

Preoperative Erythropoietin Administration in Patients With Prostate Cancer Undergoing Radical Prostatectomy Without Transfusion

Byung Woo Lee, Min Gu Park, Dae Yeon Cho, Seok San Park, Jeong Kyun Yeo

Department of Urology, Inje University Seoul Paik Hospital, Seoul, Korea

Purpose: In this study, we administered erythropoietin preoperatively to patients who underwent open radical prostatectomy without transfusion to increase their hemoglobin levels and investigated the efficacy of this procedure.

Materials and Methods: We evaluated 62 patients who underwent open radical prostatectomy performed by the same surgeon between June 2005 and January 2011. The 22 patients who refused transfusion were assigned to group 1; the patients who accepted transfusion were assigned to group 2. Before surgery, we administered erythropoietin beta to group 1 patients whose hemoglobin levels were < 12 g/dL and retrospectively compared the clinical data of the two groups. We used the t-test and the chi-square test for statistical analysis.

Results: Mean preoperative hemoglobin levels in group 1 after erythropoietin administration (14.5 g/dL) were significantly higher than those in group 2 (13.59 g/dL, $p=0.003$). Moreover, the difference in the mean hemoglobin levels before and after surgery for group 1 patients (3.55 g/dL) significantly exceeded that for group 2 patients (2.08 g/dL, $p=0.000$). Additional analysis revealed no statistically significant differences in perioperative complications between the groups.

Conclusions: Preoperative erythropoietin administration increased the safety margin of hemoglobin levels, and this strategy worked sufficiently well in our experience.

Keywords: Blood transfusion; Bloodless medical and surgical procedures; Erythropoietin; Jehovah's witnesses; Prostatectomy

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Corresponding Author:

Jeong Kyun Yeo
Department of Urology, Inje University Seoul Paik Hospital, 9 Mareunnae-ro, Jung-gu, Seoul 100-032, Korea
TEL: +82-2-2270-0080
FAX: +82-2-2270-0226
E-mail: yeoluvk@hanmail.net

INTRODUCTION

For localized prostate cancer, radical retropubic prostatectomy is considered the standard treatment. However, during this surgery, patients lose large amounts of blood and may therefore require blood transfusions. Patients unwilling to accept transfusions present a challenge to the surgeon. In this study, we administered erythropoietin preoperatively to patients who underwent open radical retropubic prostatectomy without transfusion to increase their hemoglobin levels. We investigated the efficacy of this approach and also discuss other ways to reduce such risks and promote favorable clinical outcomes in radical retro-

pubic prostatectomy without transfusion.

MATERIALS AND METHODS

Our study was conducted on patients who underwent radical retropubic prostatectomy between June 2005 and January 2011. All surgeries were performed by the same surgeon. Of these patients, 22 refused transfusion (group 1), and 40 accepted transfusion (group 2). All patients signed an informed consent form that stipulated the risks of the surgery. We administered 2,000 IU/d of erythropoietin before surgery to the patients in group 1 whose hemoglobin levels were < 12 g/dL until their levels reached 14 g/dL.

TABLE 1. Clinical data for the two groups

Variable	Group 1	Group 2	p-value
Age (y)	67.73	69.30	0.401
Preoperative PSA (ng/mL)	26.95	20.20	0.560
Preoperative Gleason score	7.18	6.30	0.057
Operation time (min)	351.82	397.50	0.009
NPO time (d)	2.68	2.38	0.045
Hospitalization days	15.45	14.00	0.329
Foley indwelling days	14.18	14.45	0.823
Estimated blood loss (mL)	1,331.82	1,411.00	0.739
Perioperative complications (%)	13.60	15.00	0.884 ^a
Wound dehiscence (%)	4.55	2.50	
Transient increase in creatinine levels (%)	4.55	5.00	
Ileus (%)	-	2.50	
Atelectasis (%)	4.55	2.50	
Anastomosis leakage (%)	-	2.50	

p-values were calculated by using the independent t-test, p-values < 0.05 were considered significant.

PSA, prostate-specific antigen; NPO, nil per os.

^a:p-value was calculated by using the chi-square test, p-values < 0.05 were considered significant.

TABLE 2. Hemoglobin (Hb) levels of the two groups

Variable	Group 1	Group 2	p-value
Baseline Hb (g/dL)	12.82	13.59	0.104
Preoperative Hb (g/dL)	14.50	13.59	0.003
Postoperative Hb (g/dL)	10.94	11.51	0.134
Hb difference (g/dL)	3.55	2.08	0.000
Estimated blood loss (mL)	1,331.82	1,411.00	0.739

p-values were calculated by using the independent t-test, p-values < 0.05 were considered significant.

Clinical and laboratory measurements were obtained for both groups, and the data were analyzed. The following parameters were assessed: preoperative factors (age, prostate-specific antigen [PSA] levels, Gleason score); intraoperative factors (operation time); perioperative complications; postoperative factors (changes in hemoglobin levels 1 day after surgery, nil per os [NPO] time after surgery, hospitalization days, time required to remove the Foley catheter); and oncologic factors (postoperative T stage, margin positivity, capsule involvement). We used the t-test and the chi-square test to determine whether there were any statistically significant differences between the groups.

RESULTS

The mean ages of groups 1 and 2 were 67.73 and 69.30 years, respectively, with no statistically significant difference (p=0.401) (Table 1). Moreover, no significant differences were observed in preoperative PSA levels or Gleason scores between the groups. Furthermore, for group 1, the mean preoperative hemoglobin levels before and after erythropoietin administration were 12.82 g/dL and 14.50 g/dL, respectively; notably, the mean hemoglobin levels of group 1 patients receiving erythropoietin significantly exceeded

TABLE 3. Oncologic factors

	Group 1	Group 2	p-value
Postoperative T stage			0.597
1	0	2	
2	14	28	
3	6	8	
4	2	2	
Margin positivity			0.068
+	14	30	
-	6	10	
Capsular extension			0.271
+	10	24	
-	12	16	

p-values were calculated by using the chi-square test, p-values < 0.05 were considered significant.

those of group 2 patients (13.59 g/dL, p=0.003) (Table 2). Differences in mean hemoglobin levels before and after surgery were 3.55 g/dL and 2.08 g/dL for group 1 (with preoperative erythropoietin administration) and group 2, respectively, and this difference was statistically significant (p=0.000) (Table 2). However, no statistically significant differences were observed in the estimated blood loss (1,331.82 mL and 1,411.00 mL for groups 1 and 2, respectively). The mean operation time was 351.82 minutes for group 1 and 397.50 minutes for group 2, with the operation time for group 2 being significantly greater than that for group 1 (p=0.009) (Table 1). Conversely, the postoperative NPO time was greater for group 1 (2.68 days) than for group 2 (2.38 days, p=0.045). However, no statistically significant differences were observed in the number of hospitalization days, Foley catheter indwelling days, or perioperative complications between the groups (Table 1). The perioperative complications included wound de-

hiscence, transient increase in creatinine levels, ileus, atelectasis, and anastomosis leakage (Table 1). Furthermore, no severe perioperative complications (shock, sepsis, etc.) were observed in either group; the postoperative T stage of cancer, margin positivity, capsule involvement, and seminal vesicle involvement were not significantly different between the groups (Table 3).

DISCUSSION

Radical retropubic prostatectomy can result in significant blood loss. The median estimated blood loss associated with radical retropubic prostatectomy is 900 mL [1]. Therefore, patients who opt for surgery but refuse transfusion present a challenge. Radical retropubic prostatectomy without transfusion should encompass a coordinated multidisciplinary approach [2]. Senior surgical, anesthetic, and theater staff should discuss such cases in advance, and the skill sets and number of support staff should be optimized to facilitate blood conservation strategies [2]. Surgery should be performed with meticulous attention to hemostasis [2]. Absorbable cellulose or collagens can help to reduce blood loss [2].

Preoperative erythropoietin beta administration can be used as a hemoglobin booster [3]. As presented in our study, erythropoietin administration effectively increased the preoperative hemoglobin levels. Erythropoietin beta is well tolerated and revealed no serious adverse effects in a previous study [3]. Other studies have reported that preoperative erythropoietin administration promotes erection recovery after nerve-sparing radical retropubic prostatectomy [4]. However, the use of angiotensin II receptor and vitamin K antagonists along with the presence of high BMIs may reduce the efficacy of short-term preoperative erythropoietin treatment [5].

Blood conservation strategies in addition to preoperative erythropoietin administration include acute normovolemic hemodilution, cell salvage machines, and low-dose tranexamic acid. Acute normovolemic hemodilution entails the preoperative phlebotomy of whole blood that contains a high concentration of red blood cells and coagulation factors while replacing the lost volume with a crystalloid or colloid infusion [5]. Relative contraindications to acute normovolemic hemodilution include severe anemia, ischemic heart disease, and renal failure [6]. In addition, cell salvage machines can be used to collect and filter the blood removed by use of suction and swabs and return it to the patient [7]. Several surgeons have been reluctant to use cell salvage because of the theoretical risk of tumor spread [8]. However, Gray et al. [9] reported that cell salvage did not increase the risk of recurrence of prostate cancer. Low-dose tranexamic acid is a safe and effective means of reducing the rate of perioperative blood transfusions in patients undergoing radical retropubic prostatectomy [10].

Careful attention to patient condition is required after surgery. Hypertension should be avoided after surgery to

reduce the possibility of bleeding, and secondary hemorrhage should be aggressively managed. In the case of severe anemia, pulsed hyperbaric oxygen therapy represents a supportive treatment [11]. Iron, vitamin B-12, folate, and recombinant erythropoietin can be administered to patients after surgery [12], and nutritional supplementation can aid recovery.

In our study, the mean preoperative hemoglobin levels were higher in group 1 than in group 2, and we concluded that this difference reflected the effects of the preoperative erythropoietin administration in group 1. Mean hemoglobin levels decreased to a greater extent in group 1, but no significant differences were observed in the postoperative hemoglobin levels between the groups. By preoperative erythropoietin administration, we effectively increased the hemoglobin levels, and this strategy worked sufficiently well in our experience. The mean operation time was shorter in group 1, and reducing the operation time in non-transfusion patients (if feasible) reduces the risks of bleeding and morbidity. Although not significantly so, the estimated blood loss was higher in group 2 than in group 1. Nevertheless, the difference in the hemoglobin levels before and after surgery was less in group 2 than in group 1, presumably because of intraoperative transfusion in group 2. Other than the NPO time after surgery, which was greater in group 1, all parameters were similar in both groups. Therefore, we conclude that radical retropubic prostatectomy without transfusion does not appreciably increase the perioperative morbidity when it is accompanied by preoperative erythropoietin administration.

A major limitation of our study was the relatively small sample size. In our hospital, we frequently use other supportive measures, including tranexamic acid administration, nutritional support, and iron therapy, in situations where transfusion is not an option; these other supportive measures can affect the surgical results, and this could be another limitation of this study.

CONCLUSIONS

Refusal of transfusion is a great challenge for surgeons. Obviously, the risks are higher in surgeries without transfusion. As described in this study, preoperative erythropoietin administration increases the safety margin of the hemoglobin levels and may therefore decrease the risk of radical retropubic prostatectomy performed without transfusion; moreover, numerous other supportive measures may likewise help when used in an adequate manner. However, further investigations and novel methods are required for safer nontransfusion radical retropubic prostatectomy.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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