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A systematic review of research into rare diseases in the educational sphere

Leire Darretxe[1]*, Zuriñe Gaintza[2] and Javier Monzon-Gonzalez[3]

[1]Department of Didactic and School Organization, University College of Teacher Training, University of the Basque Country, Spain.
[2]Department of Didactic and School Organization, University College of Teacher Training, University of the Basque, Spain.
[3]Department of Didactic and School Organization, Faculty of Education, Philosophy and Anthropology, University of the Basque, Spain.

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Rare diseases (RDs) represent a wide, varied group of illnesses characterised by their low prevalence among the population. Moreover, they can appear at any time of life, including in infancy. For this reason, the aim of this article was to review and analyse research in the field of education to find out what kind of educational response is offered by schools to pupils with RDs. The following databases were used to find the pertinent bibliography: Web of Science, Scopus, Education Database (Proquest) and Eric. After retrieving the publications included in this study, each paper was reviewed and analysed on the basis of what journal they were published in and their abstracts. Out of the 53 studies included, only six bore any relation to the school context. The results showed that while there are scientific papers on RDs, most of them are restricted to the medical sphere. It was therefore concluded that further research is needed in the field of education to advance in the schooling of pupils with RDs.

Key words: Rare diseases, inclusive education, school, systematic review.

INTRODUCTION

Rare diseases (RDs) include those disorders that affect a small fraction of the population, < 5 in 10,000 people according to the European Union definition (Taruscio et al., 2011). Despite this low prevalence, according to the World Health Organisation (WHO), RDs affect large numbers of people, there being nearly 7,000 RDs, which affect 7% of the world's population. As RDs are a public health issue, there are various sources of information and training, the first source of knowledge about education being the Orphanet database (Kovács et al., 2013). Analysis of this database reveals that many of the RDs also affect children of school age. For example, some of the RDs that affect children are:

(1) Dravet syndrome,
(2) Angelman syndrome,
(3) West syndrome,
(4) Prader-Willi syndrome,
(5) Williams syndrome,
(6) Stüve-Wiedemann syndrome,

*Corresponding author. E-mail: leire.darretxe@ehu.eus.

(7) Apert syndrome,
(8) Ehlers-Danlos syndrome,
(9) Duchenne muscular dystrophy and Interstitial lung disease.

Depending on the illness, diagnosis of RDs may be possible before birth, at a very early age or it can be taken between the ages of 5 and 30 (Tambuyzer 2010), in most cases being a period of between 10 and 15 years.

Nevertheless, it has been observed that the developmental stage at which the RD appears and is diagnosed essentially matches the school level. That is to say, many children can be diagnosed with RD from the moment they are enrolled at school, and many others will display symptoms while at school that will lead to subsequent diagnosis of RD.

Without any doubt, catering for these pupils will be a challenge for any school, since it is the job of the inclusive school to adapt and adjust the context itself to foster an education accessible to all children (Bryant et al., 2008).

As Rose (2002) points out, teaching staff must be aware of their pupils' needs and be able to give an educational response to meet these needs. But what happens when this need involves minority diversity? More so, what happens when these needs are not known, even in the medical sphere? In general terms, it can be said that teachers do not feel qualified to perform the tasks that the inclusive school sometimes demands of them (McLeskey and Waldron, 2002; Scott et al., 1998). Therefore, thought must be given to the fact that there may be a pupil in the class with an RD of which even the name is unfamiliar to them and they are unsure how to adapt their educational response in the classroom.

Faced with this situation, and in order to provide teachers with the minimum of knowledge they need to fit their educational response to pupils with RD. For this reason, the aim of this article was to review and analyse research in the field of education to find out what kind of educational response is offered by schools to pupils with RDs.

Rare disorders

While the definition of RDs is based on the concept of prevalence or the maximum number of patients in a region, ranging in approximate terms from 1 in 1,000 to 1 in 10,000 people (Ayme et al., 2015), it differs from country to country (Dragusin et al., 2013; Facey et al., 2014; Facey and Hansen 2015). There is no single description of RDs for everybody (Cui and Han, 2015). Despite this lack of consensus, RDs display common specific features, which are:

(1) Low prevalence among the population,
(2) A wide diversity of diseases and symptoms,
(3) Difficulty in diagnosing many of them and,
(4) A lack of effective therapies (Taruscio et al., 2014b).

Even though, as already pointed out, RDs are pathologies with a low prevalence, there are large numbers of people in the world with RDs, as according to the World Health Organization there are about 7,000 existing RDs. Experts estimate that around 400 million people around the world are patients with some RD or the other (von der Schulenburg & Frank 2015). This figure is corroborated by Fagnan et al. (2015), who point out that at world level RDs affect about 350 million people.

It can therefore be stated that RDs are a broad, varied group of serious, incapacitating illnesses. Many RDs are complex, degenerative, chronic and debilitating, while others are compatible with a "normal" life if they are diagnosed in time and if given suitable treatment (Moliner and Waligora, 2013). These diseases can appear at any phase of life and their diagnosis is often difficult and late (García, 2013; von der Schulenburg and Frank 2015).

Diagnosis of the disease nearly always means a cul-de-sac in treatment terms. Due to the features of RDs, providing adequate treatment is more difficult than with common diseases (Schultz et al., 2012). Treatment varies in each case and only some RDs can be treated with medication known as orphan medicines (Ramalle et al., 2015).

Unfortunately, designation of a "rare" disease is associated with some substantial profits for the companies that play a role in developing new drugs. These drugs, known as orphan medicines, have major financial implications both for pharmaceutical concerns and for insurers (Clarke et al. 2014). On the other hand, RD patients and their families often require more social and health resources than most, and have to devote a large proportion of their household budget to meeting these needs (García, 2013). This fact causes not only financial problems for patients and their families but also psychological ones (Taruscio et al., 2014a).

In view of the difficulties encountered by people with RDs, they are beginning to join together and different associations are emerging to study, explain, and combat the impact the disease has on their lives. Since the 1980s, these patients' organizations have been meeting to help advance therapies and research (Brouard-Lapointe et al., 2015).

Thus, for example, in the United States in the 80s and in Europe in the 90s certain patients' organizations helped to take care of social justice and fairness regarding questions on RDs (Rabeharisoa et al., 2014). Both in the USA, with the National Organization for Rare Disorders (NORD) and in Europe, with the European Organization for Rare Disorders (EURORDIS), these organizations have influenced policy in their respective countries. While these alliances are forming more slowly

elsewhere in the world, organizations of this kind also exist in, for example, Taiwan and Japan in the eastern Asia and in Columbia in Latin America.

References on RDs do not only appear in Europe and the United States. Research in this area is also emerging in other countries including China, Brazil, Russia and Australia. In China, public awareness on RDs has risen in the last decade, though no legislation exists on developing treatments (Cui and Han, 2015). China has no official definition for RDs, and the official World Health Organization existing definition is not sufficient to guide the Chinese government in developing specific strategies on orphan medicines.

In Brazil, RDs are receiving more attention than in the past (Fioravanti 2014). In Russia, Fedyaeva et al. (2014) state that classifying and prioritizing RDs is crucial to determining what state support measures are justified. And in Australia, despite having some of the best health indices, in the field of RDs the country is trailing behind other developed nations (Kirby, 2012).

With regard to the United States, the U.S. Food and Drug Administration's (FDA's) Office of Orphan Product Development (OOPD) defines an RD as an "orphan" disease affecting less than 200,000 patients. It is estimated that 25 to 30 million Americans are affected by one of the more than 6,800 RDs recognised by the US National Institute of Health (NIH) (Fagnan et al., 2015; Groft 2013). This means that about 6% of the general population of the USA has a rare disease (Groft and Rubinstein 2013).

In Europe, according to EURORDIS, an RD is any illness that affects a small percentage of the population (1 in 2,000). Despite their low prevalence, put together they account for 6 to 8% of the population, affecting between 27 and 36 million people (Moliner and Waligora, 2013; Taruscio et al., 2014b). The EURORDIS patients' organization is dedicated to improving quality of life for people suffering some kind of RD. In this respect, it has played a part in setting up Centers of Expertise (CE) and European Reference Networks (ERNs) for people with RDs since 2004. CEs are defined as highly specialized physical structures for dealing with and caring for patients with RDs. Their role is to offer high-quality care: to speed up the process of early, appropriate diagnosis and make adequate treatment possible for patients.

Monitoring of RDs is assured at regional, national, European or international level. Each CE specializes in a single RD or in a group of them in order to meet both the medical and social needs of patients. The designation of CEs is an important step as it provides the basis for connection to the next level of cooperation at ERN level (Ayme and Rodwell, 2014; Taruscio et al., 2014b). ERNs represent the best way to speed up access to appropriate and timely diagnosis as well as suitable care, since they are networks to share experience by connecting CEs together at European level (Andersen et al., 2014).

The same authors state that on 24th October 2011, EURORDIS contributed to the approval of the Recommendation of the European Committee of Experts on Rare Diseases (EUCERD), whose subsequent job was to make recommendations for setting up both CEs and ERNs. EUCERD was recently replaced by the Commission Expert Group on Rare Diseases (Aymeand Rodwell, 2014; Taruscio et al., 2014a). Another major step forward in the level of cooperation came about in 2009, when NORD and EURORDIS signed a memorandum of understanding, formalizing an alliance between the two organizations (Mavris and Dunkle, 2014). The purpose of this alliance is to connect patients and patients' organizations in the USA and Europe, focusing particularly on areas related to education, awareness, advocacy and public policy. Thus, it can be said that the current community of people with RDs is becoming a co-international movement.

The different levels of cooperation proposed up to now form part of an institutional framework all work as official bodies and submit their respective statutes. However, communication via social networks should not be forgotten. In the case of RDs, due to their low prevalence and the lack of experience, on the one hand patients are obliged to seek knowledge about their own condition using the net (Budych et al., 2012). Social networks of patients offer people with specific health problems the chance to share experiences as well as to seek, receive and provide information, advice and even emotional support online (Torrente et al., 2010).

On the other hand, researchers feel the need to fall back on social media to find out about a particular RD and at the same time to share knowledge with other researchers who are probably far from where they are. Like this, Facebook, Internet forums and traditional website become contexts for conducting research (Schumacher et al., 2014). According to Facey et al. (2014), new forms of research using social networks, blogs, etc. can prove to be valuable resources to connect patients all over the world and so help to describe their illness and its impact. Both social networks and the job done by patient support networks have helped to considerably raise public awareness of RDs in recent years.

In recent decades recognition that RDs are an important medical and social problem has grown constantly in the public mind as a result of the work of active advocacy groups which include academics and politicians (Schieppati et al., 2008).

Doctors must recognize the active role of patients in approaching planning processes, while patients must play a part in innovation and change (Schultz et al., 2012). In fact, it is undeniable that people with RDs are playing an active, decisive role in determining policy and research projects (Luzzatto et al., 2015; Moliner and Waligora 2013). Numerous experts opt for patient-centered research to provide better-quality services for RDs (Facey and Hansen, 2015; Kesselheim et al., 2015).

Table 1. Results from international databases.

Term in the title	Web of science	SCOPUS	Education database (Proquest)	ERIC	Total
"Rare diseases"	1119	1894	24	2	3039
+ "Education"	6	8	0	0	14
+ "Educational"	2	1	0	0	3
+ "Inclusion"	0	1	0	0	1
+ "Integration"	2	3	0	0	5
+ "Mainstreaming"	0	0	0	0	0
+ "School"	1	0	0	0	1
+ "Teacher"	0	0	0	0	0
+ "Support teacher"	0	0	0	0	0
+ "Students"	4	1	0	0	5
+ "Classroom"	0	0	0	0	0
+ "Special needs"	1	0	0	0	1
+ "Disability"	6	7	1	1	15
+ "Curriculum"	1	1	0	0	2
+ "Methodology"	10	7	0	0	17
+ "Collaboration"	7	9	0	0	16

With this study, as professionals in the educational sphere in favour of inclusive schools, we set out to consider the issue of RDs from an educational point of view. As already pointed out, the aim of this paper was to review and analyse research in the field of education to find out what kind of educational response is offered by schools to pupils with RDs.

METHODOLOGY

Search procedures

Using the Web of Science, Scopus, Education Database (Proquest) and Eric database systems, between the years 2000 and 2016, a computer search of the literature was conducted. While Web of Science and Scopus are multi-disciplinary databases, the other two databases selected (Education Database Proquest and Eric) are specific to the educational sphere.

Initially, to find out what research existed in the field of RDs, the term "rare diseases" was searched for in the title of the paper. Subsequently, to find out how many pieces of research corresponded to the educational sphere, the above term was combined with others related to education. Before beginning the search, an iterative process of searches for tests was undertaken to determine which search terms would find the widest range of relevant studies. This used term was already used in other reviews related to schools or inclusive education (Alkhateeb et al., 2016; Begeny and Martens, 2007; Demetriou et al., 2015).

In this way, 15 search terms were established: “education”, “educational”, “inclusion”, “integration”, mainstreaming”, “school”, “teacher”, “support teacher”, “students”, “classroom”, “special needs”, “disability”, “curriculum”, “methodology”, “collaboration”.

Inclusion criteria

As pointed out earlier, the searches were for the term in the title. If the title suggested that the research could meet the criteria for inclusion, the abstract of the article was then examined. If the abstract indicated that the research did deal with RDs in the educational sphere, then the paper was ordered and reviewed to determine whether the study did in fact match the criteria for inclusion. Initially, a study was included if it fulfilled the following conditions:

(1) It was published between the year 2000 and December 2016.
(2) The term was included in the title.

RESULTS AND DISCUSSION

This analysis led to a total of 80 documents being included in the review (Table 1). On the one hand, searching for the term “rare diseases” as a title of studies, both in the Web of Science database and in Scopus, gave quite a lot of results.

However, when education-specific databases like Education Database Proquest and Eric were used, hardly any academic articles relating to RDs were to be found. On the other hand, when the search term was supplemented by another related to the educational sphere, the results were considerably less. Only 3.5% in the Web of Science database and 2% in Scopus had any education-related term in the title. There was a much more drastic reduction in the number of studies in the education-specific Proquest database.

The study by Cismondi et al. (2015) that set out to develop guidelines for improving scientific knowledge about RDs found a situation similar to that shown by this study. When the database in the medical field pub MED was analysed for the period 2005 to 2014 it showed that 12,646 papers on RDs had been published, but when the

term medical education was specified the number fell to 377. The study concluded that, “the issue of medical education in RDs is not ‘specifically’ described in the articles analyzed”.

Out of the 80 shown in Table 1, a total of 27 papers were in more than one database, so in the end the study had 53 papers. These papers where there appeared to be a link between RDs and education were analysed in detail, revealing the following:

As regards the journal in which they were published, it was found that the vast majority, 97.4%, appeared in journals indexed in databases in the medical field, MEDLINE and/or Embase and/or pub Med, etc. After reading the abstracts it was found that, even though one of the terms in the educational sphere appeared in the title, the content of the paper was medical. Some were related to the training of medical and healthcare staff in the field of RDs (Jinnah, 2011; Van Karnebeek et al., 2012). Others had to do with university studies and knowledge, as in the case - for example - of the paper by Cismondi et al. (2015), which addressed the educational issues associated with particular rare diseases in the curricula of Health Sciences and Professional Training Programs. Many others presented a study related to a particular RD, for example that by Chisolm et al. (2014) or that by Smith et al. (2014).

Thus, only six (Barrio and Castro, 2008; Han, 2008; Lee and Lee, 2014; Lin et al., 2013; Silibello et al., 2016; Waldman et al., 2008) of the studies analysed were at all related or included any information of interest to the education/school sphere.

These papers showed no general pattern and each of them had its own characteristics. The paper by Lin et al. (2013) described a general demographic picture of patients with rare diseases and the prevalence of rare diseases over time, age and gender distributions.

The study highlighted that the incidence of RDs increased significantly in children from 3 to 5 years old and schoolchildren from 6 to 14 years old. This only confirms the fact that there may be pupils with RDs in schools. The study by Waldman et al. (2008) underlined that one of the common features of RDs is the social consequences that impact on schooling, these pupils' future jobs and free time with friends.

Two papers published in 2008 focused on the educational response needed by pupils with RDs, arguing that as they have more complex educational needs it is essential to offer educational support strategies (Han, 2008) as well as good coordination between school and family (Barrio and Castro 2008).

Also in the school context, the study by Lee and Lee (2014) recorded the experiences and needs of pupils diagnosed with a particular RD, specifically congenital vascular malformation. Going a little further in the analysis of the situation of people with RDs, the study by Silibello et al. (2016) recorded, through questionnaires, the voice of 154 families with children with RDs in the school context.

This study confirmed both the existence of pupils with RDs in ordinary schools and that of an educational response aimed at them. However, despite the existence of this response, parents with severely disabled children were less happy with the education system than the rest and considered family-centred attention and multi-disciplinary work to be essential (Silibello et al., 2016).

The four papers directly related to the school context all point outed that: these pupils were considered pupils with special educational needs; they needed both educational support and adaptations to the curriculum; maximum knowledge of pupils with RDs was needed in order to tailor the educational response; and multi-disciplinary work was needed between the different professionals to improve quality of life for these people and their families.

Conclusions

It can nevertheless be concluded that, on the one hand, this study shows there is interest in research into RDs in the medical sphere, and on the other that there are pupils with RDs in ordinary schools. There is very little research in the latter sphere to determine, as this study aimed to do, what kind of educational response is offered to pupils with RDs in schools. Therefore, in this sphere we see a need to call for more attention to be paid to research, to transform and make progress in the educational response to pupils with RDs within the framework of inclusive schooling.

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CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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