

RaDiCo-ACOEIL - National cohort on congenital defects of the eye: natural history, genetic determinisms and improved ocular and extra-ocular outcome prediction for better patient management

Responsable(s) : Chassaing Nicolas , Inserm U 1056
Calvas Patrick

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Général

Identification

Nom détaillé National cohort on congenital defects of the eye: natural history, genetic determinisms and improved ocular and extra-ocular outcome prediction for better patient management

Sigle ou acronyme RaDiCo-ACOEIL

Numéro d'enregistrement (ID-RCB ou EUDRACT, CNIL, CPP, etc.) CCTIRS n° 16.051 / CNIL decision DR-2016-349

Thématiques générales

Domaine médical Disability/handicap
Neurology
Ophthalmology
Rare diseases

Pathologie, précisions microphthalmia, anophthalmia, aniridia, other anterior segment dysgenesis: These ocular defects include a large spectrum of malformations mainly involving cornea or iris. They include the classical Peters, Rieger and Axenfeld anomalies^{8, 9}. Peters' anomaly corresponds to total or central clouding of the cornea associated with irido-corneal synechia. This malformation frequently leads to glaucoma or cataract. Peters anomaly can be isolated or frequently associated with a wide variety of extra-ocular features as with intellectual disability¹⁰. One syndromic form, Peters-plus syndrome is well defined and encompasses Peters anomaly, growth retardation, brachydactyly, intellectual disability, and various other malformations¹¹. Axenfeld-Rieger anomaly corresponds to iris involvement (posterior embryotoxon, iris hypoplasia, corectopia, polycoria) and synechia between iris and trabecular meshwork. Once again, this ocular developmental defect may be isolated or associated with extra-ocular features and intellectual deficiency^{12, 13}.

One syndromic form, Rieger syndrome, consists of Axenfeld-Rieger anomaly together with hypodontia, peg-shaped teeth, facial dysmorphism, and redundant periumbilical skin.

Déterminants de santé
Genetic
Healthcare system and access to health care services
Medicine
Social and psychosocial factors

Mots-clés
Ophthalmic diseases, Rare diseases, Quality of life

Responsable(s) scientifique(s)

Nom du responsable
Chassaing

Prénom
Nicolas

Adresse
Service de génétique médicale - Pavillon Charles Lefebvre
Hôpital Purpan ? CHU de Toulouse
31 059 Toulouse Cedex
FRANCE

Téléphone
+ 33 (0)5 61 77 90 55

Email
chassaing.n@chu-toulouse.fr

Laboratoire
Inserm U 1056

Organisme
Institut National de la Santé et de la Recherche Médicale / French National Institute for Health and Medical Research (Inserm)

Nom du responsable
Calvas

Prénom
Patrick

Adresse
Service de génétique médicale - Pavillon Charles Lefebvre
Hôpital Purpan ? CHU de Toulouse
31 059 Toulouse Cedex

Email
calvas.p@chu-toulouse

Organisme
Institut National de la Santé et de la Recherche Médicale / French National Institute for Health and Medical Research (Inserm)

Collaborations

Participation à des projets, des
Yes

réseaux, des consortiums

Précisions Filières de Santé Maladies Rares (National Rare Diseases Healthcare Networks): SENSGENE and ANDDIRARE

Autres Patient Associations: Microphthalmie France, Gêneris, Retina France

Financements

Financements Public

Précisions Funded by the French « Investissements d'Avenir » cohorts programme, Grant « ANR » 10-COHO-0003.

Gouvernance de la base de données

Organisation(s) responsable(s) ou promoteur Institut National de la Santé et de la Recherche Médicale / French National Institute for Health and Medical Research (Inserm)

Statut de l'organisation Secteur Public

Existence de comités scientifique ou de pilotage Yes

Labellisations et évaluations de la base de données Security audit certification of the database

Contact(s) supplémentaire(s)

Caractéristiques

Type de base de données

Type de base de données Morbidity registers

Informations complémentaires concernant la constitution de l'échantillon Patients from 0 to 7 years old
We aim to include most patients born with a developmental ocular defect. Even if most ocular defects are diagnosed during the first months of age, patients could be included in the cohort until 7 years old (age at the first neuropsychological evaluation). Given the estimated incidence of microphthalmia and anophthalmia (~1/10.000), aniridia (~1/60.000), and other anterior segment dysgenesis (~1/30.000), 80 new patients should be born each year in France (800.000 births/year) with AM, 14 with aniridia, and 27 with other anterior segment dysgenesis. We planned to enrol at least

half of these patients each year (50 patients: 25 with microphthalmia or anophthalmia, 10 with aniridia, and 15 with anterior segment dysgenesis). This estimation is based on our diagnostic activity during the past three years. Indeed, within this period, we recruited each year for diagnostic purpose, 43 unrelated patients (including 33 children) with microphthalmia/anophthalmia, 29 unrelated patients (including 14 children) with aniridia, and 25 unrelated patients (including 19 children) with anterior segment dysgenesis.

Patients over 8 years old

Affected adults and children over 8 years old will not be included in the follow-up subgroup. However their phenotype (ocular defect, extra-ocular malformations, and visual and neurological outcome) will be retrieved in the database as retrospective cases to increase collected data about outcome of patients affected by these ocular defects. We retrieved historic patients (150 patients or families with microphthalmia/anophthalmia, 100 with aniridia and 80 with anterior segment dysgenesis) in our clinical database (CNIL authorisation 1458306V0 du 09-10-2010) through our diagnostics laboratory. These patients will be contacted again by their geneticist or ophthalmologist to participate to the standard evaluation procedure. In addition to these already known patients, we are still collecting each year about 30 ?novel? adult patients through this diagnostics activity. Combining the known cases, and the newly identified adult (or children over 8 years) cases, we could expect to enrol at least 30 patients each year in this subgroup.

Study duration

- Up to ten year follow-up of patients under 7 years old at time of inclusion (incident subgroup): two evaluations after inclusion (at 6-7 years old and 9-11 years old)
- Unique evaluation of patients over 8 years old (? prevalent subgroup?) at time of inclusion.

Objectif de la base de données

Objectif principal

Main objective

The principal objective of this study is to delineate the long term outcomes of the patients with ocular developmental defects, focusing on visual and neuro-developmental issues.

Secondary objectives

I) Identification of prognostic factors (such as ocular defects, unilateral or bilateral involvement, extra-ocular malformations) that would be associated with unfavourable visual and/or neurologic outcome. These data will be essential for the formulation of recommendations to enhance diagnosis and patient management.

II) Repercussions of the ocular developmental defects on patients and families quality of life.

Exploratory objectives

Searching for potential genotype/phenotype correlations to unravel

- the frequency of implication of each gene in these ocular developmental defects;
- the phenotypic spectrum associated with mutations in these genes;
- the identification of novel genes involved in these ocular developmental defects.

Given genotyping will not be mandatory to participate to the cohort; this objective will involve only the patients who accepted it.

Critères d'inclusion

Patients from 0 to 7 years old

- Newborns and/or children from birth to 7 years old, affected with the following ocular defects:

- ? anophthalmia,
- ? microphthalmia
- ? aniridia

? anterior segment dysgenesis

whose parents will have properly evaluated risks (those related to the actual standard of care for these pathologies) and benefits (improvement of knowledge and standard of care) of the study, and will be given an informed consent to participate the protocol.

- Patients affiliated to the "Régime National d'Assurance Maladie"

- Inclusion of foreign patients will be possible through the French inclusion centers when they agreed to be charged for all medical fees.

Patients over 8 years old

- Children from 8 years old, affected with the following ocular defects :

- ? anophthalmia,
- ? microphthalmia
- ? aniridia

? anterior segment dysgenesis

whose parents will have properly evaluated risks and benefits of the study, and will be given an informed consent form to participate to the protocol.

- Patients affiliated to the "Régime National

d'Assurance Maladie"

- Inclusion of foreign patients will be possible through the French inclusion centres when they agreed to be charged for all medical fees.

Adult Patients

- Adults affected with the following ocular defects :

- ? anophthalmia,

- ? microphthalmia

- ? aniridia

- ? anterior segment dysgenesis

- Adult patients under guardianship whose guardians will have properly evaluated risks (those related to the actual standard of care for these pathologies) and benefits (improvement of knowledge and standard of care) of the study, and will be given an informed consent to participate the protocol. Indeed, intellectual disability may be associated with the ocular defects and we will need to include these patients in order to evaluate incidence of this event.

- Adult patients able to properly evaluate risks (those related to the actual standard of care for these pathologies) and benefits (improvement of knowledge and standard of care) of the study and to give their informed consent to participate to the protocol.

- Adult parents of an affected child participating to the study and willing to participate to the inheritance study (results of DNA analysis).

- Patients affiliated to the "Régime National d'Assurance Maladie".

- Inclusion of foreign patients will be possible through the French inclusion centres when they agreed to be charged for all medical fees.

- Pregnant women can be included in the study (as examination proposed have no interference or adverse effect during pregnancies).

Non-inclusion Criteria

- Patients with ocular developmental defects other than the ones listed above.

- Patient or patients' parents/tutor not able to approve or declining participation to the protocol.

- French patients not affiliated to the "Régime National d'Assurance Maladie" or foreign patients not willing to pay charges of medical services.

Type de population

Age

Newborns (birth to 28 days)

Infant (28 days to 2 years)

Early childhood (2 to 5 years)

Childhood (6 to 13 years)

Adolescence (13 to 18 years)
Adulthood (19 to 24 years)
Adulthood (25 to 44 years)
Adulthood (45 to 64 years)
Elderly (65 to 79 years)
Great age (80 years and more)

Population concernée Sick population

Pathologie Q11 - Anophthalmos, microphthalmos and macropthalmos

Sexe Male
Woman

Champ géographique National

Détail du champ géographique All French territory via rare disease reference and competence centers

Collecte

Dates

Année du premier recueil 2016

Année du dernier recueil up to 2036

Taille de la base de données

Taille de la base de données (en nombre d'individus) [500-1000[individuals

Détail du nombre d'individus 800

Données

Activité de la base Current data collection

Type de données recueillies Clinical data
Declarative data
Paraclinical data
Biological data
Administrative data

Données cliniques, précisions Direct physical measures
Medical registration

Détail des données cliniques recueillies clinical data, as well as biological, uniform molecular and comparative data of patients suffering from ocular congenital malformations. The retrieved data are dedicated to:- Implement the family history including the pregnancy and delivery follow-up; -

The description of patient's phenotype (either ocular and extra-ocular); - The collection of paraclinic investigations data; - The description of visual and neurologic status;; - The evaluation of sociological state and quality of life

Données déclaratives, précisions

Paper self-questionnaire
Internet self-questionnaire
Face to face interview

Détail des données déclaratives recueillies

SF-36 (adults) / SF-10 (children)

Données biologiques, précisions

For patients agreeing to have such analysis, molecular screening for diagnosis purposes will be performed by the genetic diagnosis laboratory led by the two principal investigators at the CHU (University Hospital) Toulouse. These analyses include the high-throughput sequencing of, to date, 25 genes known to be involved in these pathologies (ALDH1A3, B3GALTL, BCOR, C12ORF57, CYP1B1, FOXC1, FOXE3, MAB21L2, MFRP, OTX2, PAX2, PAX6, PITX2, PITX3, PRSS56, PXDN, RARB, RAX, RCN1, SIX6, SMOC1, SOX2, STRA6, TENM3, VSX2), and possibly more once new genes will be identified. These analyses are performed by Sanger, targeted sequencing (NGS).; Further molecular analysis for research purposes that may be required for identification of new or modulator genes, will be performed by the EA-4555 research laboratory (research laboratory of the two principal investigators). These analyses will be performed by whole exome and whole genome sequencing.

Existence d'une bibliothèque

No

Paramètres de santé étudiés

Health event/morbidity
Health event/mortality
Quality of life/health perception
Others

Qualité de vie/santé perçue, précisions

SF-36 (adults) / SF-10 (children)

Modalités

Mode de recueil des données

eCRF using REDCap EDC; Cloud based, secure by design web accessible platform. Certified Health Data Hosting resource

Nomenclatures employées

HPO, ICD10, Snomed CT, Orpha Codes and ORDO, Drug dictionary (DCIs)

Procédures qualité utilisées	Continuous data management; Data Management Plan and Data Validation Plan. Native controls and Query system
Suivi des participants	Yes
Modalités de suivi des participants	Monitoring by convocation of the participant Monitoring by contact with the referring doctor
Pathologie suivies	Q11 - Anophthalmos, microphthalmos and macrophthalmos
Appariement avec des sources administratives	No

Valorisation et accès

Valorisation et accès

Accès

Existence d'un document qui répertorie les variables et les modalités de codage

Yes

Charte d'accès aux données (convention de mise à disposition, format de données et délais de mise à disposition)

Access requests to RaDiCo -AC OEIL data (rough / structured), or to analytic reports will be examined by the scientific committee following submission of a Specific Research Project (SRP) synopsis, as defined in the Resource Access Charter. Must be sent to ac-oeil@radico.fr

Accès aux données agrégées

Access on specific project only

Accès aux données individuelles

Access on specific project only