Scientific Research Publishing

Open Journal of Nephrology, 2017, 7, 38-46
http://www.scirp.org/journal/ojneph
ISSN Online: 2164-2869
ISSN Print: 2164-2842

Assessment of Patient Perceptions about Use of Wepox Pen™ (Recombinant Erythropoietin Delivery Device with 30,000 IU Cartridge) in the Management of Anemia in Chronic Kidney Disease Patients*

Hanmant Barkate, Salman Motlekar, Sameer Rao, Sanjay Kamble

Department of Medical Affairs, Wokhardt Limited, Mumbai, India
Email: SMotlekar@wockhardt.com

How to cite this paper: Barkate, H., Motlekar, S., Rao, S. and Kamble, S. (2017) Assessment of Patient Perceptions about Use of Wepox Pen™ (Recombinant Erythropoietin Delivery Device with 30,000 IU Cartridge) in the Management of Anemia in Chronic Kidney Disease Patients. *Open Journal of Nephrology*, **7**, 38-46.
https://doi.org/10.4236/ojneph.2017.72005

Received: May 4, 2017
Accepted: June 20, 2017
Published: June 23, 2017

Abstract

Objective: To assess perceptions about ease of use and other benefits of Wepox Pen™ (loaded with 30,000 IU cartridge of recombinant erythropoietin) in the management of anemia in adult chronic kidney disease (CKD) patients. **Material and methods:** In this prospective, observational, multicentric post marketing surveillance, adult CKD patients treated with erythropoietin were enrolled from November 2015 to December 2016 to understand their opinions about Wepox Pen™. Ease of use of pen, ease of administering accurate dose, confidence in administration and ease of storage and disposal of cartridge were assessed on five points Likert scale: 1. very easy; 2. somewhat easy; 3. neither easy nor difficult; 4. somewhat difficult; 5. very difficult. Global assessment was performed on five points scale: 1. excellent; 2. very good; 3. good; 4. average; 5. not good. Safety was recorded by checking pain and discomfort and adverse events. **Results:** A total of 263 patients (mean age 32.87 years; 66% male; 34% female) were enrolled. Number of patients reporting ease of use as "very easy" from 209 (80.7%) at baseline increased to 245 (94.6%) and 249 (96.1%) at visit 2 ($p = 0.001$) and visit 3 ($p = 0.001$) respectively. Number of "very easy" response for accurate dose increased from 236 (91.1%) at visit 1 to 246 (95%) at visit 2 ($p = 0.84$) and 249 (96.1%) at visit 3 ($p = 0.001$). Number of the patients with "no pain" at injection site increased from 177 (68.3%) at visit 1 to 205 (79.2%) and 212 (81.9%) at visit 2 ($p = 0.001$) and visit 3 ($p = 0.001$) respectively. Improvement in number of patients with "no hurt" at visit 2 ($p = 0.538$) and visit 3 ($p = 0.286$) was not statistically significant. Number of patients reporting "somewhat easy" to "very easy" confidence in self injection increased from 251 (96.9%) at visit 2 to 255 (98.5%) at

*Patient perceptions about Wepox Pen™.

visit 3. Number of patients reporting ease of storage and disposal of cartridge as "somewhat easy" to "very easy" increased from 254 (98.1%) at visit 2 to 256 (98.9%) at visit 3. According to the global assessment, 144 (56.3%) cases reported "excellent" response. "Very good" and "Good" responses were reported by 106 (41.4%) and 6 (2.3%) patients respectively. A total of 230 (98.7%) patients said that they would prefer to use erythropoietin pen device for further treatment too. **Conclusion:** Wepox Pen™ (recombinant erythropoietin) is easy to use and does not cause significant pain or discomfort. Ability to self-administer recombinant erythropoietin with Wepox Pen™ is a great advantage which can make a significant difference for both CKD patients and doctors. Storage and disposal of cartridge is also easy.

Keywords

Anemia, Chronic Kidney Disease, Erythropoietin Pen Device

1. Introduction

Chronic kidney disease (CKD) is one of the significant clinical problems worldwide and more so in India, because of the high prevalence of diabetes, a known risk factor. According to the SEEK (Screening and Early Evaluation of Kidney Disease) study, the prevalence of CKD in India is 17.2% [1]. Of the several complications in CKD, anemia is a common clinical concern [2] [3] [4] with progressively higher rates in patients with renal impairment [3]. Indian studies have reported very high rates of anemia in CKD patients. The reported prevalence of anemia in Indian CKD patients ranges between 94% and 100% [5] [6] [7]. Anemia in CKD patients can cause cardiac complications including congestive cardiac failure and left ventricular dysfunction, increased rates of hospitalizations and frequent need of blood transfusions. Overall, anemia in CKD patients can adversely affect the quality of life and increase the risk of mortality [2] [8] [9].

Effective therapy of anemia can reduce requirement of blood transfusion and improve quality of life and survival [10] [11]. Erythropoiesis stimulating agents (ESAs) are one of the most important treatment options for anemia in CKD patients [12] [13]. As these agents need to be given as an injection, formulations/devices which are easy to use and cause less pain or discomfort may increase confidence of patients for self-administration. Wepox Pen™ is a device loaded with 30,000 IU cartridge of recombinant erythropoietin available in Indian market for the treatment of anemia in CKD patients. The device is easy to use without much inconvenience to patients with CKD. There is limited data on the patient perceptions about erythropoietin injection devices.

2. Objective

The objective of this study was to assess perception about ease of use and other benefits of Wepox Pen™ (loaded with 30,000 IU cartridge of recombinant erythropoietin) in the management of anemia in adult CKD patients.

3. Material and Methods

In this open label, observational and multi-centric post marketing surveillance (PMS), adult patients between 18 - 65 years of age with anemia due to stage 3 - 5 CKD and treated with erythropoietin were enrolled from November 2015 to December 2016 with convenience sampling method. In addition to pregnant and lactating women, patients with other medical conditions that can affect participation in the survey were excluded from the study based on the judgment of the investigator. Each enrolled patient was provided Wepox Pen™ with 30,000 IU, three milliliter cartridge of recombinant erythropoietin. The pen device was provided free of cost but the cartridges expense was borne by the patients. Patients were instructed to use Wepox Pen™ as per their dosage requirement or according to physician's discretion for four months. Patients were evaluated at three visits. Second and third evaluation was done at day 61 ± 3 and day 122 ± 3. During all visits patients were asked to fill a questionnaire which included questions related to ease of use of Wepox Pen™, pain at injection site and ease of accuracy of dose. At visits 2 and 3, in addition to these parameters, patients were also asked to rate their confidence in administration, ease of storage and disposal of cartridge. Patients were asked to complete global assessment for Wepox Pen™ use at visit 3. Ease of use of pen, ease of administering accurate dose, confidence in administration and ease of storage and disposal of cartridge was assessed on five point Likert scale; 1-very easy; 2-somewhat easy; 3-neither easy nor difficult; 4-somewhat difficult; 5-very difficult. Global assessment was performed on five point scale-1-excellent; 2-very good; 3-good; 4-average; 5-not good. Assessment of preference was checked by asking a question "Would you prefer using Wepox Pen™ for further treatment?" Safety and tolerability was checked by recording discomfort like burning or itching at the site of injection immediately after injection on six point scale-0-no hurt; 1-hurts little bit; 2-hurts little more; 3-hurts even more; 4-hurts whole lot; 5-hurts worst. Additionally, other adverse events, if any were also recorded. Wepox pen is an approved device in India and is standard of care for administration of erythropoietin in patients with anemia in CKD. The study was carried out as a post-marketing surveillance for observing the benefits of the pen device. Hence as per the country norms, ethics committee approval was not required.

4. Statistical Analysis

Continuous data are presented as mean and standard deviation whereas categorical data are presented as number and percentages. Chi square test was used to analyze difference between three visits.

5. Results

A total of 263 patients with mean age of 32.87 years and mean duration of CKD of 2.3 years were enrolled in this survey. The survey population consisted of 173 (66%) males and 89 (34%) females (Table 1).

A total of 30 (11.4%) patients had either diabetes or hypertension. Diabetes and hypertension was present in 14 (6.1%) and 16 (5.3%) patients respectively.

At baseline 209 (80.7%) patients reported the ease of erythropoietin pen device as "very easy". The number of patients reporting ease of erythropoietin pen device as "very easy" increased to 245 (94.6%) and 249 (96.1%) respectively. The improvement in number of patients reporting ease as "very easy" at visit 2 and visit 3 was statistically significant compared to baseline (Table 2; p = 0.001 at both visit 2 and visit 3).

Number of patients reporting taking accurate dose with erythropoietin pen device as "very easy" increased from 236 (91.1%) at visit 1 to 246 (95%) at visit 2 and 249 (96.1%) at visit 3. The improvement in response rate of "very easy" at visit 2 was not significant (p = 0.84); however, at visit 3 the improvement was significant (Table 2; p = 0.001).

At visit 1 177 (68.3%) of the patients had "no pain" at injection site by using Erythropoietin Pen device. The number of patients with "no pain" increased to 205 (79.2%) and 212 (81.9%) at visit 2 and visit 3 respectively. The improvement at visit 2 and visit 3 was statistically significant (Table 3; p = 0.001 at visit 2 and visit 3) compared to baseline.

Table 1. Baseline characteristics.

Parameter	Result
Age (years) (n = 263)	
Mean ± SD	32.87(+10.46)
Range	18 - 48 years
Gender (n = 262)	
Male n(%)	173(66%)
Female n(%)	89(34%)
Number of CKD years (n = 75)	
Mean (SD)	2.30(1.75)
Range	0.6 - 8 years

Table 2. Percentage of patients reporting ease of use and ease of taking accurate dose with erythropoietin pen device at three visits.

	Percentage of patients reporting ease of erythropoietin pen device use			Percentage of patients reporting ease of taking accurate dose		
	Visit 1 (N = 259) N(%)	Visit 2 (N = 259) N(%)	Visit 3 (N = 259) N(%)	Visit 1 (N = 259) N(%)	Visit 2 (N = 259) N(%)	Visit 3 (N = 259) N(%)
Very easy	209(80.7%)	245(94.6%)	249(96.1%)	236(91.1%)	246(95%)	249(96.1%)
Somewhat easy	049(18.9%)	014(5.4%)	10(3.9%)	22(8.5%)	13(5%)	10(3.9%)
Neither easy nor difficult	-	-	-	-	-	-
Somewhat difficult	001(0.4%)	-	-	1(0.4%)	-	-
Very difficult	-	-	-	-	-	-
P value (Chi-square test)		0.001 (Chi-square value 23.104)	0.001 (Chi-square value 30.160)		0.84 (Chi-square value 2.985)	0.001 (Chi-square value 5.469)

At Visit 1 245 (94.6%) of the patients had "no hurt" with erythropoietin pen device. The number of patients with "no hurt" at visit 2 and visit 3 were 248 (95.8%) and 250 (96.5%) respectively (Table 4). The improvement in number of patients with "no hurt" at visit 2 (p = 0.538) and visit 3 (p = 0.286) was not statistically significant (Table 4).

The number of patients reporting "somewhat easy" to "very easy" confidence in self injection increased from 251 (96.9%) at visit 2 to 255 (98.5%) at visit 3. Similarly, number of patients reporting ease of storage and disposal of cartridge as "somewhat easy" to "very easy" increased from 254 (98.1%) at visit 2 to 256 (98.9%) at visit 3 (Table 5).

Table 3. Percentage of patients reporting pain at injection site.

	Visit 1 (N = 259) N(%)	Visit 2 (N = 259) N(%)	Visit 3 (N = 259) N(%)
No Pain	177 (68.3%)	205 (79.2%)	212 (81.9%)
Little pain	78 (30.2%)	52 (20.1%)	46 (17.8%)
Mild pain	4 (1.5%)	2 (0.7%)	1 (0.3%)
Moderate pain	-	-	-
Severe pain	-	-	-
Worst pain	-	-	-
P value (Chi square test)		0.001 (Chi-square value 7.817)	0.001 (Chi-square value 12.645)

Table 4. Percentage of patients reporting discomfort.

	Visit 1 (N = 259) N(%)	Visit 2 (N = 259) N(%)	Visit 3 (N = 259) N(%)
No hurt	245 (94.6%)	248 (95.8%)	250 (96.5%)
Hurts little bit	14 (5.4%)	11 (4.2%)	9 (3.5%)
Hurts little more	-	-	-
Hurts Even more	-	-	-
Hurts whole lot	-	-	-
Hurts worst	-	-	-
P value (Chi square test)	-	0.538 (Chi-square value 0.378)	0.286 (Chi-square value 1.137)

Table 5. Percentage of patients with confidence in self injection and ease of storage and disposal of cartridge.

	Confidence in self injection		Ease of storage and disposal of cartridge	
	Visit 2 (N = 259) N(%)	Visit 3 (N = 259) N(%)	Visit 2 (N = 259) N(%)	Visit 3 (N = 259) N(%)
Very easy	192 (74.1%)	219 (84.6%)	205 (79.2%)	225 (86.9%)
Somewhat easy	59 (22.8%)	36 (13.9%)	49 (18.9%)	31 (12%)
Neither easy nor difficult	8 (3.1%)	4 (1.5%)	5 (1.9%)	3 (1.1%)
Somewhat difficult	-	-	-	-
Very difficult	-	-	-	-

According to the global assessment of erythropoietin pen device, 144 (56.3%) cases reported "excellent" response. "Very good" and "Good" responses were reported by 106 (41.4%) and 6 (2.3%) patients respectively. No patient reported "Average" or "Not good" response (Figure 1).

A total of 230 (98.7%) patients said that they would prefer to use Erythropoietin Pen device for further treatment too (Figure 2).

6. Discussion

Anemia is an early complication of CKD [2]. The mean CKD duration of 2.3 years in our study is in accordance with this finding. The mean age of CKD patients in our study was lesser than the age reported in the SEEK study [1] and first report of Indian CKD registry [14]. The lowest age reported in the SEEK study is 18 years, indicating possibility of CKD even in the younger age group. Diabetes and hypertension are the two common conditions responsible for CKD [1] [14]. In our study, 11.4% patients had either diabetes or hypertension. Early identification and prompt treatment of comorbid conditions may prevent complications

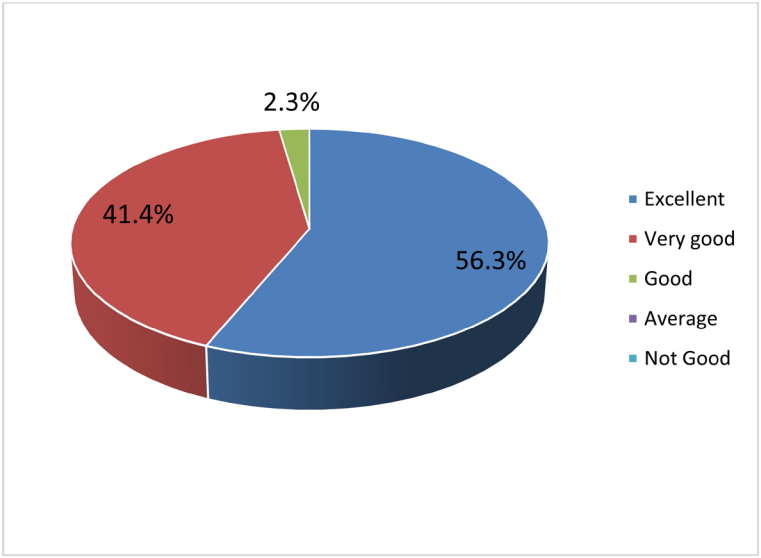

Figure 1. Global assessment of erythropoietin pen device (n = 256).

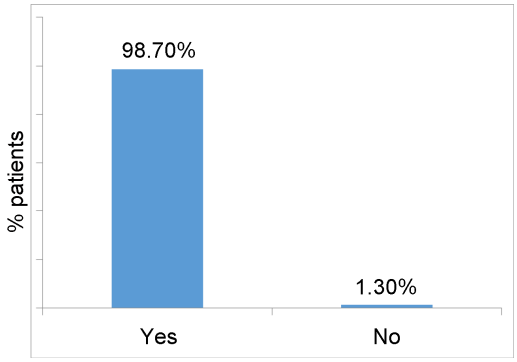

Figure 2. Assessment of preference of erythropoietin pen device (n = 233).

of CKD. Higher number of male patients in our survey is in accordance with published data from India [1] [14].

Recombinant human erythropoietin, the choice of therapy for anemia in CKD patients can be administered by subcutaneous and intravenous route [15]. Subcutaneous route has its own advantage in terms of self administration. However, noncompliance with subcutaneous use is a significant problem [16].

Patient training and confidence of patient are critical in long term success with self administration of medicine. The responses for ease of erythropoietin pen device as "very easy" in our study consistently and significantly increased from baseline to visit 2 and visit 3. The study also showed improvement in confidence of self injection at visit 2 and 3.

Delivery device plays an important role in tailoring the dose of ESA in patients with renal anemia [17]. In our study, number of patients reporting the response "very easy" in taking accurate dose with erythropoietin pen device was high at baseline (91.1%) which further increased in subsequent visits. At visit 3, the difference in improvement of response was significant (91.1% vs. 96.1% $p = 0.001$). The results prove the potential of Wepox Pen™ device in providing accurate dose. These responses are of importance given the chances of dosing errors especially at lower doses with concentrated formulations [18].

Pain is an important concern for ESA administration. Efforts have been done to change the buffer or provide local anesthetic cream to reduce the pain with subcutaneous injection [19] [20] [21]. In our study, number of patients with "no pain" at injection site progressively and significantly increased from baseline to visit 2 and 3. Pain and discomfort may cause discontinuation of therapy, adversely affecting compliance and outcomes of therapy. Wepox Pen™ device, by virtue of less pain, may increase the compliance to erythropoietin therapy. The improvement in number of patients reporting "no hurt" did not increase significantly at visit 2 and 3 compared to baseline. This might be explained by the high number of patients (94.6%) reporting "no hurt" at baseline. However, there was numeric improvement in responses at both second and third visit.

Storage and disposal of cartridge can sometimes be difficult especially for the agents required for long term use. In this study, large number of patients reported "somewhat easy" to "very easy" storage and disposal.

All these observation including pain and discomfort with injection, confidence in injection, accuracy of dosage and storage and disposal of cartridge can impact global assessment. In accordance with the responses for these individual questions, global assessment of erythropoietin pen device was also very positive. A total of 97.7% patients reported "excellent" or "very good" responses for the global assessment. Despite availability of options of "average" or "not good" response, no patient reported it. Based on their overall satisfaction, 98.7% of the patients said that they would prefer to use this pen device for further treatment too.

Overall, the study observations show confidence and ease of administration of erythropoietin with Wepox Pen™. Routine use of Wepox Pen™ has a potential

to improve compliance in CKD patients with anemia. Larger studies to confirm improved adherence/compliance with Wepox Pen™ are required.

The study is associated with some limitations. Subjective evaluation, convenience sampling and short term follow up limit generalization of observations to all CKD patients. Long term studies to evaluate compliance to treatment and outcomes of anemia in CKD patients are recommended.

7. Conclusion

Wepox Pen™, a recombinant erythropoietin delivery device with 30,000 IU cartridge is easy to use without significant concern of pain or discomfort in the management of anemia in CKD patients. Moreover, confidence of patient is high while using erythropoietin with this device. Self-administration of erythropoietin with Wepox Pen™ makes a significant difference for patients as well as doctors unlike prefilled syringe (PFS) formulation which often requires external help for injection. The reported benefits have potential to improve patient compliance and outcomes of anemia in CKD patients.

References

[1] Singh, A.K., Farag, Y.M.K., Mittal, B.V., Subramanian, K.K., Reddy, S.R.K., Acharya, V.N., *et al.* (2013) Epidemiology and Risk Factors of Chronic Kidney Disease in India—Results from the SEEK (Screening and Early Evaluation of Kidney Disease) Study. *BMC Nephrology*, **14**, 114. https://doi.org/10.1186/1471-2369-14-114

[2] Horl, W.H., Vanrenterghem, Y., Aljama, P., Brunet, P., Brunkhorst, R., Gesualdo, L., *et al.* (2007) OPTA: Optimal Treatment of Anemia in Patients with Chronic Kidney Disease (CKD). *Nephrology Dialysis Transplantation*, **22**, iii20-iii26. https://doi.org/10.1093/ndt/gfm017

[3] Shaheen, F.A.M., Souqiyyeh, M.Z., Al-Attar, B.A., Karkar, A., Al Jazairi, A.M.H. and Badawi, L.S. (2011) Prevalence of Anemia in Predialysis Chronic Kidney Disease Patients. *Saudi Journal of Kidney Diseases and Transplantation*, **22**, 456-463.

[4] Hirakata, H., Tsubakihara, Y., Gejyo, F., Nishi, S., Iino, Y., Watanake, Y., *et al.* (2010) Maintaining High Hemoglobin Levels Improved the Left Ventricular Mass Index and Quality of Life Scores in Pre-Dialysis Japanese Chronic Kidney Disease Patients. *Clinical and Experimental Nephrology*, **14**, 28-35. https://doi.org/10.1007/s10157-009-0212-4

[5] Arun, S., Venkatraya Prabhu, M., Nithyananda Chowta, K. and Bengre, M.L. (2012) The Haematological Pattern of the Patients with Chronic Kidney Disease in a Tertiary Care Setup in South India. *Journal of Clinical and Diagnostic Research*, **6**, 1003-1006.

[6] Mudiyammanavara, R.N., Dhanajaya, P.E. and Agarwal, R. (2015) Cross Sectional Study of Anaemia in Chronic Kidney Disease. *Indian Journal of Basic and Applied Medical Research*, **4**, 414-419.

[7] Talwar, V.K., Gupta, H.L. and Shashinarayan (2002) Clinicohaematological Profile in Chronic Renal Failure. *The Journal of the Association of Physicians of India*, **50**, 228-233.

[8] Schmidt, R.J. and Dalton, C.L. (2007) Treating Anemia of Chronic Kidney Disease in the Primary Care Setting: Cardiovascular Outcomes and Management Recom-

mendations. *Osteopathic Medicine and Primary Care*, **1**, 14. https://doi.org/10.1186/1750-4732-1-14

[9] Kuwahara, M., Hasumi, S., Mandai, S., Tanaka, T., Shikuma, S., Akita, W., *et al.* (2014) Effects of Three Kinds of Erythropoiesis-Stimulating Agents on Renal Anemia in Japanese Non-Dialysis Chronic Kidney Disease Patients. *Clinical and Experimental Nephrology*, **18**, 755-762. https://doi.org/10.1007/s10157-013-0919-0

[10] Carrera, F. and Burnier, M. (2009) Use of Darbepoetin Alfa in the Treatment of Anemia of Chronic Kidney Disease: Clinical and Pharmacoeconomic Considerations. *NDT Plus*, **2**, i9-i17. https://doi.org/10.1093/ndtplus/sfn175

[11] Neves, P.L., Morgado, E., Faisca, M., Carrasqueira, H., Baptista, A. and Silva, A.P. (2006) Nutritional and Inflammatory Status Influence Darbepoetin Dose in Pre-Dialysis Elderly Patients. *International Urology and Nephrology*, **38**, 811-813. https://doi.org/10.1007/s11255-006-0077-3

[12] Suzuki, M., Hada, Y., Akaishi, M., Hiroe, M., Aonuma, K., Tsybakihara, Y., *et al.* (2012) Effects of Anemia Correction by Erythropoiesis-Stimulating Agents on Cardiovascular Function in Non-Dialysis Patients with Chronic Kidney Disease. *International Heart Journal*, **53**, 238-243. https://doi.org/10.1536/ihj.53.238

[13] John, M.J., Jaison, V., Jain, K., Kakkar, N. and Jacob, J.J. (2012) Erythropoietin Use and Abuse. *Indian Journal of Endocrinology and Metabolism*, **16**, 220-227. https://doi.org/10.4103/2230-8210.93739

[14] Rajapurkar, M.M., John, G.T., Kirpalani, A.L., Abraham, G., Agarwal, S.K., Almeirda, A.F., *et al.* (2012) What Do We Know about Chronic Kidney Disease in India: First Report of the Indian CKD Registry. *BMC Nephrology*, **13**, 10. https://doi.org/10.1186/1471-2369-13-10

[15] Horl, W.H. (1992) Optimal Route of Administration of Erythropoietin in Chronic Renal Failure Patients: Intravenous versus Subcutaneous. *Acta Haematologica*, **87**, 16-19. https://doi.org/10.1159/000204783

[16] Nicoletta, P., Bernardini, J., Dacko, C., Terry, C. and Fried, L. (2000) Compliance with Subcutaneous Erythropoietin in Peritoneal Dialysis Patients. *Advances in Peritoneal Dialysis*, **16**, 90-92.

[17] Kleophas, W. (2005) Dose Tailoring Strategies in Haemodialysis Patients: A Discussion of Case Histories. *Nephrology Dialysis Transplantation*, **20**, vi31-vi36. https://doi.org/10.1093/ndt/gfh1096

[18] Spiegel, D.M. and Nemenoff, R.A. (2010) Recombinant Human Erythropoietin Dosing Errors Due to Concentrated EPO. *Clinical Nephrology*, **73**, 446-448. https://doi.org/10.5414/CNP73446

[19] Yu, A.W., Leung, C.B., Li, P.K., Lui, S.F. and Lai, K.N. (1998) Pain Perception Following Subcutaneous Injections of Citrate-Buffered and Phosphate-Buffered Epoetin Alpha. *The International Journal of Artificial Organs*, **21**, 341-343.

[20] Morris, K.P., Hughes, C., Hardy, S.P., Matthews, J.N. and Coulthard, M.G. (1994) Pain after Subcutaneous Injection of Recombinant Human Erythropoietin: Does Emla Cream Help? *Nephrology Dialysis Transplantation*, **9**, 1299-1301.

[21] Veys, N., Dhondt, A. and Lameire, N. (1998) Pain at the Injection Site of Subcutaneously Administered Erythropoietin: Phosphate-Buffered Epoetin Alpha Compared to Citrate-Buffered Epoetin Alpha and Epoetin Beta. *Clinical Nephrology*, **49**, 41-44.