Khartoum Journal of Pharmaceutical Sciences
2020 Volume (1) , Issue (1), Pages (7-12)
http://onlinejournals.uofk.edu/

Research Article

Retrospective Comparison of Efficacy and Safety of Basiliximab and Antithymocyte Globulin in Kidney Transplant Recipients

Article Information
Received
27 Jan 2020
Accepted
24 Aug 2020
Published
1 Sep 2020

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Abstract

Background: Induction therapy with biological agents as anti-thymocyte globulin (ATG) or an interleukin 2 receptor antagonist (IL2-RA) is essential to reduce the risk of acute rejection. Though ATG is used selectively in patients with high immunological risk, the decision for induction treatment stays a matter of discussion in a patient with high immunological risk.

Objective: To compare the efficacy and safety of Basiliximab versus Antithymocyte Globulin (ATG) in kidney transplant recipients (KTRs).

Methodology: A retrospective study was conducted at Ahmed Gasim Hospital, Cardiac Surgery and Renal Transplantation center. Data was collected from all renal transplant recipients with intermediate immunological risk from January 2017 to August 2018. Data included the patient's demographics, efficacy, and frequency of adverse effects.

Results: Out of 75 patients, 44 (58.7%) patients were treated with ATG, and 31(41.3%) with Basiliximab. Patient survival at one year was 97.7 % in the ATG treated group and 100 % in the Basiliximab treated group.While graft survival was similar in both groups (100%), and there was no delayed graft function in both groups, the incidence of acute rejection was 6.8 % and 6.5 % in the ATG and the Basiliximab treated group respectively. Infections were more prevalent in the ATG treated group 22.7% compared to 9.7% in Basiliximab treated group. Moreover, the rate of hematological disorders was significantly higher in ATG treated group (61.4%) in comparison to Basiliximab treated group (29%)

Conclusion: Both, ATG and Basiliximab induction therapy decreased acute rejection rates and they were associated with excellent one-year graft and patient survival rates. Basiliximab was effective as ATG in intermediate immunological risk patients with lower infections and hematological disorders rates and lower mortality rates.

Keywords: Anti-thymocyte globulin, Basiliximab, kidney transplant recipients

Introduction

Kidney transplantation is the treatment of choice for stage five chronic kidney disease patients. Except for transplantation between identical twins, all kidney transplant recipients (KTRs) need immunosuppressive medications to prevent rejection.The goal of immunosuppressive therapy is to prevent organ rejection, prolong graft survival, patient survival, and consequently improve the quality of patient's life. Many studies reported that short-term (1–2 years) survival after transplantation has improved dramatically.As patients live longer after transplantation, the focus of therapy has shifted to survival and management of long-term complications. [1,2].

The genetic compatibility between donor and recipient can have a major impact on acute rejection, graft function, graft survival, and patient survival.Therefore, according to human leukocyte antigen typing and related factors, the recipient is classified into low, intermediate or high immunological risk groups [5].

Induction therapy is treatment with a biologic agent, either lymphocyte-depleting agent as Anti-Thymocyte Globulin (ATG) antibody or an interleukin 2 receptor antagonist (IL2-RA) as Basiliximab. While Lymphocyte-depleting agents have been used since the 1980s, non-depleting IL2-RA was introduced in the 1990s [3]. Both induction therapy regimens have different tolerance profiles. ATG is administered (1.5 mg/kg/day) for 3 to 10 days after transplantation. Basiliximab dose is 20 mg IV given 2 hours before the transplant on days 0, followed by a second 20-mg dose on postoperative day four. Although Basiliximab has better tolerance, lower risk of hematological disorders, infection and malignancy rate, it has lower immunogenicity. Therefore, it appears to be the most effective in immunologically low-risk patients, whereas, in high-risk patients, its use may be limited [2, 4, 7]. In high-risk patients, ATG is superior to prevent acute rejection. Furthermore, some reports suggested an additional effect of ATG to prevent or reduce the incidence of delayed graft function (DGF) through the suppression of alloimmunity and ischemia-reperfusion injury [8]. The choice of induction treatment remains a matter of debate, especially for a recipient with intermediate risk of rejection. ATG is used in about 60% of kidney transplantations in the United States, with IL2RA induction being used in only about 20% of cases. In contrast, in Europe, IL2RA induction is more widely used than ATG or other depleting agents Antithymocyte globulin (ATG) and Basiliximab are the most commonly used in induction therapy [3]. In Sudan,There is an essential need to conduct such studies to minimize the risk of organ rejection and improve the quality of patient life.The current study aimed to compare the efficacy and safety of Basiliximab and Antithymocyte Globulin (ATG) in intermediate immunological risk kidney transplant recipients (KTRs)

Methodology

Study design

A descriptive retrospective study was conducted among kidney transplant recipients from paper-based patients' hospital records. The study was conducted from January to August 2019 at Ahmed Gasim Hospital, Cardiac Surgery, and Renal Transplantation Center. Ahmed Gasim Hospital is a specialized hospital located in Khartoum North, Sudan. It incorporates one of the largest Renal Transplantation Centers in Sudan.

Study population

All kidney transplant recipients received either ATG or Basiliximab induction with a subsequent triple immunosuppressive protocol consisting of tacrolimus, mycophenolate,and steroid.

Inclusion and exclusion criteria

All males or females aged from 18-65 years with intermediate immunologic risk patients were

included in the study. Patients with high immunologic risk, incomplete records, missed contact information and who changed maintenance immunosuppressant regimen were excluded. Total coverage of all study population was carried out.The study population 75 patients.

Data collection

A data collection sheet was used to collect data from paper-based patient hospital records Targeted information from the records included the following variable; demographic and background characteristics of recipients, efficacy, and frequency of adverse events during a one-year follow-up. The efficacy was evaluated by the incidence of acute rejection, delayed graft function, graft and patient survival within one-year follow-up by using patient's records, and direct Telephone contact with patients. Moreover, the safety of induction therapy was assessed by comparing adverse effects, namely; microbial infections and various hematological disorders.

Ethical consideration

Ethical clearance and approval to conduct the study were taken from the Ministry of Health, Khartoum State and Ahmed Gasim Hospital. Verbal consent was taken by telephone from all participants after clarification of the purpose of research and confidentiality of all data collected was ensured.

Statistical analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 24. Results were expressed in the form of tables and figures. Pearson Chi-square correlation and Fisher's Exact Test were performed to determine the significance of the difference between Basiliximab and ATG. and p-value < 0.05 was considered statistically significant.

Results

A total of 75 patients were included in the study, 44 (58.7%) patients treated with ATG and 31(41.3%) with Basiliximab. Patients' demographics are outlined in (Table 1). There were no significant differences in the demographic features among both groups. Moreover, time on dialysis before transplantation and the reasons for renal disease requiring transplantation were similar.

Table 1. Demographic characteristics of the study group (75)

Demographic Data	**ATG treated group (n:44)**		**Basiliximab treated group (n:31)**	
Age (years)	**Frequency**	**(%)**	**Frequency**	**(%)**
< 20	2	4.5	3	9.7
20-30	9	20.5	3	9.7
31-40	14	31.8	12	38.7
41-50	10	22.7	4	12.9
51-60	7	15.9	6	19.4
> 60	2	4.5	3	9.7
Total	44	100.0	31	100.0
Gender	**Frequency**	**(%)**	**Frequency**	**(%)**
Male	32	73%	23	74.2
Female	12	27%	8	25.8
BMI	**Frequency**	**(%)**	**Frequency**	**(%)**
underweight	1	2.3	2	6.5
Normal	36	81	23	74.2
overweight	5	11.4	3	9.7
Obese	2	4.5	3	9.7

Out of 75 patients, 68% of patients were with unknown causes of renal failure. The second risk factor was long-standing hypertension (12%). The two treatment groups had the same morbidity background (p-value 0.233). The distribution of two treatment groups according to risk factors is presented in Table 2.

Most of the kidney donors were first degree relatives, 86.40% for ATG treated group and 77.40% for Basiliximab treated group. In both groups, only about 12.00% of donors have no geological relation to receipts. There was no statistically significant difference between the type of donors in the two groups (p-value 0.353).

Table 2. Distribution of risk factors in ATG and Basiliximab treated groups

Risk factor	ATG treated group (n:44)		Basiliximab treated group (n:31)		Total	
	Frequency	(%)	Frequency	(%)	Frequency	(%)
Unknown	30	68%	21	68%	51	68%
Hypertension	5	1 1%	4	1 3%	9	1 2%
Glomerulonephritis	4	9%	0	0%	4	5%
Focal segmental glomerulosclerosis	2	4. 5%	0	0%	2	3%
Stone	2	4. 5%	0	0%	2	3%
Nephrectomy	1	2%	1	3%	2	3%
diabetes mellitus. Hypertension.Stone	0	0%	1	3%	1	1%
Obstructive uropathy	0	0%	1	3%	1	1%
Obstructive Uropathy Nephrectomy	0	0%	1	3%	1	1%
Obstructive Uropathy, Hypertension	0	0%	1	3%	1	1%
Systemic lupus erythematous Nephrectomy	0	0%	1	3%	1	1%

To compare the efficacy and safety of Basiliximab versus ATG, the Creatinine level was used as a surrogate marker for the incidence of delayed graft function (DGF). The occurrence of DGF was zero in both treated groups (Figure 1). Moreover, Fisher's Exact test was done to investigate the incidence of acute rejection in two groups.

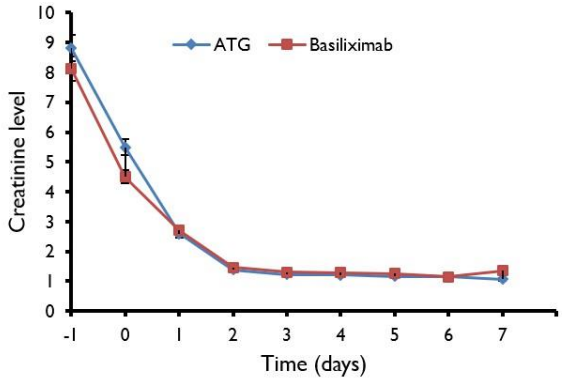

Figure 1. Mean of creatinine concentration in ATG and Basiliximab treated groups pre- and post-operation (-1: one day before the operation, 0: operation day, 0 <: post operation)

As shown in Figure 2, there was no significant difference between the ATG treated group and Basiliximab treated group (P-value: 0.664). Regarding the survival rate, there were no statistically significant differences between the two treatment groups (P-value = 0.587). While Graft survival was 100% for two treatment groups, the patient survival was 97.7% in ATG treated group and 100% in Basiliximab treated group (Figure 2). Although the infection rate was higher in the ATG treated group than in Basiliximab treated group, there was no statistically significant difference between the two groups.

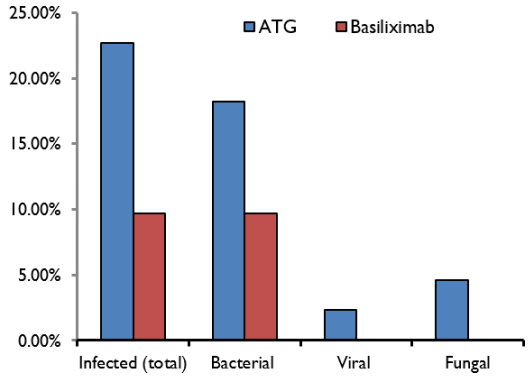

Figure 2. Incidence of infections in ATG treated group(n:44) and Basiliximab treated group and (n: 31)

To determine the rate of the hematological disorder, Fisher's Exact test was done and results are presented in Figure (3). Importantly, there was a statistically significant difference between the two treatment groups;The rate of development of hematological disorders in the ATG treated group and Basiliximab treated group was 61.4% and 29% respectively. Among patients with hematological disorders, anemia was the most common disorder in both groups, it was 52.3% in ATG treated group compared to 25.8% in the Basiliximab treated group. Other observed hematological disorders include thrombocytopenia and leukopenia alone or in addition to anemia.

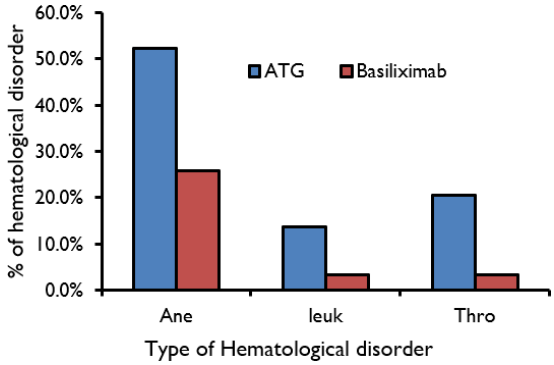

Figure 3. The distraction of different hematological disorders in ATG treated group (n:44) and Basiliximab treated group (n:31). Ane: Anemia,Thro: thrombocytopenia. Leu: leukopenia

Discussion

In recent years, there has been a significant improvement in the short-term outcome following renal transplantation; however, improvement has not been shown in the long-term graft survival. Hence, the primary concern has been shifted to long-term outcomes with an emphasis on fewer complications. Induction therapy prevents the early acute rejection episodes, which may help in improving the long term outcome in renal transplantation. Some studies have shown that the renal allograft half-life was longer in patients who never had acute rejection episodes. Different induction regimens are used to improve the early graft function, thereby improving the short- and long-term graft survival [9]

There is moderate-quality evidence across a broad range of patients with different immunological risk and concomitant immunosuppressive medication regimens, which shows that compared to Basiliximab,ATG reduces acute rejection but increases the risk of infections and malignancies [1, 2]. One study done by Ulrich *et al* (4) Compared the long-term outcome of ATG and Basiliximab with double immunosuppression therapy concluded that the rate of acute rejection was slightly higher in the ATG group. In this study, the incidence of acute rejection was slightly higher in the ATG group (6.8%), however, it was not statistically significant when compared with the Basiliximab group (6.5%). Post-operative analysis indicated no delayed graft function in both treatment groups. This could be attributed to the fact that all patients received kidneys from live donors and were considered as a low-risk group for delayed graft function. Serum creatinine reduction in the first postoperative week was similar in both groups. A recent study showed a favorable effect of ATG compared to Basiliximab in terms of reduced delayed graft function [4]. Furthermore, both groups showed excellent graft survival rate (100%), and there was no graft loss, this may be due to the absence of delayed graft function in all patients.

The patient survival rate at the end of the one-year follow-up period was slightly lower in ATG treated group (97.7%) than in Basiliximab treated group (100 %). In a study conducted by Ulrich F *et al*. reported 91.7% survival rates in ATG treated group and 85% in Basiliximab treated group [4]. In the current study, the cause of death in the ATG treated group may be attributed to adverse events of ATG,especially

The rate of infections including bacterial, fungal, or viral infections was markedly higher in ATG treated group (22.7%) than in Basiliximab treated group (9.7%), this may have contributed to the observed higher mortality in ATG treated patient.Importantly, a high incidence of hematological disorders; anemia, thrombocytopenia, and leukopenia was observed with ATG treated group (61.4%) in comparison to the Basiliximab treated group (29%). Furthermore, the current study revealed a significant relationship between the type of induction therapy and the incidence of anemia; the most common hematological disorder (Figure 3). This finding was in agreement with the study conducted by Ulrich *et al* (4) which concluded

that the rate of adverse events and the infection rates were significantly higher in the ATG treated group than in the Basiliximab treated group.

Conclusion

From the findings of the current study, both ATG and Basiliximab induction therapy decreased the rate of acute rejection and were associated with excellent one-year graft and patient survival rates. Although ATG is effective as Basiliximab in intermediate immunological risk patients, it was associated with higher infection rates and hematological disorders. Also, the mortality rate was relatively higher in ATG treated patients. Although our findings showed that Basiliximab wa effective as and safer than ATG in intermediate immunological risk recipients, further studies in a large population and more long follow up period to confirm long term outcomes.

Conflict of interest

The authors declare no conflict of interest.

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