Protocol Review: Evidence used and rationale

Protocol name: Anaemia in Children

Rationale: A new study into maternal and child health is due to commence in the Kimberley in 2015/2016. A review of the maternal and child health protocols to reflect the best evidence was requested in order to inform that study. In particular, review of the anaemia in children, healthy child and growth faltering protocols.
Last updated:2011

Initial Working Group:
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Further review from: Kimberley Maternal and Child Health Sub-committee

The CARPA guidelines were recently reviewed and updated in August 2014. The population served by the CARPA manuals is very similar to the population in the Kimberley. This updated guideline is aligned closely with the CARPA manual, in order to enable standardised treatment across our regions for patients and clinicians alike. There are a few areas that this protocol differs from the CARPA manual, and these are discussed below.

Discussion points:

Screening at 4 Months of Age

There was some discussion about whether to keep 4 month screening of premature infants as in the previous protocol, in which case we would need reference ranges and treatment options for abnormal values. Consensus was that we should keep 4 month screening for premature infants < 37 weeks. This would allow us to identify infants that should be on routine iron treatment who may not be compliant (or check that they are), as well as premature infants that do not require routine iron treatment that may be anaemic. The reference range for infants < 6 months was obtained from the Pathwest QEII haematology reference ranges.

Length of Prophylaxis for Premature Infants

There was disagreement in the available protocols in regards to length of prophylaxis for premature infants. KEMH guidelines advise from 1-4 months. CARPA guidelines advise from 1-12 months and old KAMS guidelines from 1-6 months. There have been two recent systematic reviews (Long, 2102; Mills, 2012). Neither really demonstrated good evidence

for length of treatment. The majority of our premature infants will be delivered at KEMH, and transferred back to the Kimberley from there. It would be reasonable to stay consistent with those guidelines and treat from 1-4 months of age. The updated Kimberley protocol advises checking Hb for premature infants at 4 months, which would allow identification of any infants that may need continuation of treatment.

Treatment of Low Birth-Weight Infants

Should we routinely treat low birth weight infants (regardless of gestation) and if so what birth weight? KEMH drug treatment guidelines are not based on birth weight but rather gestational age. CARPA suggests routinely treat for BW < 2500g which would significantly change our management. Old KAMS guidelines say routinely treat for BW < 1800g. The two systematic (Long, 2102; Mills, 2012) don't give very good guidance. However, there was a study done (Berglund 2010) which demonstrates decreased risk of anaemia and iron deficiency in the treatment group for marginally low birth weight (2000-2500g). This is likely the evidence CARPA are basing their guidelines on. On discussion with our working group, consensus was that despite this single study, there is currently not enough evidence to change our management. Hence routine prophylaxis for LBW infants will stay at < 1800g.

Is HemoCue testing accurate?

There was concern expressed amongst staff in regards to the accuracy of the HemoCue and basing treatments on those results. Studies suggest that the HemoCue is very accurate when maintained properly and used with venous or arterial blood (Sanchis-Gomar, 2012). Using capillary blood leaves potential for interstitial fluid in the sample leading to dilution of the sample and a low reading. The correct technique for obtaining a capillary sample to reduce the risk of this has been attached to the protocol. Capillary HemoCue testing is a sensitive test for anaemia, in that a normal result is likely to be a true normal. Given the risk that an anaemic result may be a false positive, we have elected to introduce venous Hb sampling prior to initiation of IM iron treatment.

Use of IM iron

There are many difficulties with iron supplementation in our communities, and the challenges we face are different to inner-city practices.

1. Oral iron is the preferred option of treatment for iron deficiency anaemia. Unfortunately if the child has a concurrent infection or chronic disease, gut absorption of iron can be low decreasing the efficacy of its use. Despite perfect compliance, some children will fail oral iron therapy. Iron preparations are also not very palatable for children, and often despite best efforts of parents and clinicians, younger children will spit it out. We would always like to give the child/family and the clinic the option to succeed with oral iron prior to the use of parenteral iron.
2. There are two options for parenteral iron. IM and IV. Currently we use IM iron in our clinics. Reasons for this include that it is quick and efficacious, it is safe, it is acceptable to parents and we are able to start treatment immediately. It has some side effects discussed below including pain and the risk of skin tattooing.

3. IV iron is an option that we would be open to develop in our clinics. In order to be able to safely offer IV iron infusions in our clinics, we need an IV preparation which has good safety data in children, can be infused over a short space of time < 15 minutes, and is able to give the full dose in one infusion to avoid multiple cannulations. Currently we don't have such a preparation available. The use of iron carboxymaltose (ferrosig) is something we are watching with interest, as this may be a good alternative to the use of IM iron. Currently this is not authorised for use in children. We would also like there to be good experience and protocols in our clinics for the use in adults before moving to the use in children.

There was a lot of discussion in regards to the use of IM iron in children.

Efficacy

There is good evidence for the efficacy and safety of IM iron treatment versus oral iron supplementation in children with iron deficiency anaemia (Hussain, 2015; Afzal, 2009). There is also evidence for the efficacy of IM iron polymaltose compared to IV iron for the treatment of iron deficiency anaemia in children (Surico, 2002).

Skin tattooing

Skin tattooing is a known risk when giving IM iron injections. This is because the iron contained in liquid form can stain the skin if it leaks into the skin. Ways to prevent this while giving IM iron is by using the correct technique of injection and forming a z-track. Generally this prevents most forms of tattooing, however it still remains a risk.

Skin tattooing is also a risk when giving IV iron infusions for the same reason. If the cannula is not secure or leaks, the iron infusion may also leak into the skin causing tattooing. This risk may be increased in children with difficult cannulations, movement, and the inability to verbalise the pain associated with extravasation of iron into the skin.

Pain

IM injections are painful and we do not give them lightly. However, when the benefit outweighs the risk, it is deemed reasonable to give IM injections for medical treatment. For example giving a Long Acting Bicillin injection for tonsillitis or skin sores and giving routine immunisations. IV cannulation is also painful, as well as being a technically difficult procedure. Often in children multiple attempts are needed, especially by staff inexperienced in the procedure in this age group. This is not a reason not to cannulate a child, however it does not make it a more feasible option in terms of pain.

Use of routine micronutrient use such as Sprinkles

There is evidence that routine iron supplementation of food reduces rates of anaemia in populations similar to ours (Suchdey, 2012). There is however some evidence that this also increases the rate of infection, in particular diarrhoeal illness (Gera, 2012). There is also an increased risk of malaria, which is not of concern in the Kimberley. On reviewing the evidence, we have concluded that better evidence of the safety of food supplementation is required before introducing it in our communities.

The dose of iron in sprinkles is much lower than that in oral iron preparations. However some studies have indicated that it is as efficacious as oral iron, although the treatment success rates are still quite low around 50% (Al-Mamari, 2014).

Further areas to look at when developing the anaemia protocol in the future.

1. Use of routine micronutrient supplementation such as sprinkles in the community. Currently there is not enough evidence that the benefit is outweighed by the risk of infection. However if further evidence in support of routine micronutrient supplementation it is an option to look at.
2. Other forms of oral iron. Currently Ferro-liquid is the only liquid form of iron available in Australia. Further oral iron formulations can be reviewed for efficacy and palatability when/if they become available
3. We watch with interest the development of IV iron preparations which require only short infusion times. Currently they are not recommended for use in children < 14, however studies are currently evaluating this (Crary, 2011; Laas, 2014).
4. New data and evidence as it becomes available on the role of hepcidin in iron metabolism. The possibility of using hemosiderin as a diagnostic test and being able to distinguish iron deficiency due to inflammation or chronic disease from other forms of iron deficiency. Being able to distinguish if/when not to treat with iron, in the presence of infection and inflammation.

Resources used:

Guidelines

1. CARPA Standard Treatment Manual, 6th Edition. Updated 30 September 2014. Pgs 118-122
2. Reference Book for the Remote Primary care manuals (Carpa). Updated August 2014. Pgs 118-127
3. KEMH NCCU Medication protocols http://www.kemh.health.wa.gov.au/services/nccu/guidelines/drug_protocols/FerrousSulphate.pdf
4. Pathwest QEII Haematoogy reference ranges

Other References:

1. Afzal M, Qureshi SM, Lutafullah M, Iqbal M, Sultan M, Khans SA. Comparative study of efficacy, tolerability and compliance of oral iron preparations (Iron edetae, iron polymaltose complex) and intramuscular iron sorbitol in iron deficiency anaemia in children. The Journal of the Pakistan Medical Association. Nov 2009; 59 (11): 764-
2. Al-Mamari A, Al-ehami MA, Al-Hag S, Al-Buryhi M. Prevalence of Iron Deficiency and Iron Deficiency Anemia in Infants and Children and Treatment with Microencapsulated Iron II Fumarate and Supplied Ascorbic Acid as “Sprinkles” . Pharmacology & Pharmacy, 2014; 5: 716-724

3. Berglund S, Westrup B, Domellöf M. Iron Supplements Reduce the Risk of Iron Deficiency Anemia in Marginally Low Birth Weight Infants. Pediatrics Volume 126, Number 4, October 2010; e874-e883
4. Crary SE, Hall K, Buchanan GR. Intravenous iron sucrose for children with iron deficiency failing to respond to oral iron therapy. Pediatr Blood Cancer, 2011;56:615-619 http://www.ncbi.nlm.nih.gov/pubmed/21298748
5. Gera T, Sachdeve H P S, Effect of iron supplmementation on incidence of infectious illness in children: systematic review. BMJ. 2012;325:1142
6. Hussain S, Ahmad TM, Sabir MUD, Tarar SH. Comparison of Efficacy of oral and intramuscular iron supplementation for treatment of iron deficiency anaemia in children. Pakistan Armed Forces Medical Journal. Feb 2015: 153-150
7. Laass MW, SStraub, S Chainey, GVirgin and T Cushway. Effectiveness and safety of ferric carboxymaltose treatment in children and adolescents with inflammatory bowel disease and other gastrointestinal diseases. BMC Gastroenterology 2014, 14:184. http://www.biomedcentral.com/1471-230X/14/184
8. Long H, Yi JM, Hu PL, Li ZB, Qiu WY, Wang F, Zhu S. Benefits of Iron supplementation for low birth weight infants: a systematic review. BMC Pediatrics. 2012; 12:99
9. Mills RJ, Davies MW. Enteral iron supplementation in preterm and low birth weight infants. Cochrane database of Systematic Reviews 2012, Issue 3. Art No: CD005095
10. Sanchis-Gomar F, Cortell-Ballester J, Pareja-Galeano H, Banfi G, Lippi G. Hemoglobin Point-of-Care Testing: The HemoCue System. Journal of Laboratory Automation. 2012; 198-205
11. Suchdey PS, Ruth LJ, Woodruff BA, Mbakaya C, Mandava U, Flores-Ayala R, Jefferds ME, Quick R. Selling Sprinkles micronutrient powder reduces anemia, iron deficiency, and vitamin A deficiency in young children in Western Kenya: a cluster-randomized control trial. The American Journal of Clinical Nutrition. 2012;95:1223–30
12. Surico G, Muggeo P, Muggeo V, Lucarelli A, Martucci T, Daniele RM, Rigillo N. Parenteral iron supplementation for the treatment of iron deficiency anaemia in children. Ann Hematol 2002 81: 154-157