Anaphylaxis Kit Utilization and Evaluation of Infliximab and Vedolizumab Therapy in Home Infusion

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Background

The emergence of monoclonal antibody therapies such as infliximab and vedolizumab has led to advances in drug therapy for a range of disease states including but not limited to rheumatoid arthritis, psoriatic arthritis, and inflammatory bowel disease. However, due to the rates of infusion related reactions with both of these drugs (13% n=60 infliximab, and 4% n=1434 vedolizumab[1,2]), there has been hesitation regarding administration in alternate care settings, including the home. The data regarding infusion related reactions with each medication has been previously demonstrated, with similar results.[3] Many studies, including a systematic review by Lichenstein et al.[3] indicated that the incidence of infusion related reactions with infliximab specifically was reported to range from 5-23% in inflammatory bowel disease (IBD) patients and required minor intervention, very rarely being EMS activation or admission to the hospital.

If infliximab or vedolizumab is administered in the home setting, patients within the organization may be prescribed anaphylaxis kits consisting of diphenhydramine, epinephrine, and 0.9% sodium chloride. The need to send an anaphylaxis kit in a first dose situation within the organization is handled on a case by case basis per policy, upon review of patient's clinical history and allergic potential of the drug.[4] As such, there is no universal requirement for the dispensing of anaphylaxis kits with infliximab and vedolizumab. Although the data regarding the frequency of use of anaphylaxis kits within the organization is available, it has not yet been analyzed to determine established dispensing criteria.

Purpose

The purpose of this study is to quantify the usage of anaphylaxis kits in home infusion patients administered infliximab (Remicade®, Inflectra®)[5] or vedolizumab (Entyvio®), and incidence of infusion related reactions. Outcomes include increasing patient safety, cost reduction, and improvement of patient care.

The outcomes from this study will provide the objective data from which to further standardize the anaphylaxis kit dispenses associated with infliximab and vedolizumab. It may also allow for policy updates to be made regarding anaphylaxis kit dispensing requirements including but not limited to frequency of dispensing beyond the first dose.

Methods

Patients who received infliximab or vedolizumab between June 2019 and June 2020 were included. Drug utilization reports through the electronic medical records were used to determine dispenses of infliximab or vedolizumab in conjunction with an anaphylaxis kit. We randomized a pool of 1,174 infliximab patients and 522 vedolizumab patients to a total of 200 patients (100 per drug group). A report from the internal adverse event reporting software was also incorporated into data collection.

The primary endpoints in this study included infusion related reactions (i.e. hypersensitivity, chest pain, shortness of breath, infusion site reactions, rash) and the use of an anaphylaxis kit. Secondary endpoints included the interventions made during therapy in response to infusion reactions (i.e. infusion stopped, slowed) as well as comorbid conditions in patients who experienced an infusion reaction (i.e. hypertension, asthma). Other considerations during data analysis included the cost of anaphylaxis kit dispenses. Endpoints reviewed and frequency reported as a percentage. This study was deemed to be IRB exempt.

References

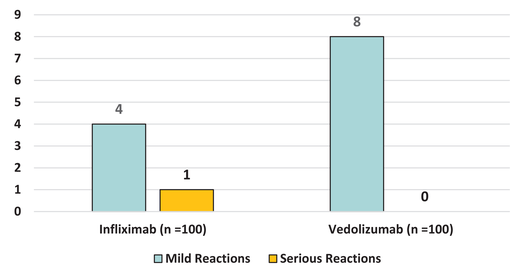
[1] infliximab (Remicade) package insert. Horsham, PA; Janssen Biotech, Inc; 2009 April
[2] vedolizumab (Entyvio) package insert. Deerfield, IL; Takeda Pharmaceuticals America, Inc; 2014 May
[3] Lichtenstein L, Ron Y, Kivity S, et al. Infliximab-Related Infusion Reactions: Systematic Review. J Crohns Colitis. 2015;9(9):806-815. doi:10.1093/ecco-jcc/jjv096
[4] Option Care Health (2020). Anaphylaxis Treatment and Management. Unpublished internal policy.
[5] infliximab (Inflectra) package insert. New York, NY; Pfizer Inc, 2016
[6] Lexicomp Online, Lexi-Drugs Online, Hudson, Ohio: UpToDate, Inc.; 2021; February 16, 2021.

Table 1:

Variable	Infliximab (n=100)	Vedolizumab (n=100)
Age, median (IQR)	45 (13-77)	50.5 (14-87)
Dosage	250 mg – 1000 mg	300 mg
Gender		
Male, n(%)	53 (53%)	43 (43%)
Female, n(%)	47 (47%)	57 (57%)
Comorbid Conditions[a]	6 (6%)	19 (19%)
Infusion Reaction		
Nausea	1 (1%)	2 (2%)
Headache	-	3 (3%)
Elevated Blood Pressure	-	2 (2%)
Chest Tightness	-	1 (1%)
ED Visit	1 (1%)[d]	1 (1%)[e]
Rash and/or Hives	2 (2%)	-
Abdominal Discomfort	1 (1%)	-
Total Mild Reactions[b]	4 (4%)	8 (8%)
Total Serious Reactions[c]	1 (1%)	0 (0%)
Disease State		
IBD[f]	93 (93%)	100 (100%)
Other[g]	7 (7%)	-

[a] asthma, diabetes, hypertension, heart disease
[b] nausea, headache, elevated BP, chest tightness, ED visit w/o admission, rash, hives, abdominal discomfort
[c] ED visit with admission, anaphylaxis
[d] patient was admitted to hospital categorizing visit as serious reaction
[e] patient was not admitted to hospital categorizing visit as mild reaction
[f] Crohns disease, ulcerative colitis, ulcerative rectosigmoiditis, both crohns and ulcerative colitis
[g] Hidradenitis suppurativa, sarcoidosis, rheumatoid arthritis, chronic iridocyclitis

Figure 1: Reactions by Drug



Results

Two-hundred patients were randomly selected utilizing a random number generator during the time span of June 2019 – June 2020 (100 per drug group). The age span of the patients ranged from 13-87 years old. Of the patient population, 48% were male, and 52% were female. Of these 200 patients disease states were as follows, 122 (61%) Crohn's disease, 60 (30%) Ulcerative Colitis, 5 (2.5%) Ulcerative Rectosigmoiditis, 6 (3%) both Ulcerative Colitis and Crohns Disease, 2 (1%) Hidradenitis Suppurativa, 2 (1%) Sarcoidosis, 2 (1%) Rheumatoid Arthritis, 1 (0.5%) Chronic iridocyclitis. Vedolizumab patients were on a consistent dose of 300mg whereas the infliximab patient doses ranged from 250mg-1200mg. Of these 200 patients, 25 (12.5%) had a comorbid condition *(see Table 1)*.

These patients were then further examined to determine if there were any adverse reactions to infliximab or vedolizumab therapy. Of the 200 patients, there was a total of 13/200 (6.5%) patients who had a mild reaction *(see Table 1)*. Only 1 patient out of 200 (0.5%) was found to have a serious adverse reaction *(see Figure 1)*. Interventions made in the infliximab group included one incidence of slowing the infusion rate, and one incidence of utilizing by mouth medications. Interventions made in the vedolizumab group included one instance of a patient who went to the emergency department and was observed overnight, however, nothing was noted. Of the 200 patients, there were approximately 232 anaphylaxis kit dispenses (~1.16 kits/patient).

Discussion

The incidence of infusion related reactions, both mild and severe, was low at 7% and lower than previous studies. There was no difference in incidence of reactions across ages, genders, diagnoses, and other co-existing comorbidities. The two incidences of ED admission can be considered outliers as no other cases had similar results. Epinephrine was not used in any of the 200 patients during the study timeframe. Interventions made for the infliximab group included 1 use of by mouth (PO) medications, and 1 rate slowed. Interventions made for the vedolizumab group included 1 instance of patient reporting to the emergency department with no admission.

Limitations of this study include small sample size and retrospective design. Additionally, patients who may have previously experienced severe reactions necessitating drug discontinuation were not included.

The average drug cost associated with an anaphylaxis kit is $20.[6] When considering the average cost of providing anaphylaxis kits with these therapies, the savings for 200 patients could be extrapolated to an estimated 3,000 total dispenses of anaphylaxis kits for a potential savings of approximately $60,000 annually.

Conclusion

Infliximab and vedolizumab demonstrated low incidence of infusion related reactions and no utilization of anaphylaxis kits. This data supports less restrictive policies related to anaphylaxis kit dispensing with infliximab or vedolizumab. The data, although specific to one organization, may be utilized in future studies to evaluate the safety of infliximab and vedolizumab in the home setting. Furthermore, the framework of this study supports future potential studies to evaluate the safety of other outpatient monoclonal antibodies in the home setting.

Disclosures

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation: Julia Cowell, Craig Gardner, Maria Giannakos, Christopher Czech, Warren Rogers: Nothing to disclose.

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