

**Running head:** Infusion reaction curriculum for rheumatology fellows

**Title:** How Well Do Rheumatology Fellows Manage Acute Infusion Reactions? A Pilot Curricular Intervention

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**ABSTRACT**

*Background*

Infusible DMARDs are commonly prescribed in rheumatology and other fields. There are no published formal educational curricula rheumatology fellowship programs can use to teach infusion reaction management skills to fellows. We aimed to better understand this

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educational gap, and implement and assess the effectiveness of an experiential curriculum on acute infusion reaction management.

### *Methods*

We included current rheumatology fellows and recent graduates from five fellowship programs. Using a novel behavioral checklist we assessed fellows' performance managing an infusion reaction in a simulation, followed by a didactic focused on infusion reactions. Pre and post-surveys assessed experiences to determine relevance, as well as attitudes and knowledge.

### *Results*

Despite ubiquitous prescribing of infusible biologic DMARDs, >50% of fellows were uncomfortable managing infusion reactions. Only 11% of fellows reported infusion reaction training during fellowship, but 56% reported managing actual patient infusion reactions. In the simulated infusion reaction, fellows managed grade 1 reactions appropriately, but grade 4 reactions poorly, meeting <50% of objectives. All fellows discontinued the infusion in the setting of anaphylaxis, but only 56% administered epinephrine. There was no difference in performance or written knowledge by training year. All fellows felt more prepared to manage infusion reactions post-curriculum and were satisfied with the experience.

### *Conclusion*

We confirmed an education gap in rheumatology fellowship training regarding infusion reactions, both in knowledge and performance. We developed and implemented a brief experiential curriculum including simulation of a high-risk patient care scenario. This curriculum was well received and is easily exportable to other programs.

## **SIGNIFICANCE AND INNOVATIONS**

1. This is the first report of an educational curriculum on acute infusion reactions for fellows in any medicine field.
2. Only 11% of surveyed rheumatology fellows in the collaborative received training on the management of infusion reactions during fellowship.
3. Among fellows, practical knowledge about how to manage an infusion reaction was poor, with only half of fellows ordering epinephrine to manage a simulated grade 4 infusion reaction, indicating either knowledge deficiencies or failure of recognition.
4. As infusible biologic medications are becoming more common, this brief, intensive curriculum can be easily implemented in other fields of medicine.

## **INTRODUCTION**

Biologic disease-modifying anti-rheumatic drugs (DMARDs), which target disease specific pathways, are commonly prescribed to manage rheumatic diseases. All biologic DMARDs have the potential to cause serious adverse effects including injection site reactions (ISRs) and infusion reactions. Up to 30% of patients in clinical trials of injectable DMARDs

experience ISRs (1). Infusion reactions are also common, affecting nearly 10% of patients receiving infliximab, with an incidence of 6.1% (2). Reported rates are as high as 45% with pegloticase in phase 3 clinical trials (3). As learning to appropriately “prescribe, monitor and assess response to pharmacotherapy, including immunomodulatory agents” is a core competency of rheumatology fellowship training, it seems infusion therapy management would be a part of all fellowship curricula (4, 5). However, informal surveying of rheumatology program directors from the Carolinas Fellows Collaborative (CFC) revealed no formalized curricula. To date there are no published educational curricula for rheumatology providers addressing infusion reaction management. Furthermore, there are no published studies of how often rheumatology fellows, practicing rheumatologists or physicians from other fields who prescribe infusion medications manage infusion reactions.

Based on lack of formal education about this topic, we hypothesized current rheumatology fellows’ knowledge about infusion reactions would be poor. We also assumed rheumatology fellows and recent graduates would agree infusion reaction management should be taught because of the high potential for morbidity to patients. To address this potential education gap, we developed and implemented a brief and intensive educational curriculum that included a needs assessment survey, a practical simulation with immediate corrective feedback and an instructive didactic to summarize the topic. We then collected feedback about this experiential curriculum. Finally, we assessed practice patterns with infusible DMARDs and experiences managing infusion reactions.

## MATERIALS AND METHODS

The Duke University Institutional Review Board determined this study exempt from review.

**Study population.** We included current rheumatology fellows and recent (2015-2016) graduates from five programs: Duke University, Wake Forest University, the University of North Carolina at Chapel Hill, Medical University of South Carolina and Massachusetts General Hospital. These fellows attended the annual CFC Winter Conference at Duke in 2017, during which one half-day is dedicated to performance assessment and feedback through a multiple station objective structured clinical examination (OSCE).

**Pre-curriculum Assessment.** A pre-survey assessed prior experience, attitudes and knowledge about infusion reactions. Attitudes and comfort with management were measured by Likert scale. Knowledge questions included symptom/sign reaction grading (defined by the National Cancer Institute Terminology Criteria for Adverse Events [NCI-CTCAE]) and infusion management decisions by reaction grade (6). Twenty-two fellows were emailed a Qualtrics® (Provo, Utah) link to the pre-curriculum survey. Graduates were emailed a link to a similar survey omitting the knowledge assessment in an attempt to shorten the survey and improve participation.

**Simulation-based Assessment.** One week pre-conference, fellows received brief descriptions of the OSCE, describing one station as “Infusion: You will speak with an infusion center nurse regarding patient management.” This station simulated the experience of an on-call rheumatologist, paged by an infusion center nurse about a patient having an acute infusion reaction to a biologic DMARD. The station was proctored by phone, with an allotted time of 12-minutes, followed by 3-minutes of face-to-face feedback. This station began with the fellow managing a patient having a grade 1 infusion reaction,

which evolved into a grade 4 infusion reaction. Proctors assessed performance using a behavior checklist.

The station scenario and performance checklist were developed based on published reports, local infusion center protocols and NCI-CTCAE reaction grading (6-12). The checklist included three sections with a maximum score of 24 points (1 point/item): History taking (10 points), Grade 1 reaction management (4 points) and Grade 4 reaction management (10 points).

**Curriculum and Post-Survey.** The day following the OSCE, fellows attended a 15-minute interactive didactic session. Session objectives were 1) differentiate immediate versus non-immediate drug hypersensitivity reactions (DHRs), 2) teach the pathophysiology of DHRs, 3) compare and contrast anaphylactoid reactions versus anaphylaxis, 4) define the NCI-CTCAE grading schema and 5) teach appropriate initial assessment and management of infusion reactions. Session attendees completed a post-survey again assessing attitudes, comfort and knowledge about infusion reactions.

**Statistical analysis.** Descriptive statistics were used for demographics and prior experience. Fischer's exact test estimated differences in attitude and comfort Likert scale responses, OSCE performance by fellowship training year (year 1 compared to years 2 & 3) and knowledge matching questions. Likert scale responses were grouped into categories of "Agree" and "Disagree." A two-sided t-test of the means was used for determination of differences between fellowship training years on the overall OSCE performance scores. All analyses were conducted in SAS 9.4 (Cary, North Carolina).

## RESULTS

**Demographics.** Eighteen rheumatology fellows completed the pre-survey: 15 (83%) adult, 1 (6%) pediatric and 2 (11%) combined adult/pediatric rheumatology. Respondents included 8 first years and 10 second year of training or beyond. Eighteen adult rheumatology fellows participated in the OSCE: 8 first, 9 second and 1 third year. Twenty-two fellows (9 first, 9 second, 3 third and 1 fourth year) attended the didactic session and 21 completed the post-curriculum survey.

Surveys were emailed to 25 CFC adult rheumatology graduates. Ten (40%) completed the survey: 7 graduated in 2015 and 3 in 2016. Nine of 10 respondents were actively practicing rheumatology: 4 (45%) described their practice as a multi-specialty private practice, 2 (22%) as single specialty, 1 (11%) as solo practice, 1 (11%) as academic health center and 1 (11%) as hospital based.

**Attitudes, Comfort, and Experience with Infusion Reactions.** The attitude of nearly all fellows both before and after this curriculum, and of all graduates, was that the topic of acute infusion reactions is important to learn (Table 1). Most (15 [83%]) fellows and graduates (9 [90%]) disagreed that acute infusion reaction management was “the job of the infusion service provider and not my responsibility.” All graduates recommended current fellows be taught how to manage acute infusion reactions. Reasons given included: “We are usually responsible for managing infusion reactions,” “Applicable to any fellow regardless of future career path,” “We prescribe them, we should be able to manage the reaction,” and “Knowledge of management is imperative if you are prescribing these drugs, especially in your clinic site, I feel my rheumatology training was lacking in this aspect.” Pre-curriculum, 11 (61%) fellows agreed their “knowledge is poor in the management of acute infusion reactions.”

Regarding comfort, 8 (44%) current fellows reported feeling comfortable managing infusion reactions; of the 7 fellows physically involved in such a situation, 3 (43%) were uncomfortable with their ability to manage the reaction. Surveyed post-curriculum, all fellows answered they felt comfortable managing an infusion reaction. All 10 graduates reported feeling comfortable with their ability to manage a patient with an acute infusion reaction. All respondents reported a preference for prescribing subcutaneous biologic DMARDS over IV therapies (Table 2). Two (11%) fellows on the pre- and 5 (24%) on the post-survey, along with 2 (20%) graduates, agreed this preference was due to concerns about their ability to manage an acute infusion reaction.

Practice patterns among fellows and graduates differ. While all respondents reported prescribing intravenous (IV) medications to treat rheumatic diseases, graduates (nearly all in private practice) primarily infuse DMARDS within the immediate clinic area, while fellows use a variety of infusion services (supplemental). Over half of graduates reported <10% of their patients were receiving infusion medications, while more than half of current fellows estimated 10-25% of their patients were receiving infusible medications. Though both groups prescribed many different medications, all current fellows and only half of graduates prescribed cyclophosphamide.

Regarding experience with infusion reactions (Table 2), few current fellows reported education/training prior to (3 [17%]) or during (2 [11%]) fellowship. Half of this reported training was informal advice from supervising physicians. Six (60%) graduates reported their training included education about infusion reactions; 3 (50%) recalled dedicated lectures and 2 (33%) cited presentations during training program orientation. Despite minimal training, 10 (56%) fellows reported being paged and 7 (39%) had physically been

involved in managing a patient having an acute infusion reaction; 3 (17%) felt direct harm was sustained by a patient. Four (40%) graduates reported managing a patient during fellowship and 5 (50%) in current practice for an acute infusion reaction; all reported multiple occurrences.

**Knowledge Assessment.** OSCE performance did not vary by training year (Table 3). Fellows reliably requested the patient's vital signs, examination findings and infusion pre-medications. For the grade I reaction, no fellows discontinued the infusion; 15 (83%) recommended decreasing the infusion rate and 15 (83%) prescribed antihistamines. All fellows' performance was highest managing the grade 1 infusion reaction, with a mean score of 3.3 (of 4) points. The overall mean performance in history taking was 4.1 (of 10) and grade 4 infusion reaction management was 4.3 (of 10).

During the grade 4 reaction simulation, all fellows appropriately discontinued the infusion. Most fellows activated the emergency response system and ordered continuous non-invasive hemodynamic monitoring. There was a non-significant higher rate of upper level fellows providing transition of care to EMS/ED providers and updating the patient's emergency contact. No fellow spontaneously asked the nurse to add the medication to the patient's allergy list, nor did any fellow mention contacting the prescribing rheumatologist. Ten (56%) fellows appropriately ordered epinephrine for the grade 4 reaction (anaphylaxis). Inappropriate management was recommended by many fellows, with 13 (72%) ordering steroids and 10 (56%) ordering antihistamines.

In the pre-didactic knowledge assessment (supplemental), current fellows demonstrated a generally poor understanding of NCI-CTCAE infusion reaction grading through their inability to correctly match signs and symptoms to the correct reaction grade. However, when given an infusion reaction grade and asked to determine if they would 1) continue, 2) decrease the rate or 3) stop the infusion, most fellows chose the correct management option, except in grade 3 in which only 55% chose correctly (discontinue the infusion). There was no statistical difference in performance by training years.

After the OSCE and didactic presentation, all fellows performed similarly on the post-intervention knowledge assessment. Eleven (52%) fellows correctly identified anaphylactoid reactions as the most common infusion reaction cause and all recognized the importance of prolonged monitoring for a grade 4 reaction. Only 1 (5%) fellow matched a grade 3 reaction clinical scenario correctly. All fellows recognized epinephrine as important in the management of anaphylaxis. Four (18%) fellows answered acetaminophen and 7 (32%) antihistamines as important in the management of anaphylaxis.

**Curriculum Evaluation.** All participants rated their overall experience as being somewhat or extremely satisfied. All fellows agreed their knowledge about the management of acute infusion reactions had improved, their awareness of IV medication related adverse effects had increased and the training was important and worth their effort. Eight (38%) fellows answered they plan on prescribing IV DMARDs more based on information learned from the curriculum.

## DISCUSSION

We created and tested an easily transferrable educational curriculum on acute infusion reactions. We confirmed a gap in training, with minimal formal education about acute infusion reactions prior to or during fellowship. Nonetheless, most current fellows had been called to manage infusion reactions, and nearly half reported feeling uncomfortable with their ability to manage these patients. Poor OSCE performance confirmed that fellows should feel uncomfortable managing infusion reactions, since their average score was only 4.3/10 in simulated management of a grade 4 infusion reaction. These findings are concerning, since most graduates who enter private practice can expect an office-based infusion center. Of interest, while this sample of recent graduates reported comfort managing infusion reactions, all reported a preference for subcutaneous DMARDs and nearly 20% related this preference to their discomfort managing infusion reactions. Certainly, though, the ultimate decision on biologic formulation is not made in isolation, considering factors including disease-activity, cost/insurance coverage, patient preference, convenience, co-morbid risk factors and current/prior medications.

This brief experiential curriculum is grounded in assumptions of several adult-learning theories. As per Knowles' assumptions, we established curriculum relevance, setting the stage prior to delivery through a survey requiring fellows to reflect on their comfort with the topic and a brief knowledge assessment to highlight their own learning needs. Fellows were notified they would face a simulated infusion reaction situation, giving them opportunity to pre-read about infusion reactions. The simulated event took place during an annual conference, when fellows were "in the mode" of learning, consistent with the Theory of Margin. Finally, experiential learning through an OSCE followed by a didactic with high-

quality information for managing a future, similar situation, is consistent with Jarvis' theory of transformational learning (13).

We identified differences between written knowledge and clinical performance. While most fellows correctly matched infusion reaction grade with appropriate management decisions, grade 4 reaction management was poor on the OSCE. All fellows appropriately recognized the need to discontinue an infusion for a severe infusion reaction, but only 56% recommended epinephrine for anaphylaxis, suggesting either limited anaphylaxis recognition or inadequate management knowledge. Prior studies have shown poor recognition and management of anaphylaxis in other specialties (14, 15). We presume fellows had not previously learned about the NCI-CTCAE grading system for infusion reactions, although their gestalt regarding whether to discontinue an infusion was generally correct. Learning the NCI-CTCAE grading system provides a foundation for gauging the severity of and appropriately managing acute infusion reactions, promoting favorable outcomes.

Limitations of this study include the use of not yet validated tools to assess knowledge and OSCE performance (none currently exist) and small sample size. Additionally, survey and knowledge assessments were anonymous, preventing correlation of confidence with competence for individual fellows. Since this was the initial implementation of this curriculum, determining improved knowledge during fellowship was not possible.

Graduates reported a higher rate of training/education during fellowship compared to current fellows. We are not aware of any substantial curricular changes within the 5 fellowship programs and attribute this difference to the possibility of recall bias, sampling

bias and individual fellow interest as well as experience gained in practice after fellowship training.

Study strengths include representation of fellows from multiple institutions, varied training years and types. The use of multiple assessments through surveys, written testing and simulation also represent strengths. Additionally, this form of curriculum is unique in that a practical assessment of ability was performed before the formal curriculum, to provide context, and it simulated a very high-risk clinical scenario without putting patients at risk.

Post-knowledge testing revealed opportunity for curriculum improvement. For example, only about 50% of fellows distinguished anaphylaxis from anaphylactoid reactions and only 1 correctly recognized a grade 3 reaction based on written scenarios. Future iterations can place more emphasis on reaction grade assessment and distinguishing between DHR types. Recording the didactic session will make it usable by other programs.

In summary, we successfully developed and implemented an acute infusion reaction educational curriculum for rheumatology fellows, meeting an important educational need for safe future practice. All participants felt this topic was important, some graduates commented they wished their training programs had provided this education. As a rheumatologist, management of both rheumatic disease and medication related adverse effects are critical to patient care. This curriculum can easily be implemented by any training program, with the ability to simulate a high-risk clinical scenario by phone. With the exploding use of targeted biologic infusion therapies in multiple fields, this curriculum can be widely adapted for multiple specialties.

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## **TABLES**

See attachments

## **LEGENDS**

Table 1

\*1/21 (4.8%) responded as not applicable

†1/21 (4.8%) responded as not applicable

‡1/10 (10%) responded as not applicable

## Table 2

\*"Residency lecture," "from senior resident"

†Institutional GME training, "advice from 2 attendings" – reported little to moderate amount of influence

‡6/7 reported 2 or more times (85%); 1/7 reported more than 10 incidents

§None resulted in death

¶13/18 (16.7%) had concerns about their ability to manage an infusion reaction affecting preference

#2/6 during fellowship orientation, 3/6 general academic lecture, 1/6 dedicated conference course, 2/6 other - "from rheumatology attending I worked with" and "preceptor bringing me along when called to manage an infusion reaction"

\*\*5/5 reported between 2-10 incidents per graduate

††2/10 had concerns about their ability to manage an infusion reaction affecting preference

## Table 3

\*Most common rate reduction was by 50%

## SUPPLEMENTARY MATERIAL

See attachments

Table 1. Surveyed attitudes, comfort and self-reported knowledge of rheumatology fellows and graduates.

|               |                                                                                                                          | Fellow<br>Pre-Survey<br>Agree<br>n =18 (%) | Fellow<br>Post-Survey<br>Agree<br>n=21 (%) | Graduate<br>Survey<br>Agree<br>n=10 (%) |
|---------------|--------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|--------------------------------------------|-----------------------------------------|
| Attitudes     | Having a working knowledge on the assessment of an acute infusion reaction is important to me.                           | 17 (94.4)                                  | 21 (100)                                   | 10 (100)                                |
|               | As a rheumatologist, I should be able to manage a patient having an acute infusion reaction from a DMARD.                | 18 (100)                                   | 21 (100)                                   | 9† (100)                                |
|               | The management of an acute infusion reaction is the job of the infusion service provider and not my responsibility.      | 3 (16.7)                                   | 5 (23.8)                                   | n/a                                     |
|               | I plan on prescribing IV DMARDs more based on what I learned from this curriculum.                                       | n/a                                        | 8* (38.1)                                  | n/a                                     |
|               | This training was worth my time and effort.                                                                              | n/a                                        | 21 (100)                                   | n/a                                     |
| Comfort       | I am uncomfortable with managing an acute infusion reaction.                                                             | 10 (55.6)                                  | n/a                                        | n/a                                     |
|               | I am <i>comfortable</i> managing an acute infusion reaction.                                                             | n/a                                        | 21 (100)                                   | 10 (100)                                |
|               | I prefer to prescribe SQ over IV medications because I am <i>uncomfortable</i> with managing an acute infusion reaction. | 2 (11.1)                                   | 5† (23.8)                                  | 2 (20)                                  |
| Knowl<br>edge | My knowledge is poor in the management of acute infusion reactions.                                                      | 11 (61.1)                                  | n/a                                        | n/a                                     |
|               | My knowledge about acute infusion reactions is improved.                                                                 | n/a                                        | 21 (100)                                   | n/a                                     |
|               | I am more aware of IV medication related adverse effects.                                                                | n/a                                        | 21 (100)                                   | n/a                                     |

Table 2. Reported prior education, experience and relevance by rheumatology fellows and graduates.

|                                                                                                                               | Fellows n (%) |           | Graduates n (%) |          |
|-------------------------------------------------------------------------------------------------------------------------------|---------------|-----------|-----------------|----------|
|                                                                                                                               | Yes           | No        | Yes             | No       |
| <b>Prior Education and Experience</b>                                                                                         |               |           |                 |          |
| Infusion reaction training/education <i>prior</i> to fellowship                                                               | 3* (16.7)     | 15 (83.3) | n/a             | n/a      |
| Infusion reaction training/education <i>during</i> fellowship                                                                 | 2† (11.1)     | 16 (88.9) | 6# (60)         | 4 (40)   |
| Current practice, were you required to complete any training for infusion reaction management                                 | n/a           | n/a       | -               | 10 (100) |
| Prior experience working in an infusion clinic with primary role of administering medication                                  | -             | 18 (100)  | n/a             | n/a      |
| During fellowship ever been <i>physically</i> involved in managing an acute infusion reaction                                 | 7‡ (38.9)     | 11 (61.1) | n/a             | n/a      |
| During fellowship ever been <i>paged</i> regarding a patient having an acute infusion reaction                                | 10 (55.6)     | 8 (44.4)  | n/a             | n/a      |
| During fellowship, did you ever assess or manage a patient having an acute infusion reaction (either in person or by phone)   | n/a           | n/a       | 4 (40)          | 6 (60)   |
| Since graduation from fellowship, has one of your patients had an acute infusion reaction                                     | n/a           | n/a       | 2 (22.2)        | 7 (77.8) |
| Since graduation, have you had to assess or manage a patient having an acute infusion reaction (either in person or by phone) | n/a           | n/a       | 5** (50)        | 5 (50)   |
| Change a patient's therapy because of an infusion reaction                                                                    | 11 (61.1)     | 7 (38.9)  | n/a             | n/a      |
| Has a patient you were treating sustained direct harm, to include death, related to an infusion therapy being prescribed      | 3§ (16.7)     | 15 (83.3) | n/a             | n/a      |
| <b>Relevance</b>                                                                                                              |               |           |                 |          |
| During fellowship, have you prescribed IV medications for the direct treatment of a rheumatic disease                         | 18 (100)      | -         | n/a             | n/a      |
| Since graduation from fellowship, have you prescribed IV medications for direct treatment of a rheumatic disease              | n/a           | n/a       | 9 (90)          | 1 (10)   |
| Given the option, do you prefer to prescribe subcutaneous over IV medications                                                 | 18¶ (100)     | -         | 10++ (100)      | -        |
| Do you recommend fellows be taught how to manage acute infusion reactions                                                     | n/a           | n/a       | 10 (100)        | -        |

Table 3. OSCE checklist results

|                                             | Rheum Fellow<br>Year 1<br>n=8 (%) | Rheum<br>Fellow<br>Years 2&3<br>n=10 (%) | Combined<br>Years<br>n=18 (%) | p-value |
|---------------------------------------------|-----------------------------------|------------------------------------------|-------------------------------|---------|
| <b>History Taking &amp; Assessment</b>      |                                   |                                          |                               |         |
| Current vital signs                         | 5 (62.5)                          | 8 (80)                                   | 13 (72.2)                     | 0.6     |
| Examination findings                        | 7 (87.5)                          | 8 (80)                                   | 15 (83.3)                     | 1.0     |
| Current medications                         | 1 (12.5)                          | 2 (20)                                   | 3 (16.7)                      | 1.0     |
| Co-morbidities                              | 1 (12.5)                          | 0                                        | 1 (5.6)                       | 0.4     |
| Onset of symptoms (time)                    | 1 (12.5)                          | 4 (40)                                   | 5 (27.8)                      | 0.3     |
| Date of last infusion                       | 5 (62.5)                          | 3 (30)                                   | 8 (44.4)                      | 0.3     |
| Prior difficulties with infusion            | 4 (50)                            | 2 (20)                                   | 6 (33.3)                      | 0.3     |
| Infusion pre-medications                    | 7 (87.5)                          | 6 (60)                                   | 13 (72.2)                     | 0.3     |
| Infusion rate                               | 2 (25)                            | 5 (50)                                   | 7 (38.9)                      | 0.4     |
| Interventions already completed             | 1 (12.5)                          | 1 (10)                                   | 2 (11.1)                      | 1.0     |
| Mean Score ( $\pm$ SD)                      | 4.3 ( $\pm$ 1.9)                  | 3.9 ( $\pm$ 1.7)                         | 4.1 ( $\pm$ 1.7)              | 0.7     |
| <b>Grade 1 Infusion Reaction Management</b> |                                   |                                          |                               |         |
| Continue infusion/no change                 | 1 (12.5)                          | 2 (20)                                   | 3 (16.7)                      | 1.0     |
| Continue infusion and decrease rate*        | 7 (87.5)                          | 8 (80)                                   | 15 (83.3)                     | 1.0     |
| Discontinue infusion                        | 0                                 | 0                                        | 0                             | 1.0     |
| Maintained IV                               | 2 (25)                            | 7 (70)                                   | 9 (50)                        | 0.1     |
| Repeat vital signs                          | 8 (100)                           | 9 (90)                                   | 17 (94.4)                     | 1.0     |
| Update on patient status with intervention  | 7 (87.5)                          | 8 (80)                                   | 15 (83.3)                     | 1.0     |
| <b>Adjunct Medications Recommended</b>      |                                   |                                          |                               |         |
| Antihistamine                               | 7 (87.5)                          | 8 (80)                                   | 15 (83.3)                     | 1.0     |
| Acetaminophen                               | 0                                 | 1 (10)                                   | 1 (5.6)                       | 1.0     |
| Mean Score ( $\pm$ SD)                      | 3.1 ( $\pm$ 0.6)                  | 3.4 ( $\pm$ 0.8)                         | 3.3 ( $\pm$ 0.8)              | 0.4     |
| <b>Grade 4 Infusion Reaction Management</b> |                                   |                                          |                               |         |

|                                                |                   |                   |                   |     |
|------------------------------------------------|-------------------|-------------------|-------------------|-----|
| Discontinue infusion                           | 8 (100)           | 10 (100)          | 18 (100)          | 1.0 |
| Activate emergency response system             | 7 (87.5)          | 7 (70)            | 14 (77.8)         | 0.6 |
| Continuous non-invasive hemodynamic monitoring | 6 (75)            | 6 (60)            | 12 (66.7)         | 0.6 |
| Placed patient on oxygen                       | 4 (50)            | 4 (40)            | 8 (44.4)          | 1.0 |
| Response to interventions                      | 2 (25)            | 5 (50)            | 7 (38.9)          | 0.4 |
| Rituximab placed on patient's allergy list     | 0                 | 0                 | 0                 | 1.0 |
| Transition of care with EMS/ED provider        | 1 (12.5)          | 5 (50)            | 6 (33.3)          | 0.2 |
| Updated patient's emergency contact            | 0                 | 3 (30)            | 3 (16.7)          | 0.2 |
| Contacted prescribing rheumatology provider    | 0                 | 0                 | 0                 | 1.0 |
| <b>Adjunct Medications Recommended</b>         |                   |                   |                   |     |
| Epinephrine                                    | 5 (62.5)          | 5 (50)            | 10 (55.6)         | 0.7 |
| Steroids                                       | 6 (75)            | 7 (70)            | 13 (72.2)         | 1.0 |
| Antihistamine                                  | 5 (62.5)          | 5 (50)            | 10 (55.6)         | 0.7 |
| IV Fluids                                      | 5 (62.5)          | 5 (50)            | 10 (55.6)         | 0.7 |
| Nebulizer/Albuterol                            | 1 (12.5)          | 2 (20)            | 3 (16.7)          | 1.0 |
| Acetaminophen                                  | 3 (37.5)          | 4 (40)            | 7 (38.9)          | 1.0 |
| Mean Score ( $\pm$ SD)                         | 4.1 ( $\pm$ 1.1)  | 4.5 ( $\pm$ 1.5)  | 4.3 ( $\pm$ 1.3)  | 0.6 |
| Total Mean Score ( $\pm$ SD)                   | 11.5 ( $\pm$ 1.4) | 11.8 ( $\pm$ 1.4) | 11.7 ( $\pm$ 1.4) | 0.8 |