the frequent need to be accompanied by relatives or friends;
- psychological problems due to patients' reluctance to prolong care within hospital and other healthcare structures; lack of motivation and a refusal to accept the unattractive traditional methods of rehabilitation.

Like other people affected by chronic diseases, patients with haemophilia (PWHs) often suffer from low adherence to their therapeutic programmes, and particularly to exercise programmes for rehabilitation[8,9]. In spite of the fact that the World Federation of Haemophilia and most clinicians recommend regular physical activity, more than half of the patients with severe and moderate haemophilia fail to satisfy recommendations concerning the quantity and quality of the exercise they have to do[8,9]. In order to achieve exercise targets, the programme and type of exercise should be more interesting for the patients and should stimulate their participation. This highlights the need to change the pattern of provision of exercise programmes, integrating them with self-management strategies based upon modern information technologies.

In the context of self-management, and for the improvement of healthcare in general, telemedicine is becoming an increasingly attractive option. The American Telemedicine Association defines telemedicine

as the distant supply of healthcare services and clinical assistance using information and communication technologies, such as the internet, wireless systems, and mobile phones[10-13]. It consists of virtual strategies that do not require any direct physical contact between the patient and healthcare professionals. These strategies include: distant monitoring, education, counseling and training, all based on networking tools. Among the different branches of telemedicine, telerehabilitation is based upon the use of information and communication technologies in order to provide people with disability who need to be rehabilitated remote services in their homes. The main potential for telerehabilitation in people with disability due to musculoskeletal disease is the possibility of increasing the frequency, intensity and enjoyment of exercise programmes and thus their regular implementation, allowing patients to stay at home. This saves travelling to healthcare facilities and the need to be accompanied. PWHs are an ideal target for telemedicine in general, and particularly for telerehabilitation[10], owing to their lifelong inherited coagulation defect that, despite ever more successful modern management[14-16], is still frequently associated with the occurrence of some degree of functional impairment of the musculoskeletal system. This article addresses the potential use of telemedicine in PWH, with a special emphasis on telerehabilitation.

Telemedicine for haemophilia

Videoconferencing

The use of videoconferencing allows verbal and visual interactions between the participants, providing consultations, diagnostic evaluations and also therapeutic interventions. Broadband computer connections are required for the necessary clarity of the image and to provide simultaneous access to several people during the one session. As part of their treatment, PWH regularly use telephones and e-mails to communicate with the specialised treatment centres and discuss their individual clinical problems. For instance, in the context of an episode of acute bleeding, videoconferencing may facilitate early and appropriate management, reducing the time between the onset of bleeding, its assessment and the actual implementation of replacement therapy. Videoconferencing can also facilitate integrated patient care, allowing interactions between more than one member of the comprehensive management team by means of 3-4 virtual rooms visible through a personal computer monitor. However, despite this potential, there is little information on the use of videoconference for PWH. According to Jacobson and Hooke[17], in a small experience carried out for one whole year in 12 paediatric cases, videoconferences helped to improve the interactive management at home of bleeding episodes, as witnessed by patients and their caregivers[17]. However, the use of videoconferences has obvious limitations because it may not always be easy to define the dosing and pattern of replacement therapies based upon remote images.

Mobile phones

In recent years, there has been a huge growth in wireless connectivity, and more than two-thirds of the global population owns a mobile phone. The use of mobile phones should help not only to improve the long-term management and control of chronic diseases such as haemophilia, but may also permit faster diagnosis and treatment of acute clinical manifestations, reducing unnecessary visits to hospitals and emergency rooms, with a likely favorable impact on costs of care and patient's quality of life. In PWH, the availability of mobile technology may help to improve management in these principal ways:

- supply information on the disease by means of a wide range of formats, including written texts, photos and videos;
- provide warnings to remind PWH to carry out treatments as prescribed;
- record the data entered by the user and potentially offer instant advice as to the best treatment;
- identify adverse effects related to the new treatments that are currently becoming available.

In PWH, adherence to prophylaxis regimens of replacement therapy may decrease dramatically during adolescence[18,19]. Adoption of self-infusion at home also means that many adolescents with haemophilia no longer regularly report the occurrence of their bleeding episodes to the treatment centre, nor their own compliance with the prescribed regimens, making it difficult for healthcare professionals to monitor them properly. Therefore, a range of electronic tools and softwares have been proposed to record the use of coagulation factors by PWH[20]. Initial attempts concerned laptops, an effective alternative to paper-based data collection forms. However, this cumbersome pattern of data collection did not survive the growing adoption of mobile phones. There are several specific apps, most are developed and provided to PWH by the pharmaceutical industry: for instance HemMobile®, developed by Pfizer, records the use of coagulation factors, the reasons for an infusion, bleeding details, pain scores and scales, as well as the impact of the haemorrhagic episode. Other similar or improved apps made available by industries are HemaGo (Novo Nordisk), Factor Track (Bayer), Beat Bleeds (Baxter) and Helitrax (CSL Behring). Even though the pharmaceutical companies should not have access to patient data, the problem of data protection and confidentiality is looming large. In addition to issues of

privacy, there is the additional problem of when patients switch therapeutic products and perhaps find that the company-related apps are no longer suitable. With so many apps developed by the industry, metrics such as the number of visits and number of pages browsed should be divulged and made easily available to the community of PWH and their caregivers, particularly in the current world of big data analysis. Given these possible gaps in knowledge, an important independent initiative was Haemtrack, developed in 2008 by the United Kingdom (UK) Haemophilia Centre Doctor Organisation. This electronic home treatment diary run on mobile phones was conceived to improve the timeliness and completeness of treatment records, including time of bleed onset, dose and batch of product administration, reason for treatment, pain score, and outcome. The Haemtrack system is being regularly used by as many as 2,683 UK patients with bleeding disorders (mainly PWH), with a median rate of overall compliance of 78%[21]. A new strategy intended to improve patient reporting compliance is now being developed[21]. In Ireland, the National Centre for Hereditary Coagulation Disorders has also produced a mobile phone app with the aim of tracking and tracing the antihaemophilic products used in hospital and at the patients' homes. The initiative was enthusiastically received by both patients and their caregivers, and hopefully the data obtained will be made more widely available.

In Italy, the Angelo Bianchi Bonomi Hemophilia and Thrombosis Centre recently developed an interactive online register also accessible to patients through a free smartphone app and web portal called mAPPHemo. This app is designed for surveillance of the new antihaemophilic drugs that are being licensed, with the goal of strengthening pharmacovigilance and to report adverse reactions to the competent regulatory agencies. This initiative is consistent with ad hoc recommendations made by the International Society on Thrombosis and Haemostasis (ISTH)/Scientific and Standardization committee (SSC) subcommittee on Factor VIII, Factor IX and Rare Coagulation Disorders. Apps on mobile phones also have a great potential to connect to social networks created specifically for PWH with the aim of providing this patient community with peer interactions. This resource is particularly needed when children move from paediatric to adult treatment centres, at a time when many adolescents report feelings of isolation[19]. Both social networks and mobile phones, which play an important role in the life of most adolescents, offer health benefits to those with rare and chronic conditions, reducing isolation, exploring the advantages of mutual support, and encouraging positive health choices. A pioneer example for PWH is SixVibe, developed by the Haemmet charity and endorsed by the UK Haemophilia Society. It is a website that provides peer-to peer support and a source of disease-related information to teenagers with haemophilia and related disorders. New has reached us that this website has recently been closed down in the UK, perhaps because over there young PWH felt little need to interact with their peers with haemophilia. However, this experience may be implemented with more success in other countries. An ongoing and more successful example is the Alisei® app (both Android and iOS), designed and developed in Italy by the Paracelso Foundation (www.fondazioneparacelso.it). Its main goals are to create a platform that connects PWH from different countries, allowing, for example, information that is needed when a patient is travelling to be shared. Once registered, a PWH can establish the days and times when he is available and be contacted by other users who need help and information. Travellers can simply open a map to locate other users and contact them via the app, WhatsApp or email. Besides providing information on the nearest treatment centre, the Alisei community members can also obtain advice on matters that are important for them at the time of travelling, such as, for example, accessibility to beaches, museums and restaurants.

Wearable sensors

In PWH, arthropathy and the fear of further bleeding tend to cause inactivity. This may lead to a higher consumption of factor replacement therapy because subjects are overweight, but also to a vicious circle of undue burden on the musculoskeletal system. Moreover, it is generally well established that poor levels of physical activity is one of the main risk factors for cardiovascular diseases, diabetes and cancer, ailments that do not spare the ageing PWH. Wearable fitness trackers have been designed as wellness devices offering potential benefits in healthcare. They are able to monitor daily physical activity, with the broad goal of walking a certain number of steps or other physical activity targets. Perez Alenda *et al.*[22] evaluated their usefulness in 26 patients with severe haemophilia on prophylaxis regimens who used the Fitbit Charge bracelet for 13 weeks. After the trial, participants filled in a questionnaire that assessed the perceived utility of fitness tracking, ease of use, attitudes towards use, and the actual use of the tracker. The number of daily steps were found to be satisfactorily high throughout the study period, and PWH perceived the tool to be useful for self-checking daily physical activity and stimulating a more active lifestyle[2].

Serious games (exergames) for telerehabilitation

Motivation and sharing are key factors when a rehabilitation programme is prescribed to patients, because these features influence the achievement of the desired objectives. This is particularly true when

exercise programmes have to be carried out at home, where the absence of the healthcare provider can very quickly reduce motivation. Driven by the recent increase in the popularity of videogames, their potential in the field of healthcare, and particularly in rehabilitation, is being explored by means of the so-called exergames or serious games, which are recreational activities developed for rehabilitation or educational purposes[23]. They are particularly important for younger users, who appreciate messages on health topics offered in the form of competitive video games. These programmes also allow greater user autonomy and effectiveness because of their flexibility in terms of where and when they can be accessed. Traditional rehabilitation requires a therapist that prescribes exercises in the context of healthcare settings, modulates them at the right level of difficulty, monitors patient movements, and involves him/her in evaluating the feasibility of the most difficult exercises. These elements must be also present when rehabilitation is carried out at home without the presence of the physiotherapist, because otherwise exercises may become ineffective or even detrimental. For this reason, monitoring by the therapist and the motivation of the user are both crucial requirements when rehabilitation systems are designed for a home setting. It is also essential that the therapist is included in the process, to ensure that appropriate programmes are developed for each individual patient, and also to actually evaluate his/her performances.

Devices like Nintendo® (Kyoto, Japan), Wii™, Balance Board™ and Microsoft® Kinect (Redmond, WA, USA) make the video game interface more natural and intuitive. The ability to measure and monitor the movements of the players was soon recognised as an important step forward towards the creation of reliable rehabilitation systems, in which the patient can be guided through exercises by appropriate video games. However, available video games, originally developed for the entertainment market, are not suitable for the pace and objectives of rehabilitation in PWH, because they demand fast interaction, which does not really correspond to the limited functional capabilities of some PWHs. Moreover, the numerous destructors included in videogames make usability poor and may produce tension and anxiety. Another important problem in the application of exergames to PWH is the definition of programmes based upon important training principles. For example, programmes should progress with an increasing level of difficulty, mapped on the rehabilitation plan and its objectives. In order to try to tackle these problems, within the framework of the Rehabilitative Wayout In responsive home Environments (REWIRE) project, Borghese *et al*.[24] have developed the Intelligent Game Engine for Rehabilitation (IGER), originally designed to improve posture and balance in patients with stroke involved in rehabilitation programmes after hospital discharge. Exergames can be implemented at three hierarchical levels:

- *Patient station*: installed in the patient's home, it consists of a computer connected to a TV screen, a Microsoft® Kinect sensor, and a balance board. The patient watches himself/herself or an avatar on the TV screen that moves in the frame of a virtual game to carry out the activities selected by the therapist. Physiological and movement data are also combined so as to set the exercises at the appropriate level of difficulty and to assess the potential risks. If the sensors detect that an exercise has not been performed correctly, corrections are implemented by means of visual feedback (such as an avatar representing a virtual physiotherapist) or warning signals.
- *Hospital station*: this is set up at the hospital facilities of the clinical staff (for example, the physiotherapist) to define, plan and monitor the rehabilitation exercises required. The hospital station can see and record the movements and data collected while the patient remains at home. Thus, the therapist understands whether or not the prescribed exercises are carried out regularly and is able to analyse the outcome of the sessions, both in the short and in the long term. This allows the degree of success and failure of the process to be evaluated, and to provide a solid base for more effective rehabilitation planning.
- *Networking station*: this additional item can be installed at a wider regional level, in order to allow to gather more global data. Linked in a collective way to the rehabilitation of individual patients, its role is to analyse, interpret and use data from the multiple network-associated hospitals. These data are able to create collective knowledge and allow common characteristics and trends of rehabilitation treatments among different hospitals and regions to be identified. Therefore, using this additional networking station, researchers and health service officials will be able to evaluate and have access to a larger amount of data in order to answer questions related to epidemiology and penetration of healthcare programmes and patient compliance.

With this background, REWIRE was used as a model for a project developed to test the exergames also in haemophilia. In a joint collaboration project between the Department of Computer Science of the University of Milan and the Angelo Bianchi Bonomi Hemophilia and Thrombosis Centre at Milano Policlinico Hospital, we developed a game system that uses some tools of other platforms (Microsoft® Kinect and a balance board) and offers young PWH

exercises aimed at strengthening lower and upper limb and trunk muscles, and to improve proprioception and body balance, thus helping to achieve correct and functional locomotion control. The exercises done at home are controlled and adapted day by day at a distance by the physiotherapist who can check through the personal computer portal of each PWH to verify if and how the programmes are being carried out. The programme can then, therefore, be modified to make it as effective and personalised as possible. Preliminary results of this programme of exergames have been reported in abstract form[25].

Conclusions

Telemedicine should become a more widely used tool in the broad management of PWH, thus helping to reduce the time and costs needed to reach the treatment centres and allowing a better adherence to the prescribed treatments, as already attempted in the frame of more common chronic conditions such as COPD and heart failure. Among the various tools of telemedicine, videoconferencing can provide health providers with a faster and more focused assessment of actual bleeding episodes. The use of mobile phones and related apps allows patients to better handle, manage and monitor replacement therapies, particularly for the many new products that are becoming available in haemophilia. They also allow peer interactions through dedicated social networks. In order to improve lifestyle, easy-to-use portable sensors can establish the goal of a given number of daily walking steps, and thus stimulate PWH to do more physical activity and get fitter. Finally, exergames are more recent tools for telerehabilitation with benefits for the musculoskeletal system while at the same time motivating PWH by exploiting the leisure characteristics of videogames.

All the technologies discussed here have only just started to be used in PWH. In general, telemedicine is a recent and rapidly evolving field, and the few related studies published so far have only involved a small number of PWH, and mainly tested the feasibility and acceptability of this new form of healthcare delivery. Solid data on the effectiveness of tools such as exergames in order to tackle rehabilitation after orthopaedic procedures or management of the muscoloskeletal problems associated with target joints are currently lacking. Therefore, more extensive data are needed in the near future through the involvement of different centres specialised in haemophilia. The goals are to establish more objectively the actual health benefits of telemedicine through follow up over time, and to evaluate the effects of telerehabilitation on important clinical outcomes such as the maintenance of the functional integrity of the musculoskeletal system.

Of course, telemedicine has its own limitations. It may encourage the tendency of some patients, particularly adolescents and older adults, to slacken the relationship with the haemophilia treatment centres. Telemedicine cannot replace physical examination of the patient and the compilation of such important scores as the Haemophilia Joint Health Score. The issue of privacy protection must be tackled. Patients should be adequately informed and signing an informed consent form should be mandatory.

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