plasma cholesterol levels and premature development of atherosclerotic cardiovascular disease. Evolocumab is a high-cost monoclonal antibody to PCSK-9, an enzyme critical in cholesterol homeostasis. It is a subcutaneous injection commissioned for HoFH in children ≥12 years with persistently raised LDL-cholesterol (LDL-C) despite maximal tolerated lipid-lowering therapy. There is an unmet clinical need to allow patients ≥6 years meeting the same treatment threshold to access evolocumab and attenuate progression to invasive lipid apheresis or liver transplantation. However, as there are no published studies with PCSK-9 inhibitors in children <12 years, no established dosing regimen exists.

Aims and objectives

- Propose a safe, efficacious and cost-effective dose of evolocumab to be administered to eligible patients aged 6 to 12 years old with HoFH.
- Review all patients at 12 weeks to determine if 30% target LDL-C reduction is achieved thereby warranting treatment continuation in line with commissioning criteria.
- Review all patients at 12 months to establish if LDL-C reduction sustained.
- Assess all patients for incidence and nature of treatment-related adverse effects.

Method

- Proposed evolocumab dosing determined using four criteria: potential dosing adjustments required based on population physiological and pharmacokinetic data, drug safety profile, practicalities of administration and cost implications.
- Clinic letters for all patients were reviewed 12 weeks and 12 months after treatment commenced.

Results

In children <12 years dosing was proposed to start at 140 mg every 2 weeks, as this is the lowest administrable dose but is clinically equivalent to the 420 mg monthly dose (if information is extrapolated from heterozygous familial hypercholesterolemia studies) and more cost-effective in terms of number of injections required. Furthermore, dose reduction in younger patients unlikely to be required as blood volume-dependent clearance of monoclonal antibodies and synthetic rates of PCSK-9 production do not significantly vary with age.

Wide therapeutic index is implied as doses can be increased to 420 mg every 2 weeks and PCSK-9 has a limited physiological role with negligible ‘off target’ toxicity due to its inhibition. Therapeutic drug monitoring is not currently an option. Evolocumab was initiated using the proposed dose regimen in two eligible patients. Patient 1 had a 65% reduction in LDL-C (5.9 mmol/L to 1.9 mmol/L) at week 12, marginally subsidising at 12 months (2.7 mmol/L). No adverse effects reported and patient not yet progressed to lipid apheresis or liver transplantation. Patient 2 had only a 7% reduction in LDL-C (6.97 mmol/L to 6.48 mmol/L) at week 12 therefore evolocumab was stopped. No adverse effects were experienced. Lipid apheresis was continued throughout treatment.

Conclusions and Discussion

Extrapolated dose of 140 mg every 2 weeks was safe and well-tolerated. Larger patient numbers are needed to further determine efficacy and safety, particularly due to promissory significant and sustained LDL-C reduction in one patient. Licensed dose increases due to poor response in patients ≥12 years warrant investigation in younger population to allow potential treatment escalation for refractory patients. Therapeutic drug monitoring and antibody level testing are possible future research opportunities.

REFERENCES

using a compounder or via other method (8% each). Organisations not using AIO PN: 43% of organisations were not planning to use AIO PN or didn’t know and 15% planned to start in the future. 42% selected ‘other’ and gave comments, primarily relating to avoiding AIO PN for neonates, e.g. need to use neonatal network PN (split-phase) or prefer flexibility to stop lipid in case of adverse effects. Eleven organisations answered, ‘Why are you thinking of using AIO PN?’ – examples included releasing aseptic capacity, reducing administration errors/improving safety and the long shelf life of triple-chamber AIO bags. 

Conclusion AIO PN appears to be an appropriate and safe for local use and should be taken into account in national standard paediatric PN formulation design where practicable.

P43 CONCENTRATED STANDARDISED PN TO OPTIMISE NUTRITION IN PRETERM INFANTS

Zoe Price*, University Hospitals Bristol NHS Foundation Trust

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Background In 2010, the NCEPOD1 report demonstrated a lack of good nutritional care for preterm infants. Since that time various approaches have evolved including standardisation of PN,2 concentrated standardised PN3 and publication of a national framework from BAPM.4 The delivery of nutrition to preterm infants on our unit has been continuously monitored, evaluated and adapted.

Aims The aim of this audit was to evaluate whether reformulating our PN recipes would improve nutritional intake and growth parameters over the first 14 days after birth.

Methods Data was collected from our EMMA system and analysed retrospectively from all infants born at our unit <28 weeks gestation or <1Kg from 16/4/2016 to 15/4/2017 (audit 1) and from 1/6/2018 to 31/5/2019 (audit 2).

Results Data from a total of 33 patients was analysed using Excel™. The mean gestation and weight were similar for both audit cycles. Audit 1: gestation 26.5 weeks, weight 0.75 kg; audit 2: gestation 26.7 weeks, weight 0.74 kg. The average time from birth to PN was less in audit 2 (12 hrs 8 mins vs 13 hrs 12 mins), however the time from PN being prescribed to being administered took over 3 times longer (5 hrs 1 min vs 1 hr 30 mins). No patient received PN within 6 hours of birth in audit 2 compared to 20% in audit 1. The average nitrogen intake was higher in audit 2 than audit 1 (0.41 g/kg/day vs 0.36 g/kg/day) and the highest protein intake increased from 0.55 g/kg/day to 0.69 g/kg/day respectively; the average energy intake decreased from 73.5 kcal/kg/day in audit 1 to 68 kcal/kg/day in audit 2. The non-nitrogen energy to nitrogen ratio was lower in audit 2 versus audit 1 (165.3 kcal/g nitrogen vs 204.7 kcal/g nitrogen). There was no change in the percentage of patients requiring insulin: 40%. More patients had started receiving lipid infusion in the first 2 days after birth in audit 2 compared to audit 1 (94% compared to 33%). Both audits had 2 patients that had still not reached their birth weight by day 14, however the patients in audit 2 gained on average 9.12 g/kg/day compared to 4.96 g/kg/day in audit 1.

Conclusion Reformulating the PN resulted in higher nitrogen intakes and higher weight gain by day 14, although the full benefit may not have been achieved due to the lower kcal intake and non-nitrogen energy to nitrogen ratio. The time from birth to PN and the time taken to administer PN once prescribed were longer so work needs to be done on addressing these issues and reducing barriers to nutrition. The total nitrogen intake with PN and EN also needs to be reviewed to prevent excessive nitrogen intake which may result if enteral feeds increase and the rate of PN is maintained.

REFERENCES


P44 VACCINE IN PEDIATRIC CHRONIC KIDNEY DISEASE (CKD) AND HEMODIALYSIS

Aichetou Camara,1 Anaïs Razurel,1 Christelle Moreau,1 Thérèse Kwon,1 Marion Caseris,2 Olivier Boudon,5 Sonia Prot-Labarte,1 Service de Pharmacie, AP-HP, Hôpital Robert-Debré, Paris, France; 2Service de néphrologie pédiatrique, AP-HP, Hôpital Robert-Debré, Paris, France; 3Equipe Opérationnelle d’Infectiologie, AP-HP, Hôpital Robert-Debré, Paris, France; 4Service de pédiatrie, AP-HP, Hôpital Robert-Debré, Département de pharmacie clinique, Université Paris Descartes, Paris, France; 5Service de pharmacie, Equipe Opérationnelle d’Infectiologie, AP-HP, Hôpital Robert-Debré, Paris France

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Aims Chronic kidney disease is a major risk factor of vaccine preventable infectious diseases due to the altered immune system and the natural evolution of the disease. There are differences in the prescription of some vaccines for this population. The aim of this study is to elaborate a vaccination protocol for chronic kidney disease and haemodialysis patients for a better immunization coverage, care and prevention against preventable infectious diseases.

Methods The study was conducted by a multidisciplinary team composed by pharmacists, infectious disease paediatrician and nephrology paediatricians. After a literature research (in Medline with MeSH terms: ‘Kidney Failure, Chronic’, ‘Renal Dialysis’ and ‘Vaccines’)1 2, we compared the French immunization schedule3 for the general population with patient with chronic kidney disease or haemodialysis patients and confront it to the physician practice in our nephrology unit. For each vaccine, we collected the following data: indication, any difference concerning dose, schedule, re-administration, antibody titration and reason for these differences.

Results The literature analysis showed disparate practices among countries and even medical centres. The most concerned vaccines were: hepatitis A and B virus vaccine, pneumococcal vaccine, flu and measles vaccines. The difference between vaccine scheduled concerned the indication (meningococcus A, B, C, Y and W135, papillomavirus), dose (hepatitis B), the schedule (hepatitis B, hepatitis A, pneumococcal, measles), re-administration (hepatitis B, varicella), antibody titration (hepatitis B, varicella). Patients with chronic kidney disease are more susceptible to develop hepatitis B infection. As for adult population, the haemodialysis patients are vaccinated with double dose4 of hepatitis B vaccine. The antibodies

Abstracts