ANAKINRA FOR USE IN NON- JUVENILE IDIOPATHIC ARTHRITIS (JIA) RELATED HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH): EVIDENCE BASE AND FUNDING

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Background Non JIA related HLH is a life-threatening complication that is increasingly recognised in paediatric patients, particularly in those who are unwell in the paediatric intensive care unit (PICU). Untreated or insufficiently treated HLH has a significant mortality rate (up to 53%).

Aim To review the evidence base for the use of anakinra in paediatric patients with non-JIA HLH refractory to systemic corticosteroids in patients who are not fit for treatment as per HLH 2004 protocol.

Methods A PubMed search with words ‘anakinra’ and ‘haemophagocytic lymphohistiocytosis’ was carried out on July 2018 to find out the evidence base with regards to the use of anakinra in non-JIA related HLH. Any published peer reviewed clinical studies or trials (including but not limited to retrospective or prospective controlled trials, comparative studies and observational/cohort studies) were considered. Case reports and series were considered if better evidence studies were not available. A recent case study from a tertiary paediatric centre will be used to illustrate the pathway followed to diagnose non-JIA related HLH and funding options.

Results Although a protocol exists for primary HLH treatment (HLH 2004), including chemotherapy and stem cell transplantation, there is no consensus on how to treat secondary HLH. The literature mainly showed case reports and small case series, describing the use of anakinra collectively for 35 patients (median age 14 to 48 years) who met the HLH 2004 diagnostic criteria with an overall survival rate of up to 88% at time of discharge from the PICU. Anakinra was used at standard doses always in combination with corticosteroids. Some patients also received intravenous immunoglobulin (IVIG) and ciclosporin at the discretion of the medical teams.

Conclusion The evidence for use of anakinra in non JIA secondary HLH is limited to retrospective observational studies and mostly restricted to adult populations. Despite this caveat, these studies have demonstrated that anakinra therapy alongside other non-etoposide immunomodulatory therapies is associated with an improvement in short term survival. In patients with multi-organ dysfunction, who are too unstable to receive the existing etoposide based HLH-2004 treatment regimen due to concerns regarding significant treatment toxicity, personalised non-etoposide therapies including dexamethasone, IVIG, ciclosporin and anakinra may be better tolerated and provide a bridge to future more standardised treatment. Evidence to date shows that relapse of secondary HLH is possible with ciclosporin therapy. In JIA related HLH, anakinra was considered better than ciclosporin at inducing remission and having a lower incidence of adverse effects, and NHS England granted funding for the treatment based on these findings. The available evidence did not show any serious adverse events related to anakinra.

Recommendations This tertiary centre approved the use of anakinra for this patient and future patients with this indication despite lack of reimbursement from NHS England for the drug. An urgent interim policy review will be put together by a team of the British Society of Paediatric and Adolescent Rheumatology (BSPAR) and presented to the NHS England commissioners to seek funding for anakinra for paediatric patients with this indication.

REFERENCES

oncology/bone marrow transplant and haematology ward (Starlight) in 2016 showed that only 33% of fluid prescriptions for PN were written before 6pm. During 2016–2017 Starlight ward piloted a new prescribing system whereby nurses administered PN directly from the prescription used to order PN from the aseptic unit. An audit in early 2018 showed that PN was routinely set-up, checked and started by 1800 hours, nurses were able to plan their time effectively and oncall doctors were only involved if patient condition warranted review. In March 2018 the pilot was replaced with similar redesigned process.

Aim To eliminate the process of prescribing volumes and flow rates for PN on fluid prescriptions. To trial a new PN prescription process on one ward, refine and improve as necessary then adopt across the whole of the hospital.

Methods On Starlight ward in March 2018 a new process for prescribing and administering PN was implemented. Nurses used the prescription for ordering PN from the aseptic unit plus the product insert to set-up, start and sign for administration. A new aseptic unit prescription was created, nursing training was provided and written guidance was issued for nurses on how to perform set-up checks. PN prescriptions were kept on the ward. Stickers that highlighted the patient required PN were placed onto fluid prescriptions to prevent PN inadvertently not being administered.

Results All patients prescribed PN on Starlight ward received it as expected. As nurses had flexibility in PN set-up time once the product was on the ward, patient routine and preference (e.g. going out for day leave) was increasingly taken into account leading to PN often starting after 18 hours. One minor incident relating to stickers occurred which did not affect the patient. Nursing feedback was very positive. By eliminating transcribing, the process was perceived as safer. In July the trial was evaluated and one change was made to the prescription to allow clearer adjustment of PN rate/volume after the infusion began. The prescribing process was implemented on a surgical ward in August and will be rolled out across the rest of the hospital pending the outcome.

Conclusion Simplifying the prescribing process meant PN was administered at a time that suited the patient and nurse. Nurse satisfaction was improved and avoiding transcription was perceived as safer. The process will be rolled out in stages to the rest of the hospital.

Methodology The pharmacy dispensing system was used to trace which BMT, haematology or oncology patients required parenteral nutrition. A combination of the medical notes and the electronic Medway system for those patients’ notes was used to collect data. Data was collected over a 12 month period from March 2017 until February 2018, a total of 29 patients were identified and audited.

Results Alternative feeding routes to PN were deemed inappropriate in all 29 patients. A full plan had only been recorded in the patient notes in just 4% (1/29) of cases. Biochemistry was routinely provided prior to initiating PN but there was a failure to monitor patients needing long term biochemistry with only 11% (1/9) of patients having long term bloods reported. Only 38% (10/26) of patients had PN discontinued when the patient reached two-thirds of their target enteral intake.

Conclusion A plan for PN is often omitted in the medical notes. There should be an expected duration, a desired outcome, IV access and a plan around what other (if any) nutrition can be given alongside. We plan to develop a PN plan proforma which can be used to stick into the notes which prompts the medical team responsible to enter this information. There is a lack of timely long term biochemistry bloods on those patients that have PN for longer than a month. This is important clinically because long term PN patients can develop deficiency in micronutrients which need replacement. We hope that educating the medical and nursing teams about this aspect of the clinical guideline will improve our practice. Lastly, the aim of PN must be to establish nutritional requirements where otherwise calorie input would not be met. Stopping early will lead to a calorie deficit and stopping too late would mean unnecessary extra clinical risk and potential inpatient stay. There were several instances where patients would have been discharged because they were otherwise clinically well but feeds were not adequate to stop PN. Other times PN is continued at 25% of requirements, where we should be stopping as soon as patients are established on 66% of oral calorie intake. This should be part of the wider team education about PN.

REFERENCE

P025 CLINICAL PEARL: TREATING INFANT BOTULISM ON A PAEDIATRIC INTENSIVE CARE UNIT (PICU)

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Problem A call was received out of hours by the specialist PICU pharmacist (SP). A five month old baby with rapidly spreading paralysis of unknown cause had been admitted to the unit. A toxin had been extracted from the stool culture and tested on mice. Within hours all mice had died, confirming a positive result for Botulism toxin. The SP was asked to obtain an urgent supply of Human Botulism Anti-Toxin however the only worldwide manufacturer/supplier, the Infant Botulism Treatment and Prevention Program (IBTPP), is based in California.1 BabyBIG, Botulism Immune Globulin Intravenous (Human) (BIG-IV), is an orphan drug that consists of human-derived anti-botulism toxin antibodies that is approved by the U.S. Food and Drug Administration for the