Official Journal of the European Paediatric Neurology Society

Original article

Ethical management in the constitution of a European database for leukodystrophies rare diseases

Nathalie Duchange [a,*], *Sylviane Darquy* [a], *Diane d'Audiffret* [a], *Ingrid Callies* [a], *Anne-Sophie Lapointe* [a], *Boris Loeve* [a], *Odile Boespflug-Tanguy* [b], *Grégoire Moutel* [c,1]

[a] *Université Paris Descartes, EA 4569, Ethique Médicale, 75006 Paris, France*
[b] *Assistance Publique – Hôpitaux de Paris, Hôpital Robert Debré, Service de Neuropédiatrie, 75020 Paris, France*
[c] *Assistance Publique – Hôpitaux de Paris, HEGP – Hôpital Corentin Celton, Unité de Médecine Sociale, 92133 Issy-Les-Moulineaux, France*

ARTICLE INFO

Article history:
Received 16 August 2013
Received in revised form
17 February 2014
Accepted 4 April 2014

Keywords:
Rare disease
Leukodystrophy
Health database
Ethics committee
Ethical management

ABSTRACT

Background: The EU LeukoTreat program aims to connect, enlarge and improve existing national databases for leukodystrophies (LDs) and other genetic diseases affecting the white matter of the brain. Ethical issues have been placed high on the agenda by pairing the participating LD expert research teams with experts in medical ethics and LD patient families and associations. The overarching goal is to apply core ethics principles to specific project needs and ensure patient rights and protection in research addressing the context of these rare diseases.

Aim: This paper looks at how ethical issues were identified and handled at project management level when setting up an ethics committee.

Methods: Through a work performed as a co-construction between health professionals, ethics experts, and patient representatives, we expose the major ethical issues identified.

Results: The committee acts as the forum for tackling specific issues tied to data sharing and patient participation: the thin line between care and research, the need for a charter establishing the commitments binding health professionals and the information items to be delivered. Ongoing feedback on the database, including delivering global results in a broad-audience format, emerged as a key recommendation. Information should be available to all patients in the partner countries developing the database and should be scaled to different patient profiles.

Conclusion: This work led to a number of recommendations for ensuring transparency and optimizing the partnership between scientists and patients.

* *Corresponding author*. Ethique Médicale, EA 4569, Université Paris Descartes, Faculté de médecine, 45 rue des Saints-Péres, 75006 Paris, France. Tel.: +33 (0) 1 42 86 41 35; fax: +33 (0) 1 42 86 41 33.
E-mail address: nathalie.duchange@inserm.fr (N. Duchange).
[1] Present address: Equipe Management des organsiations de santé (MOS), PRES Sorbonne Paris Cité/EHESP, France.
http://dx.doi.org/10.1016/j.ejpn.2014.04.002
1090-3798/

1. Introduction

Patient registries and databases are key tools for the development of biomedical and clinical research – particularly in the field of rare diseases which faces specific challenges tied to small patient populations and variations among disease subtypes. Gathering information on a large scale has considerable potential for helping to improve diagnosis and treatment, promote the development of clinical trials, and facilitate recruitment.[1,2]

One aim of the EU LeukoTreat program (www.leukotreat.eu) is to develop a supranational database geared specifically to leukodystrophy (LD) – the LeukoDataBase (LeukoDB). Collecting clinical data on LD patients will improve understanding of the natural history, epidemiology and genotype–phenotype correlations of these disorders. The challenge is to connect, enlarge and improve pan-European databases on LDs and other genetic diseases affecting the white matter of the brain. Addressing this challenge entails organizing the collection and management of clinical and biological data, including genetic information. The objective is to foster the emergence of innovative therapeutic strategies as part of translational research designed to accelerate the clinical application of fundamental research results.

LDs are a group of rare genetically inherited neurodegenerative diseases of the white matter and its main component, myelin. LDs predominantly affect young children but can also hit adults, causing cognitive deficits and potential loss of autonomy. The overall prevalence of LDs is approximately 1 in 10,000 of the population, with around 1000 new cases every year in Europe. Despite great strides forward made over the past decade in terms of advance in each individual LD, there is currently still no curative therapy (see, Ref. 3,4 for review).

LeukoTreat has placed ethics issues high up the agenda by pairing the participating LD expert research teams with experts in medical ethics and LD patient families and associations. The overarching goal is to apply core ethics principles to specific project needs and ensure patient rights and protection in research addressing the context of these rare diseases. The ethical approach was integrated right from the project's outset to handle the sharing of medical information at a European level in the context of LD patients, which are a heterogeneous population characterized by variable clinical expression and age of appearance. This approach also considers the harmonization of information and consent on existing practices in national databases.

This paper looks at how ethical issues were identified and handled at project management level during the project lifetime.

2. Synergy between an ethics committee and an ethics research group

Before starting LeukoTreat, the proposal first received approval from the EC ethics review board, which is an integral component of the research evaluation procedure under FP7.[5] The EU report singled out the plan to form a project-long ethics committee as a positive. Indeed, a stand-out feature of LeukoTreat was that it attached a LeukoTreat Ethics Committee (LEC) to the ethics research group involved in the project.

The LEC is composed of two categories of members: project members (clinicians and the ethics research group) and independent non-project members, including international experts in medical ethics, human sciences and law professionals as well as representatives of patient organizations. The LEC was put together in accordance with EU recommendations for ethics review panels.[5] The LEC is dedicated to the LeukoTreat project and is thus a separate entity to Institutional Review Boards (IRB) or Research Ethics Committees (REC) whose role is to review research proposals involving humans. The LEC is responsible for the ethical management and follow-up of the project during its lifetime. Its role is to help identify specific issues and facilitate discussion and awareness among project partners, especially those involved both in care and research. The LEC is a forum for discussion and debate: one of its main objectives is to offer guidance to LeukoTreat partners on the issues addressed in the project and on other issues that the Committee may identify over the course of the project.

One of the LEC's first tasks was to produce recommendations and documents framing the database. Together with the ethics research group, the Committee carried out evaluations in the existing national-level procedures with a dual objective: 1) to elaborate rules governing data sharing within the database, and 2) to harmonize information and consent documents.

The work was performed as a co-construction between health professionals, ethics experts, and patient representatives relaying patient expectations. The standpoints and expectations of patients and families were also concurrently investigated via a survey led with French families participating in the annual meeting of the European Leukodystrophies Association (ELA), where 55 questionnaires were returned and analyzed (unpublished results). This approach resulted in the production of a charter defining the binding commitments and responsibilities of health professionals in terms of the preservation, use and sharing of participants' data. Based on international texts and recommendations issued by international organizations,[6–10] the charter develops the main principles on data privacy, regulation of potential value and the exploitation of data, as well as issues tied to consent, information and release of results. The charter anchors transparency as a core functional requirement and an essential tool for answering patients/families' questions on individual elements included in information and consent documents. Indeed, McCormack et al. highlighted that a particular concern and possible source of anxiety for patients and families are ownership of the registry/database and the data contained, as it defines who controls how the data are used.[11] The charter is accessible on the dedicated LeukoTreat website (http://www.leukotreat.eu/leukodatabase-ethics.php).

3. Data sharing in LeukoDB

The primary concern of the LEC was to establish ethical rules governing the sharing of data. The database gathers socio-