favoured on the unit over the cheaper first line alpha-2 adrenergic agonist clonidine. Our 'Guidelines for Analgesia and Sedation in Children on the Paediatric Intensive Care Unit (PICU)'[1] were updated in 2020 to include guidance on the use of dexmedetomidine, including approved indications, for the first time. We aimed to assess compliance and efficacy of dexmedetomidine in hospitalised children on the PICU or Paediatric High Dependency Unit (PHDU) against indications and doses in our updated guidelines between September 2020 and May 2021:

- IV dexmedetomidine should be prescribed for one of the listed indications
- The dose of IV dexmedetomidine should not exceed 1.4 microgram/kg/hour
- The duration of IV dexmedetomidine should not exceed 72 hours

Method The audit was registered with the trust. Children prescribed IV dexmedetomidine on the PICU or PHDU were identified using the electronic prescribing system. Indication was identified using electronic medical notes. COMFORT scores were documented before and after dexmedetomidine initiation.[2] Education on the updated guidelines were provided before the data collection period and an update in January 2021 was delivered in the format of a monthly 'DRUGgle'.

Results 33 patients with a median age of 2.2 years (range 2 months – 14.4 years) received IV dexmedetomidine. 32/33 prescriptions (97%) were as per the agreed indications. One patient (3%) was prescribed dexmedetomidine despite not having a trial of standard therapies. 18/32 (56%) of the courses for approved indications were to aid extubation, 12 (36%) for sedation in patients on non-invasive ventilation, and 2 patients (6%) received dexmedetomidine after prolonged use of standard therapies failed. In the 14 patients (total of 18 dexmedetomidine courses) for indications other than to aid extubation, COMFORT scores were recorded for 15 courses, but none had documented target scores. Patients remained or moved into a comfortable sedation score (12–17 COMFORT-B, 18–25 for COMFORT-Original) in 9 cases, 5 were slightly over sedated (10–11 COMFORT-B, 14–17 COMFORT-Original) and 1 infusion resulted in over sedation (<13 COMFORT-Original). IV dexmedetomidine did not exceed the maximum dose of 1.4 microgram/kg/hr in any of the patients identified. IV dexmedetomidine infusion was administered for more than 72 hours in 3 patients (9%): in two, a transition to clonidine was not attempted in a timely manner, in the third this was not successful due to labile blood pressure, bradycardia and restlessness. The main limitation was clarity on documented indications.

Conclusion Overall, compliance to approved indications for dexmedetomidine prescriptions was high; with 97% of all prescriptions as per updated guidelines. The dose never exceeded the recommended, but an infusion was administered for more than 72 hours in 9% of patients. COMFORT scores were maintained in comfortable range in almost all cases. A repeat audit will be carried out.

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P13 TRAMETINIB FOR CHYLOTHORAX MANAGEMENT IN NOONAN SYNDROME: DISCUSSION ABOUT EFFICACY, SAFETY AND TOLERABILITY

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Introduction Trametinib is a novel medicine that inhibits the mitogen-activated protein kinase enzyme (MEK), part of the mitogen-activated protein kinases (MAPK) signalling pathway. MAPKs regulates cell behaviour by controlling DNA transcription and subsequent protein production. It was developed to inhibit growth of cancers with an up-regulated MAPK signalling pathway. However, its role is expanding to other conditions which also have a link to MAPK pathways. Noonan syndrome is a genetic multisystem disorder which is linked to dysregulation of MAPK pathway.[1] Lymphatic abnormalities, most commonly peripheral lymphoedema, are estimated to be present in up to 20% of individuals. There had been one case report in literature whereby a patient with Noonan's syndrome was treated with MEK inhibitor (trametinib) with remodelling of lymphatic vasculature and complete resolution of symptoms.[2]

Situation A 3-year-old girl with previous intensive care admissions for chylothorax. Background issues included Noonan syndrome (RIT1 mutation), hypertrophic obstructive cardiomyopathy (HOCM), multiple congenital cardiac abnormalities, and spontaneous bowel perforation with a history of high output ileostomy. Previous failed treatments for the chylothoraces using conventional methods included medium-chained triglyceride (MCT) diet, parenteral nutrition (PN) and octreotide. Trametinib was accessed through Novartis' compassionate scheme as a rescue treatment. Patients treated with MEK inhibitors are likely to encounter adverse effects including skin irritation, diarrhoea, hypertension, vision changes and pneumonitis. Dosage adjustment or withholding treatment is required if renal, hepatic or worsening cardiovascular impairment occurs. It was felt that this child needed a bespoke side effect management protocol due to their comorbidities. The protocol was devised by the pharmacist in consultation with the mother of the child, dietitian, cardiologist and general surgeon. It was important to particularly target the management of skin rashes, increased stoma losses, pneumonitis, hypertension and cardiac impairment. Tolerability and side effects were monitored and the protocol was followed and adjusted as clinically appropriate based on multidisciplinary team (MDT) and family discussions.

Lessons Learnt This medication is only routinely used in oncology patients in an outpatient setting. Therefore, the side effect management is based on practice within this patient cohort.[3] In this situation the treatment was novel, using a theoretical pathway to guide its use. In addition, this child had comorbidities which complicated assessment of side effects. The side effects seen were skin irritation, increased stoma output and nausea, despite proactive management. Skin irritation was managed with short courses of steroid cream and regular emollients under guidance from a dermatologist. High stoma losses (>20 mL/kg) occurred despite maximum dose of loperamide and withholding most enteral nutrition, allowing small bites of fat-free food for comfort, and drinks of rehydration solution as part of a stoma losses replacement plan. In total, 12 weeks of treatment was given, with no chylothorax reoccurrence seen at 10 weeks post-treatment. In conclusion, our

experience has demonstrated that it is possible to manage the side effects of trametinib in a patient with multiple comorbidities using a patient centred and MDT approach.

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P14 FLUCTUATION OF SIROLIMUS DOSING IN A CHILD (NEONATAL TO INFANCY) WITH CARDIAC RHABDOMYOMAS

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Introduction Sirolimus is a mammalian target of rapamycin (mTOR) inhibitor and well-known for its anti-tumour effect increasing the tumour disappearance rate of rhabdomyoma. Cardiac rhabdomyomas are a rare condition associated with tuberous sclerosis. They present antenatally as benign tumours which grow for six months postnatally. Mostly, the tumours regress without treatment. Rhabdomyomas are problematic when they cause cardiac arrhythmias and obstruction to cardiac blood flow. Larger tumours can cause life-threatening obstruction of the ventricular outflow tracts or cardiac dysfunction; only treatment options are surgical resection or sirolimus. Sirolimus undergoes metabolism in the intestinal wall and liver. Sirolimus is primarily metabolised by O-demethylation and/or hydroxylation via CYP3A4 and P-glycoprotein forming metabolites which are pharmacologically inactive. These metabolic pathways and enzymes can mature at different ages, although the exact timings and effect this has on medications is unknown.

Situation A 10-day 39/40 neonate (3.75kg) with antenatal diagnosis of multiple cardiac rhabdomyomas; including potential life-threatening obstruction of the left ventricular outflow tract and moderate obstruction of the right ventricular outflow tract. To avoid surgical resection a treatment course of sirolimus was commenced to prevent further growth of the tumours and lead to a reduction in size. Sirolimus is unlicensed in this indication/cohort and dosing experience is limited. Dosing of 0.25 mg (1 mg/m^2) daily with a target blood concentration of 5–15ng/mL was used based on the prospective cohort study.[1] This led to a concentration of 16.2ng/mL after 4 days and 19.8ng/mL after a further week, with two doses omitted and dose reduced to 0.12 mg (0.48 mg/m^2) daily. Three further doses were omitted and the dose reduced to 0.05 mg (0.2 mg/m^2) daily giving stable concentrations of 5–7ng/mL until approximately 3 months of age when concentrations dropped to 2.9ng/mL. At this point multiple dosage increases were needed to maintain concentrations within the target range, with a final dose of 0.5 mg (1.47 mg/m^2) daily (infants weight 5.99kg) being sufficient, ten times the original dose required to maintain target concentrations.

Lessons Learnt It is theorised that a metabolic pathway involved in the metabolism of sirolimus may have matured during the neonatal to infant period, causing an increased clearance rate. CYP3A4 activity is very low at birth and gradually increases to adult activity throughout infancy.[2] There is a large increase in activity of CYP3A4 during the first 3 months of life, with nearly no activity during the first few days[3] which may have contributed to the initial high sirolimus concentrations observed in this patient. However as this is a single case interpatient variability could play a role. The medication was well tolerated with few side effects. Mild neutropenia (1.33 10^9/L) was observed with high sirolimus concentrations, but resolved when sirolimus concentrations returned to the target range. It is clear from this case that close blood concentration monitoring is required for neonates and infants requiring sirolimus treatment in order to achieve target concentrations consistently and to reduce the risk of toxic concentrations which could lead to dose dependent adverse effects.

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P15 TWO-CYCLE AUDIT ON PAEDIATRIC VANCOMYCIN PRESCRIBING AND MONITORING: TERTIARY CENTRE EXPERIENCE

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Aims In 2018, a new guideline for the use of intravenous vancomycin in children was implemented in a tertiary centre. The guideline differed from BNFC recommendations,[1] with increased dosing and increased frequencies. These differences were based on the results of a national NPPG project in 2016.[2]

The aim of this two-cycle audit was firstly to investigate compliance with the guideline, and secondly to assess the impact of changes made after the first cycle, on compliance and the quality of vancomycin prescriptions and monitoring.

Methods This two-cycle audit was carried out on all paediatric patients (>30 days and <17 years) who received intravenous vancomycin at a tertiary centre, during the two audit periods. Retrospective, fully anonymised data collection was completed between the dates of 1st January 2019 and 30th June 2019 for the first cycle, and between 1st August 2021 and 31st January 2022 for the second cycle. Exclusion criteria were patients who received intrathecal doses, single isolated surgical prophylaxis doses, and patients who were treated under Paediatric Haematology or Oncology. Descriptive analyses were performed, and categorical variables were reported as percentages. Data analyses, statistical analyses and graphs were performed or produced using R (R Version 3.4.1) and Microsoft Excel.

Results A total of 29 patients were included for the first cycle, and 28 patients for the second cycle. In the first cycle, 75.9% of patients were prescribed the correct frequency, but only