Department of Pediatrics Fellowships
Quality Assurance / Quality Improvement (QA/QI) Project

QA/QI Project

As part of the ABP credentialing requirements, all fellows must complete at least one QA/QI project during their subspecialty training. The QA/QI project, also called the practice-based learning and improvement (PBLI) project, focuses the trainee's critical awareness on the systems in which they work, as well as self-awareness of their own practice. The skills acquired through this process provide the trainee with useful tools he/she can use throughout his/her career. The QA/QI project should be selected through discussion between the fellow, a faculty mentor, and the program director. When the project is completed, the fellow will provide the director with a written summary of the project for his/her permanent file in addition to one completed form.

Attach a separate sheet if necessary

Trainee Name: Walaa Elfar, MBBCh Date Submitted: 6/7/17

Project Title: The management of Infliximab acute infusion reaction in our pediatric infusion center

Project Aim / Goals:

Our overall aim for the project was to improve the nurses and provider satisfaction and level of knowledge in regards of the identification and management of the acute infliximab infusion reactions in the outpatient setting. We created a short teaching session and obtained before and after intervention survey to assess the level of knowledge and satisfaction.

How has completing this project influenced your insight on your current practice?

I was able to better understand the types of Infliximab infusion reactions and their subcategories. I was also able to manage those reactions in a more standard way and feel confident teaching the young fellows and nurse how to deal with those reactions when they occur. Distinguishing between the different categories of acute reactions can be challenging at times and may lead to cancellation of infusions at times patients are in need for those infusions.

How will you enhance your practice with the information gleaned from this project?

I will be able to better teach and guide the new providers and nurses in regards of the acute infliximab infusion reactions and how to manage them appropriately. I will have a plan on how to restart the infusion after a patient had developed a previous reaction.

Fellow's Signature	6/7/17 Date
N. Patel Mentor's Signature	6/7/17 Date
Program Director's Signature	6/8/17 Date

Revised 09/20/2013

Quality Assessment/Improvement Project
Acute Infliximab infusion reactions management

Name: Walaa Elfar, MB.BCh **Date: 6/7/17**
Mentor: Nishaben Patel, MD

Proposed Need for Improvement: Infliximab infusion reaction trouble shooting in the setting of outpatient based Infliximab infusion practice with paucity of GI providers at times

Background Information: the overall incidence to infliximab infusion reaction is estimated to be 5%. Infusion reactions to infliximab are categorized as either acute or delayed. Management of an acute reaction is directed towards alleviating the signs and symptoms, which most commonly include: fever, chest pain, hypo/hypertension or dyspnea. Typically symptoms resolve or improve significantly after treatment with antihistamine, acetaminophen, steroids and/or epinephrine.

In our center, the infliximab infusion is outpatient based practice and is run by a nurse practitioner and qualified infusion center nurses with indirect supervision of GI physicians. Those nurses notify the covering gastrointestinal provider if there are any concerns prior to starting the infusion and in the setting of developing any infusion reactions.

The aims of this project is to:

- Improve the knowledge of acute infliximab infusion reaction by assessing the ability to:
    - Identify the common sign/symptoms that prevents starting infliximab infusion
    - Identify the common reactions to the infliximab infusion
- Create a protocol for the immediate evaluation and management of those reactions
- Improve the nurses and providers regarding current protocol and proposed changes.

Methods: We searched the literature for current accepted protocols for the management of acute infliximab infusion reactions. We then created an algorithm for pre- infusion evaluation as well as an algorithm for any acute or subsequent infusion reactions using as a guide the published data from the division of clinical immunology infusion center, Mount Sinai Medical Center as well as the pediatric infusion center in the Cleveland clinic. I scheduled a short teaching session with the providers and nurses

separately. Prior to the teaching session, I asked the learners to fill up a pre-intervention survey (see attached) to assess the level of satisfaction and knowledge of the Infliximab reactions and their management prior to the intervention. Then I conducted a short 15 minutes teaching session (slides attached). During the session, went over the common Infliximab infusion reactions, when not to infuse, how to identify different categories of acute reactions, how to manage different categories of acute reactions. We also went over the new premedication guidelines and what to do when a patient comes for a subsequent Infliximab infusion after having a reaction. After completing the teaching session, I asked the learners to fill out the same survey afterwards. The data was blinded. We calculated the mean, standard deviation and standard error of the mean using excel. We then created column charts to compare the results. We ran unpaired student t-test to compare the pre and post intervention data and consider $P<0.05$ statistically significant.

Objective:

- Pre-intervention survey to assess baseline knowledge and satisfaction
- 15 minute teaching session
    - Understand the types and categorization of acute Infliximab infusion reactions
    - Learn the immediate management plans for the different categories of acute Infliximab infusion reactions
    - Learn the management plan when patient come to infusion center for a subsequent infusion after initial infusion reaction
- Post-intervention survey to assess improvement/difference in the level of knowledge and satisfaction

Results: see attached excel sheet.

The Management of Acute Infliximab Infusion Reactions- QI project
Pre/post intervention questionnaire

1- How do you feel about the current protocol for the management of Infliximab infusion reactions? (Satisfied, dissatisfied, neutral. Explain)

2- In case of Infliximab infusion adverse reaction, how confident do you feel handling the situation? (Very confident, somewhat confident, not confident, I don't know)

3- Do you know who to call and in what order in case of infusion reaction? (Yes, Not sure, No)

4- Do you know the types of infusion reactions? (Yes, Not sure, No)

5- Are you clear on how to handle each specific type of reaction? (Yes, Not sure, No)

6- Are you satisfied with the current teaching provided to nurses prior to starting Infliximab infusions? (Yes, Not sure, No)

Please choose the correct answer for each question below.

When would you reschedule the Infliximab infusion?

1. Patient has a fever of 39
2. Patient has a sinus infection and was started on antibiotics last week
3. Patient has abdominal pain and bloody diarrhea
4. Patient has non-erythematous papular rash

What kind of reaction a patient can develop during the first 24 hours from Infliximab infusion?

1. Acute reaction
2. Delayed reaction
3. Intermediate reaction
4. None of the above

When do you use methylprednisolone as a premedication prior to Infliximab infusion?

1. Prior to each infusion as a premedication
2. If the patient developed a previous infusion reaction
3. Prior to each infusion and if the patient developed a previous infusion reaction
4. None of the above

12 years old girl with fisulizing Crohn's disease is in the infusion center today for her scheduled maintenance Infliximab dose. She never had reactions before. 30 minutes after starting the infusion, she started to develop shortness of breath and a blotchy rash on her chest. Her vital signs remained stable except for mild drop in her systolic blood pressure. What is the classification of her reaction and what to do next?

1. Mild acute reaction. Slow down the infusion
2. Moderate acute reaction. Stop the infusion and reassess
3. Severe acute reaction. Stop the infusion, maintain airway, infuse a bolus and prepare epinephrine
4. None of the above

12 years old with fisulizing Crohn's disease is in the infusion center today for her scheduled maintenance Infliximab dose. She never had reactions before. 30 minutes after starting the infusion, she started to develop palpitation, diaphoresis and headache with some skin hyperemia. Her vital signs remained stable with no changes. What is the classification of her reaction and what to do next?

1. Mild acute reaction. Slow down the infusion
2. Moderate acute reaction. Stop the infusion and reassess
3. Severe acute reaction. Stop the infusion, maintain airway, infuse a bolus and prepare epinephrine
4. None of the above

12 years old with fisulizing Crohn's disease is in the infusion center today for her scheduled maintenance Infliximab dose. She never had reactions before. 30 minutes after starting the infusion, she started to develop chest tightness and stridor. Her vital signs were noted for temp 38.5 and a blood pressure of 90/70. Her vitals prior to starting the infusion were noted for normal temperature and blood pressure of 1115/80. What is the classification of her reaction and what to do next?

1. Mild acute reaction. Slow down the infusion
2. Moderate acute reaction. Stop the infusion and reassess
3. Severe acute reaction. Stop the infusion, maintain airway, infuse a bolus and prepare epinephrine
4. None of the above

Walaa Elfar
Pediatric gastroenterology and nutrition Fellow

Infliximab Infusion Reactions Management

QI project
Walaa Elfar, MBBCh
Nishaben Patel, MD
4/6/2017

Background

- Infliximab is a chimeric monoclonal antibody used as targeted therapy to treat Crohn's disease and ulcerative colitis
- It blocks the reaction in the body to human tumor necrosis factor alpha (TNF-α).
- It is a protein. Body can recognize it as a foreign protein and start making antibodies against it→ infusion reaction
- Overall, the incidence of infliximab infusion reactions are low ~5%
- Can Develop similar reactions to other monoclonal antibodies.
- The management of acute infliximab infusion reactions has not been updated since the late 90s.
- There are new data about improvement of patient outcome and satisfaction when minimal pre-medication and faster infusion protocols are used.

Aims

- Aim 1: To improve the recognition and categorization of acute infliximab infusion reactions
- Aim 2: To unify the management plan for the acute infliximab infusion reactions in an effort to to improve nurses and provider satisfaction and level of performance

*This will act as a step towards moving forward to the one hour infusion protocol if the patient tolerates the induction doses using the 2 hour infusion protocol.

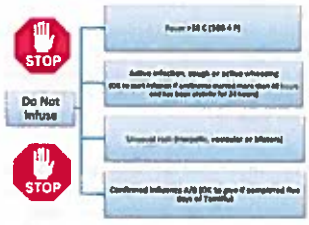
Objectives

- Understand the types and categorization of acute infliximab infusion reactions
- Learn the immediate management plans for the different categories of acute infliximab infusion reactions
- Learn the management plan when patient come to infusion center for a subsequent infusion after initial infusion reaction

Pre-infusion Assessment

- Vital signs, height and weight
- History of any recent illness or hospitalization
- History of any rashes, abscess or skin breaks

When NOT to start the Infusion?

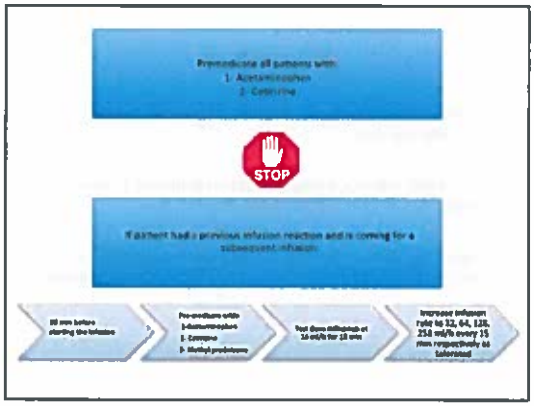


Types of Concerning Rashes

To Pre-medicate or Not?

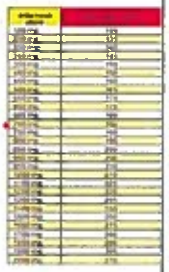
- All patients were pre-medicated with Diphenhydramine, Acetaminophen and Methyl prednisone regardless of previous history
  - Recent studies have shown that the use of antihistamine pre-medications routinely & slower infusion rates increase the likelihood that patients develop antibodies resulting in reactions and termination of therapy

Effective Soon:
All patients will get pre-medicated with **Cetirizine** and **Acetaminophen** unless they have a previously documented reaction to Infliximab infusion.



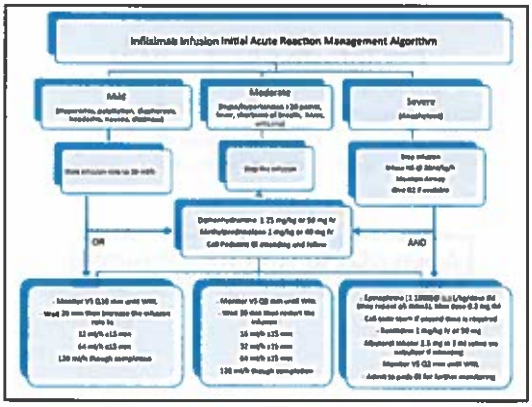
During Infusion

- ***For first three doses***: Infliximab is infused over 2 hours, titrating per the following:
  - 16ml/ h for 15 minutes
  - 32ml/ h for 15 minutes
  - 64ml/ h for 15 minutes
  - 128ml/ h for 15 minutes
- MAX rate for duration of infusion
  - MAX rate is based on total dose



Types of Infliximab Infusion Reactions

- **Acute reaction:** any adverse reaction, whether immunologically or nonimmunologically based, which occurs during or within 24 h of an initial or subsequent infliximab infusion. Can be further categorized as mild, moderate, or severe, according to the severity
- **Delayed reaction:** adverse reaction that occurs from 24 h to 14 days after retreatment with infliximab. Can be further categorized as mild, moderate, or severe, according to the severity. Symptoms of arthralgia, myalgia, urticarial rash, fever, and malaise



Mild Reaction

- Hyperemia, palpitations, diaphoresis, headache, dizziness or nausea
- What to do?
  1. Slow infusion rate to 16 ml/h
  2. Diphenhydramine (1.25 mg/kg IV; max dose 50 mg)
  3. Monitor VS every 10 min until WNL
  4. Wait 20 min, then increase infusion rate to 32 ml/h, 64 ml/h, and 128 ml/h every 15 min, respectively, as tolerated
  5. Notify GI provider

Moderate Reaction

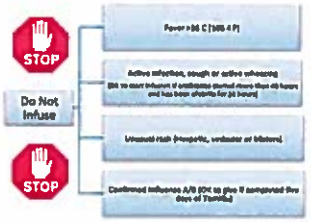
- Hypo/hypertension (≥20 points SBP), hyperemia, chest discomfort (e.g., tightening, pressure), shortness of breath, elevated temperature, palpitations or urticaria
- What to do?
  1. Stop the infusion
  2. Diphenhydramine (1.25 mg/kg IV; max dose 50 mg)
  3. Methylprednisolone (1mg/kg/dose IV; max dose of 40 mg)
  4. Monitor VS every 5 min until WNL
  5. Notify GI provider
  6. If patient stabilizes and given clearance by assessing physician, wait 20 min, then restart infusion rate at 16 ml/h for 15 min
  7. If tolerated, increase infusion rate to 32 ml/h, 64 ml/h, and 128 ml/h, every 15 min, respectively, as tolerated. Do not exceed 128 ml/h through completion.

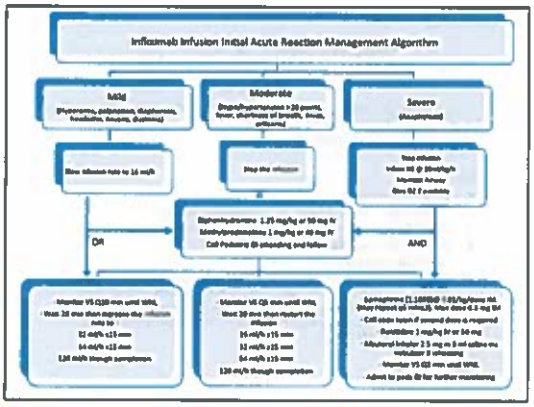
Severe Reaction (Anaphylaxis)

- Significant (≥40 points SBP) hypo/ hypertension, elevated temperature with rigors, hyperemia, chest discomfort (e.g., tightening, pressure), significant shortness of breath or stridor
- What to do?
  1. Stop the infusion
  2. Place patient in supine position with the lower extremities elevated, or if dyspneic or vomiting, place patient semi-recumbent with lower extremities elevated.
  3. Infuse normal saline rapid bolus (20 mL/kg/dose IV), re-evaluate and repeat as needed
  4. Maintain airway, give oxygen (8 to 10 L/min via facemask to keep O2 saturation >92%)
  5. Remain with patient and have inpatient GI attending/fellow paged.

Severe Reaction (Anaphylaxis)

6. IM Epinephrine (1 mg/mL preparation = 1:1000)- Give 0.01 mg/kg/ dose; max dose 0 3 mg IM in mid-outer thigh; may repeat every 5 min for three doses
7. Methylprednisolone (1mg/kg/dose IV; max dose of 40 mg)
8. H1 antihistamine: Diphenhydramine (1 25 mg/kg IV; max dose 50 mg)
9. H2 antihistamine: Ranitidine (1mg/kg/dose IV, max dose 50 mg)
10. Albuterol (for bronchospasm resistant to IM epinephrine): Give 2 5 mg in 3 mL saline inhaled via nebulizer. Repeat as needed.
11. Monitor VS every 2 min until WNL
12. Admit patient to Peds GI service overnight for monitoring and observation





Questions?

Preferences

- Am J Gastroenterol. 2003 Jun;98(6):1315-24. The incidence and management of infusion reactions to infliximab: a large center experience.
- Up to date
- Dig Liver Dis.2015 May;47(5):372-7.doi:10.1016/j.dld.2015.01.152. Epub 2015 Jan 30. a nurse –led accelerated procedure for infliximab infusion is well tolerated and effective in patients with inflammatory bowel disease.
- Expert Opin Biol Ther.2014 Mar;14(3):277-82.doi:10.1517/14712598.2014.866649. Epub 2013 Dec 21. Safty and cost benefit of accelerated infliximab infusion protocol in the treatment of ambulatory patients with inflammatory bowel disease.

Data for the Qt project

Knowledge scores

	Pre	post
Nurses	2	3
	3	2
	3	4
	2	4
	1	3
	1	6
Mean	2	3.66666667
standard deviation	0.89442719	1.3662601
standard error	0.36514837	0.55777335

	pre	post
providers	2	6
	4	6
	4	6
	2	3
	5	4
Mean	3.4	5
standard deviation	1.34164079	1.41421356
standard error	0.6	0.63245553

pre	0.36514837	0.6
post	0.55777335	0.63245553

Satisfaction scores

	pre	post
Nurses	15	19
	13	18
	13	19
	12	19
	13	19
	17	17
Mean	13.8333333	18.5
standard deviation	1.09544512	0.4472136
standard error	0.4472136	0.18257419

	pre	post
providers	16	19
	10	19
	6	19
	14	18
	12	18
Mean	11.6	18.6
standard deviation	3.84707681	0.54772256
standard error	1.72046505	0.24494897

pre	0.4472136	1.72046505
post	0.18257419	0.24494897

Knowledge scores

	pre	post
providers	3.4	5
Nurses	2	3.7

satisfactio scores

	pre	post
providers	11.6	18.6
Nurses	13.8	18.5

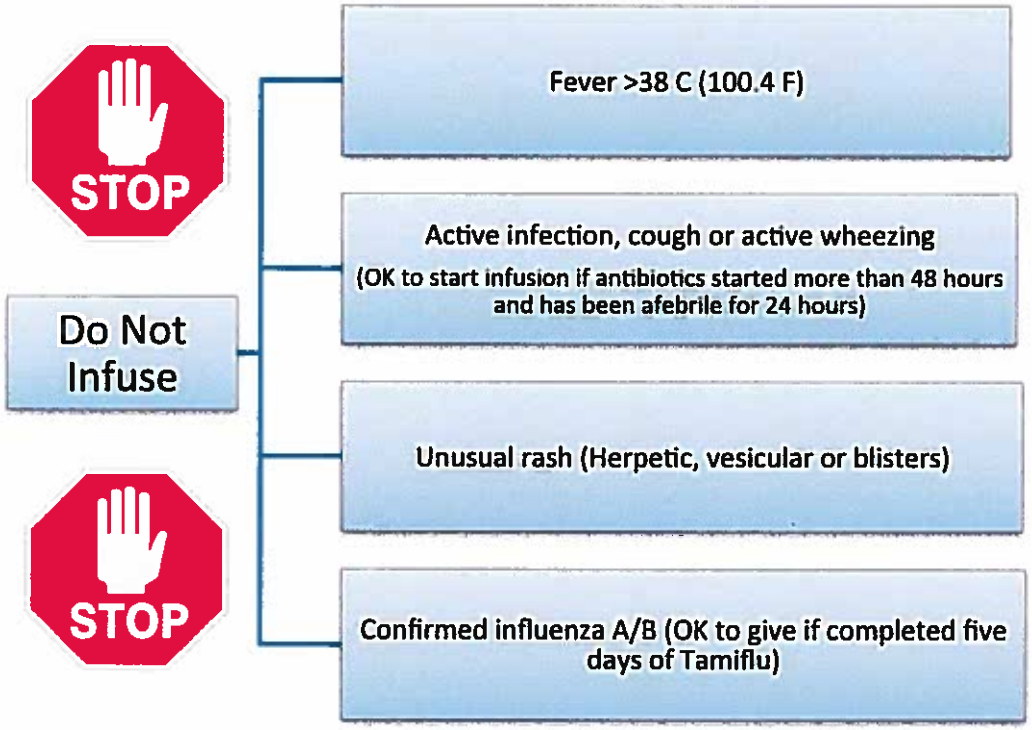
Nurse satisfaction t-test
0.000762459

provider satisfaction t-test
0.014558334

Nurse knowledge t-test
0.034938586

provider knowledge t-test:
0.103889513

The error bars on the charts represents standard error from the mean.


STOP
Do Not Infuse
STOP
Fever >38 C (100.4 F)
Active infection, cough or active wheezing
(OK to start infusion if antibiotics started more than 48 hours and has been afebrile for 24 hours)
Unusual rash (Herpetic, vesicular or blisters)
Confirmed influenza A/B (OK to give if completed five days of Tamiflu)

Premedicate all patients with:
1- Acetaminophen
2- Cetirizine

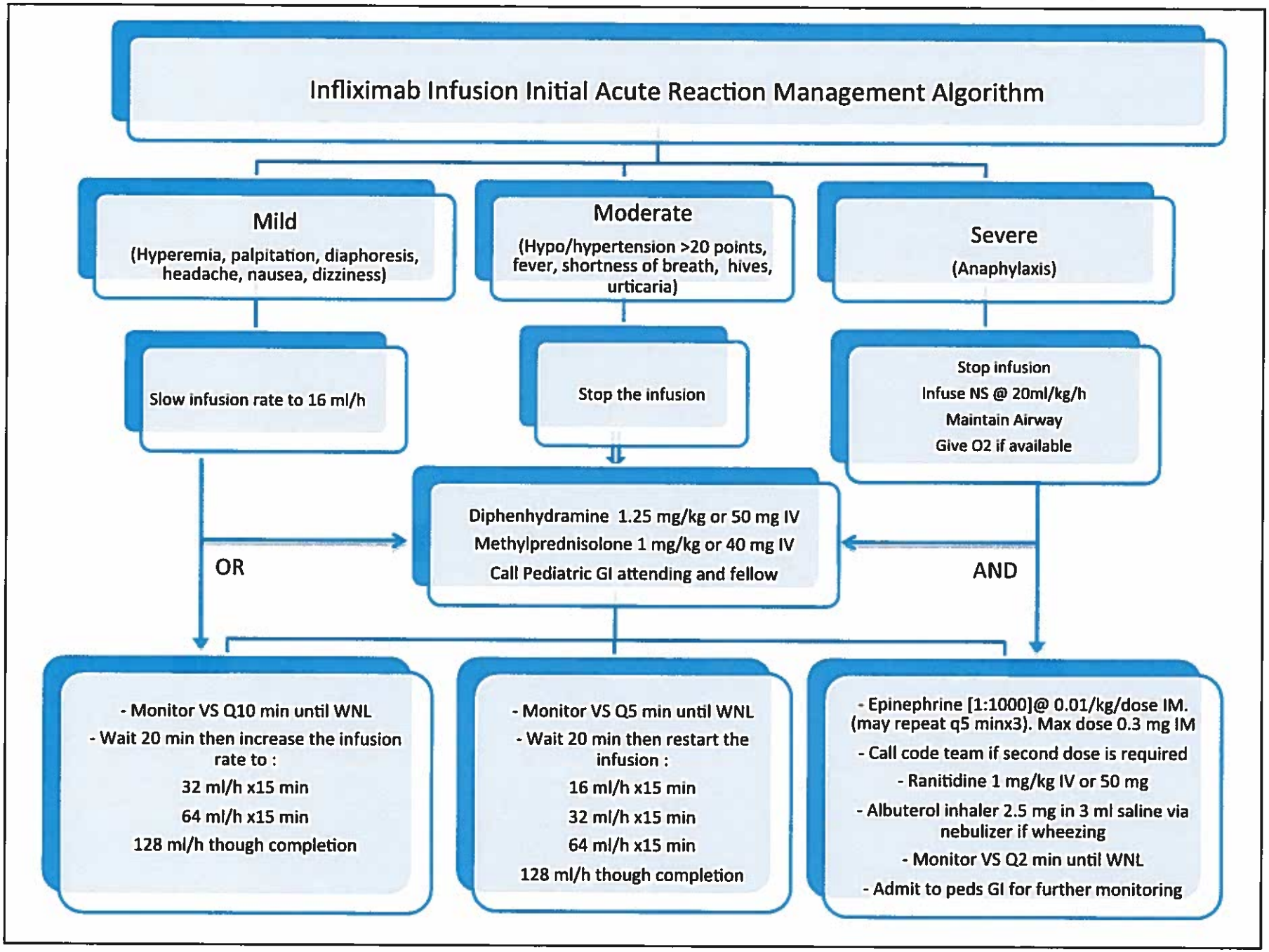
If patient had a previous infusion reaction and is coming for a subsequent infusion:

30 min before starting the infusion

Pre-medicate with:
1-Acetaminophen
2- Cetirizine
3- Methyl prednisone

Test dose infliximab at 16 ml/h for 15 min

Increase infusion rate to 32, 64, 128, 256 **ml/h** every 15 min respectively as tolerated


Infliximab Infusion Initial Acute Reaction Management Algorithm
Mild
(Hyperemia, palpitation, diaphoresis, headache, nausea, dizziness)
Moderate
(Hypo/hypertension >20 points, fever, shortness of breath, hives, urticaria)
Severe
(Anaphylaxis)
Slow infusion rate to 16 ml/h
Stop the infusion
Stop infusion
Infuse NS @ 20ml/kg/h
Maintain Airway
Give O2 if available
Diphenhydramine 1.25 mg/kg or 50 mg IV
Methylprednisolone 1 mg/kg or 40 mg IV
Call Pediatric GI attending and fellow
OR
AND
- Monitor VS Q10 min until WNL
- Wait 20 min then increase the infusion rate to :
32 ml/h x15 min
64 ml/h x15 min
128 ml/h though completion
- Monitor VS Q5 min until WNL
- Wait 20 min then restart the infusion :
16 ml/h x15 min
32 ml/h x15 min
64 ml/h x15 min
128 ml/h though completion
- Epinephrine [1:1000]@ 0.01/kg/dose IM. (may repeat q5 minx3). Max dose 0.3 mg IM
- Call code team if second dose is required
- Ranitidine 1 mg/kg IV or 50 mg
- Albuterol inhaler 2.5 mg in 3 ml saline via nebulizer if wheezing
- Monitor VS Q2 min until WNL
- Admit to peds GI for further monitoring