

## Crigler Najjar (CN) disease and liver transplantation

---

M. Sinaasappel

Erasmus MC, Rotterdam, The Netherlands

CN disease is caused by an inherited defect of bilirubin conjugation and biliary secretion resulting in an increase of plasma unconjugated bilirubin (UCB) levels. The prognosis is determined by the occurrence of kernicterus caused by toxic levels of free UCB in the brain. In case of complete absence of bilirubin conjugation this condition starts at birth, while residual capacity is associated with milder course and later presentation of the disease.

The backbone for therapy is intense skin irradiation with blue light (460-480 nm) called phototherapy. This energy source causes configurational changes in the UCB molecule resulting in changes of the lipophilic to hydrophilic characteristics associated with increased biliary secretion of UCB. The limitation of this therapy is the intensity, skin characteristics and the compliance of the patient. Increase of free UCB is seen during infectious diseases, accidental hemorrhage, and low albumin binding of UCB by competition with pharmaceuticals. Many of these conditions occur unexpectedly and are a serious risk for kernicterus. Clinical care needs careful follow up and prophylactic measures. This is very much

dependent on the experience of the team. In expert centers it is possible to prevent complications for many years but in single patient care the course is unpredictable and dangerous for the patient.

The ultimate therapy is repair of the genetic defect in the hepatocyte, but this is so far only achieved in the laboratory setting in animal models. Other possibilities are liver cell transplantation or (partial) liver transplantation.

A world survey showed that the mean time of transplantation was 9 years, but that 26 % of the patients had already neurologic defects at that time. In expert centers it is possible to extend the period to transplantation to young adulthood, but monitoring has to be very careful and finally it is expected that phototherapy alone will be insufficient. Conclusion is that liver transplantation is not a question of if but when.

---

M. Sinaasappel, MD PhD, Erasmus MC, location Sophia, Rotterdam, The Netherlands.  
E-mail: m.sinaasappel@erasmusmc.nl