**APPENDIX (ONLINE-ONLY)**

**Current protocol for management of anemia in Bloodless patients at the Institute for Patient Blood Management and Bloodless Medicine and Surgery at Englewood Hospital and Medical Center.**

***Baseline Hemoglobin >7g/dL***

1. Epoetin alfa (Procrit®): 40,000 units subQ once per week (use IV only if subQ unsuitable)
2. Iron dextran (Infed®): 100mg IV push once daily for 10 days. For first-time Iron dextran patients, administer 25mg IV push test dose, wait 30 minutes, then 75mg IV push if no reaction to the test dose.

OR

Iron sucrose (Venofer®): 100 mg IV push once daily for up to10 days (If patient is NOT a candidate for Iron dextran (Infed®). No test dose required for Venofer.

1. Folic acid (Folate): 1 mg IVPB once daily
2. Vitamin C (Ascorbic acid): 500 mg every 12 hours enterally
3. Vitamin B12 (Cyanocobalamin): 1000 mcg IM x 1 dose
4. Minimize oxygen utilization – supplemental O2
5. Aggressive nutritional support
6. Aggressive management of infection
7. DVT prophylaxis: SCDs, cautious use of heparin or enoxaparin (Lovenox®)
8. GI stress ulcer prophylaxis: Proton pump inhibitor ( IV or PO)

***Baseline Hemoglobin 5-7 g/dL***

1. Epoetin alfa (Procrit®): 20,000 units subQ once daily for 5 days (use IV only if subQ unsuitable)
2. Iron dextran (Infed®): 100 mg IV push once daily for 10 days. For first time Iron dextran patients, administer 25 mg IV push test dose, wait 30 minutes, then 75 mg IV push if no reaction to the test dose.

OR

Iron sucrose (Venofer®): 100 mg IV push once daily for up to10 days (If patient is NOT a candidate for Iron dextran (Infed®). No test dose required for Venofer.

1. Folic acid (Folate): 1 mg IVPB once daily
2. Vitamin C (Ascorbic acid): 500 mg every 12 hours enterally
3. Vitamin B12 (Cyanocobalamin): 1000 mcg IM x 1 dose
4. If weekly corrected reticulocyte count < 6% then redose Epoetin alfa (Procrit®): 40,000 units subQ once daily for 4 day
5. Monitor for tissue dysoxia:
   1. Daily 12 lead ECG
   2. q 4 hr neurological exam
   3. Metabolic acidosis
   4. Progressive renal insufficiency despite euvolemia
   5. Alternating mental status
6. Minimize oxygen utilization
   1. Strict bed rest
   2. Non-selective beta blocker: Propranolol (Inderal®) 150 micrograms (0.15 mg) IV q 4 hours as tolerated by BP. Goal HR 90 - 100 bpm or reduction of HR by 10% but no more than 15 % from baseline tachycardia.
7. Aggressive nutritional support
8. Aggressive management of infection
9. DVT prophylaxis: SCDs, no heparin or enoxaparin (Lovenox®)
10. GI stress ulcer prophylaxis: Proton pump inhibitor ( IV or PO)
11. Reduce intrapulmonary shunt
    1. Head of bed greater than 30 degrees
    2. “Standing order” bronchodilator therapy
    3. Chest PT and incentive spirometry (if not ventilated and patient able to perform)
12. If signs of end organ dysoxia:
    1. Intubation, sedation, ventilation with 100% oxygen (goal PaO2 >250, preferably >300)
    2. Remember to use PEEP to reduce intrapulmonary shunt, maintain FRC and increase PaO2 (make sure patient is euvolemic)
    3. Sedation to reduce oxygen consumption
    4. Keep euthermic, active cooling if elevated temperature ( fever increases consumption and reduces SaO2)
    5. Neuromuscular blockers (NMBs) if necessary to facilitate ventilation, minimize oxygen consumption and facilitate cooling by reducing subclinical shivering. NMB (“train-of-four”) monitoring as standard: try to keep patient at ¾.

***Baseline Hemoglobin <5 g/dL***

1. Epoetin alfa (Procrit®): 20,000 units IV every 12 hours for 5 days (use IV only if subQ unsuitable)
2. Iron dextran (Infed®): 100mg IV push once daily for 10 days. For first time Iron dextran patients, administer 25 mg IV push test dose, wait 30 minutes, then 75mg IV push if no reaction to the test dose.

OR

Iron sucrose (Venofer®): 100 mg IV push once daily for up to10 days (If patient is NOT a candidate for Iron dextran (Infed®). No test dose required for Venofer.

1. Folic acid (Folate): 1 mg IVPB once daily
2. Vitamin C (Ascorbic acid): 500 mg every 12 hours enterally
3. Vitamin B12 (Cyanocobalamin): 1000 mcg IM x 1 dose
4. If weekly corrected reticulocyte count < 6% then redose Epoetin alfa (Procrit®): 40,000 units IV every 12 hrs for 5 days
5. Maximize dissolved oxygen content: 100% Oxygen therapy
6. Monitor for tissue dysoxia:
   1. Daily 12 lead ECG
   2. q 4 hr neurological exam
   3. Metabolic acidosis
   4. Progressive renal insufficiency despite euvolemia
   5. Alternating mental status and/or inability to concentrate or sleepy
7. Minimize oxygen utilization
   1. Strict bed rest
   2. Non-selective beta blocker: Propranolol (Inderal®) 150 micrograms (0.15 mg) IV q 4 hours as tolerated by BP. Goal HR 90 - 100 bpm or reduction of HR by 10% but no more than 15 % from baseline tachycardia.
8. Aggressive nutritional support
9. Aggressive management of infection
10. DVT prophylaxis: SCDs, no heparin or enoxaparin (Lovenox®)
11. GI stress ulcer prophylaxis: Proton pump inhibitor ( IV or PO)
12. Reduce intrapulmonary shunt
    1. Head of bed greater than 30 degrees
    2. “Standing order” bronchodilator therapy
    3. Chest PT and incentive spirometry (if not ventilated and patient able to perform)
13. If signs of end organ dysoxia:
    1. Intubation, sedation, ventilation with 100% oxygen (goal PaO2 >250, preferably >300)
    2. Remember to use PEEP to reduce intrapulmonary shunt, maintain FRC and increase PaO2 (make sure patient is euvolemic)
    3. Sedation to reduce oxygen consumption
    4. Keep euthermic, active cooling if elevated temperature ( fever increases consumption and reduces SaO2)
    5. Neuromuscular blockers (NMBs) if necessary to facilitate ventilation, minimize oxygen consumption and facilitate cooling by reducing subclinical shivering. NMB (“train-of-four”) monitoring as standard: try to keep patient at ¾.

***Lab Test Schedule:***

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **ICU Day** | **Baseline (Day 0)** | **3** | **7** | **10** | **14** | **21** | **28** |
| **CBC + diff** | X |  | X |  | X | X | X |
| **CBC no diff** |  | X |  | X |  |  |  |
| **Fe** | X |  | X |  | X |  |  |
| **Ferritin** | X |  | X |  | X |  |  |
| **Tsat** | X |  | X |  | X |  |  |
| **TIBC** | X |  | X |  | X |  |  |
| **Folate** | X |  |  |  |  |  |  |
| **B12** | X |  |  |  |  |  |  |
| **Retic Abc** | X | X | X | X | X | X | X |
| **Retic %** | X | X | X | X | X | X | X |
| **IRF** | X | X | X | X | X | X | X |

If advanced directive does not exist, contact Bloodless Medicine team for assistance.

Blood sampling for all labs: use neonatal tubes; use an in-line device to minimize blood waste. For Witness patients: maintain closed system (blood to remain part of the patient’s circulation) at all times. No “standing order” or “routine” daily labs (final decision as per Intensivist) except: once a day blood gas for intubated ventilated patients, unless otherwise specified by Intensivist.

***Expected Response to the Treatment:***

Our protocol is designed to increase hemoglobin level in the shortest possible timeframe to minimize the consequences of hypoxia in severely anemic patients managed without transfusion. Our protocol and a similar one (Haemoglobin Maximisation Regimen, courtesy of Shannon Farmer, School of Surgery, Faculty of Medicine Dentistry and Health Sciences, University of Western Australia), have been used extensively in these patients and has been shown to achieve relatively rapid rises in hemoglobin level.

In 24 patients admitted to ICU over a 7-month period in 2006, a post-nadir hemoglobin rise of 0.19-0.62 g/dL per day was achieved (Ironing out problems. McMorrow J, Farmer S, Towler S, Carnley B. SHPA 2007 Abstract). Similarly, in a series of 18 patients including 6 severely anemic patients transferred to ICU with severe hemorrhage and multiple trauma and nadir hemoglobin range of 1.7-5.3 g/dL, post-nadir hemoglobin rise was 0.39-0.61 g/dL per day, with hemoglobin levels reaching 4.9-8.1 g/dL at 4-6 days and 7.3-10.8 g/dL at 10 - 12 days (2 patients had further surgery days 3 and 4 post-nadir hemoglobin level). In several other cases, the observed hemoglobin level rise achieved under this protocol was around 4 g/dL per week over the first week, 1.7 g/dL per week over the first 2 weeks and 1.6-3.4 g/dL per week over the first 3 weeks. Therefore, our observations support an initial rapid response phase to hematinics in severely anemic patient occurring within the first few days of the treatment which can be critical in minimizing the negative consequences of hypoxia in these patients.