

INTRAVENOUS IRON ADMINISTRATION

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The current K/DOQI guidelines for anemia management recommend a target range for hematocrit/hemoglobin of 33% /11 g/dL to 36% /12 g/dL for both hemodialysis and peritoneal (PD) dialysis patients¹. The majority of patients require erythropoietin (EPO) therapy in order to achieve and maintain these targets. Adequate iron stores are required for an effective response to erythropoietin; however, both absolute and functional iron deficiency are common in dialysis patients. Most patients need routine or periodic iron supplementation in addition to EPO.



Oral iron supplementation is usually inadequate to maintain sufficient iron stores and is often poorly tolerated. For PD patients intraperitoneal (IP) iron administration has been considered as an alternative. Iron dextran appears to be stable in dextrose dialysate solutions² and is absorbed through the peritoneal membrane. Although successful and effective IP administration has been reported^{3,4}, concerns regarding potential

toxicity to the membrane has hindered its acceptability^{5, 6, 7}. Intravenous iron therapy is currently the preferred administration route. K/DOQI guidelines recommend that sufficient iron should be given to maintain a transferrin saturation (TSAT) of > 20% and serum ferritin > 100ng/mL. If these targets are met and the response to EPO is poor, additional IV iron may be needed and other causes of EPO resistance investigated.

The provision of adequate iron and EPO are essential in the management of anemia of ESRD. There are however a number of significant concerns related to the safety of iron supplementation, particularly among patients with the most significant degree of anemia. The following discussion is a summary of the major concerns related to parenteral iron therapy and a synopsis of the current thinking among practicing nephrologists. For a more detailed discussion and representative references, the reader is referred to Aronoff's recent review on the safety of intravenous iron⁸.

Effect of IV iron on morbidity and mortality. The analysis of the effect of IV iron on morbidity and mortality is complicated due to the numerous variables affecting outcomes among ESRD patients, particularly the high incidence of comorbid conditions. The "judicious" use of IV iron has not been generally associated with increased morbidity among uremic patients. However, the possibilities of increased infection and oxidative stress as a consequence of excessive iron administration must be considered.

Risk of infection with IV iron. The data are contradictory with regards to the risk of bacterial infection associated with iron stores and the use of IV iron. A large prospective multicenter cohort-controlled observational trial identified central venous catheters, history of bacteremia, immunosuppressive therapy and anemia as factors associated with increased use of bacteremia⁹. The risk of bacteremia was neither related to the serum ferritin levels nor the administration of IV iron therapy. Several other large scale prospective clinical trials have come to similar conclusions.

Conversely, a single retrospective trial in HD patients reported a possible increase in infection associated with IV iron therapy¹⁰ and a recent retrospective analysis of 87 HD patients suggested an increased risk for bacterial infections at modest levels of

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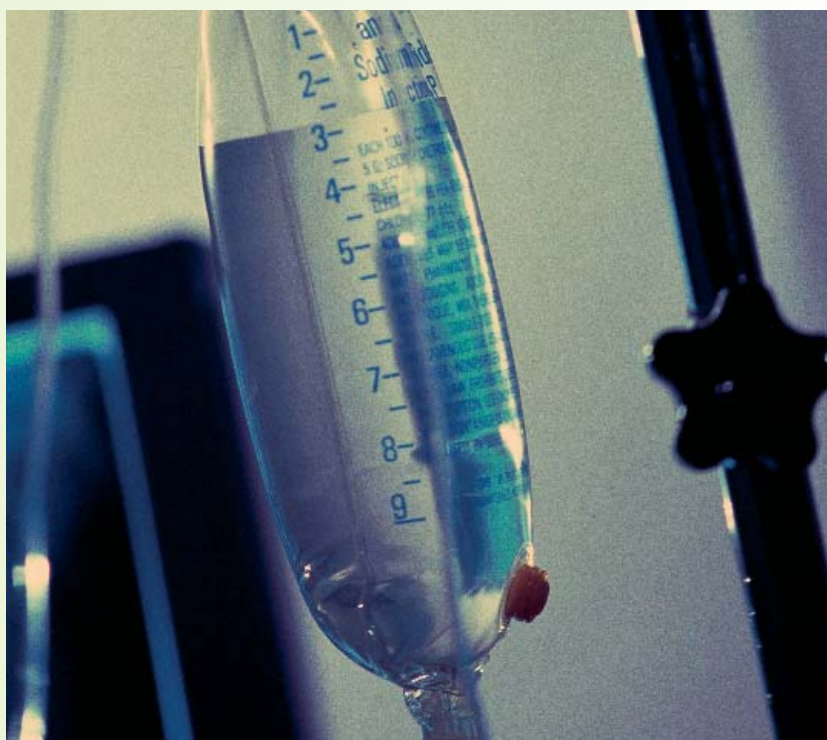
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iron stores (ferritin > 100 ng/ml and TSAT > 20%) among HD patients initiating IV iron¹¹. It is obvious that further scrutiny and large prospective studies are needed to confirm these relationships.

Defining adequate iron stores. As many as 20-40% of PD patients on erythropoietin have inadequate iron supplies. Although PD patients experience lower blood losses than HD patients, the absorption of iron is disturbed in some of them due to lower mucosal uptake and transfer¹². Other reasons for poor absorption of iron among PD patients are the concomitant ingestion of green leafy vegetables, tea, antacids, H2 blockers, omeprazole and phosphate binders.

Regular monitoring of iron status in PD patients is recommended using serum ferritin and transferrin saturation (Tsat%) at a minimum of every 3 months. The ferritin target is > 100 to < 800 ng/ml and the Tsat% > 20% to < 50%. While these measures have proven useful for the management of anemia in ESRD, they are far from perfect. The optimal target for PD may still need refinement and new diagnostic tools with better sensitivity and specificity are needed. What level of ferritin can be considered too high? There is good reason to believe that ferritin levels should not exceed 800 ng/ml. Most iron in dialysis patients with high ferritin levels is in the reticuloendothelial cells and not in tissues. There is no well qualified method of defining the optimal ferritin value among dialysis patients. Perhaps the most practical way of approaching this issue is to use the evidence accumulated on the relationship between efficacy of IV iron administration and pretreatment serum ferritin levels. Most of the available data suggest that pretreatment serum ferritin levels below 100 ng/ml or above 500 ng/ml are associated with a markedly lower success.

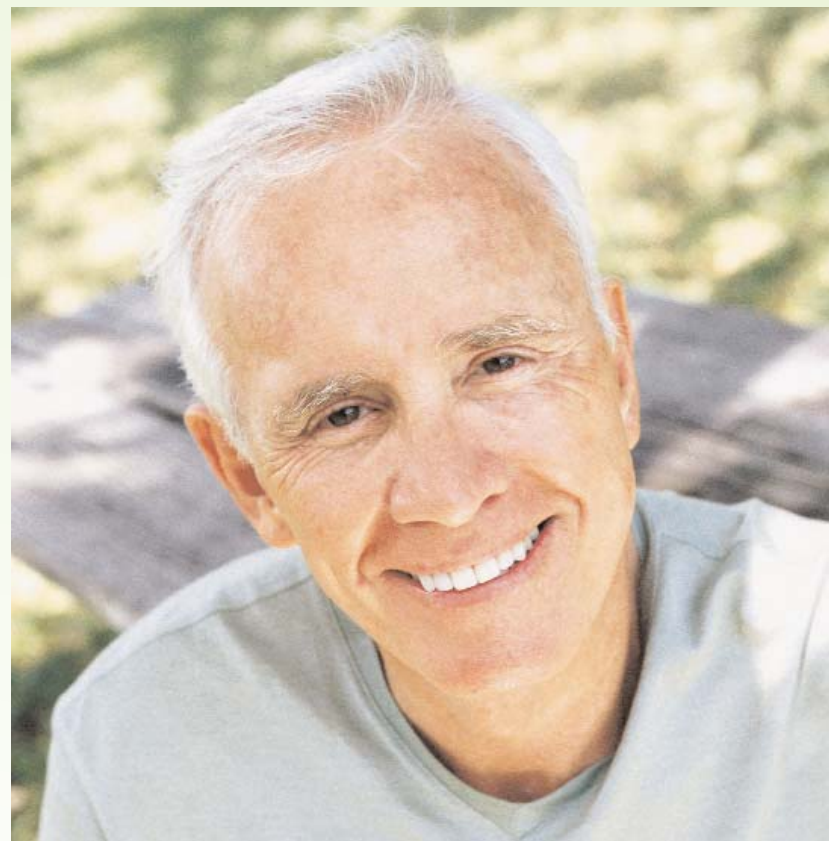


Another challenge is how to manage the patient with low Tsat% and a high ferritin level. This combination of findings suggests inflammation and demands looking for elevation in inflammatory markers. These patients often receive high EPO doses, have low Hgb and serum albumin concentrations and high C-reactive protein. Among the common sources of inflammation figure: infected central venous catheters, recent peritonitis or exit site infections, recent bacteremia or a chronic and silent graft infection.

Finally, what are the acute adverse events of administering IV iron? There are insufficient data to adequately compare the various IV iron agents in regards to allergic versus toxic reactions. However, it is important to differentiate between the two types of reactions that can and do occur with IV iron administration. A *toxic reaction* occurs when iron is given too quickly or in too high of a dose. In other words, it is dose or rate dependent. By slowing the rate or lowering the dose this

reaction is resolved. An *allergic hypersensitivity* reaction is the more serious of the two. When this occurs the patient may experience one or all of the following symptoms: hypotension, difficulty breathing, chest pain and/or rash that can occur suddenly after administration of a low, slow dose.

The administration of IV iron is an important part of treating the CKD patient. Knowledge regarding its safety and guidelines remains an integral part of providing the care for these patients.



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WHAT'S NEW? THE INTERNATIONAL SOCIETY OF PERITONEAL DIALYSIS (ISPD) RELEASES UPDATED GUIDELINES

Terri L. Crawford-Bonadio, RN, CNN

The 2005 update of the ISPD peritoneal dialysis-related recommendations were recently published. This update has been simplified and is much easier to follow than the previous release from 2000. There is greater consideration to the individual center needs by offering more alternatives for the initial and specific treatment recommendations. It no longer emphasizes the use of first and third generation cephalosporins as initial empiric therapy. Additionally, they reintroduce the use of vancomycin for specific conditions and, for the first time, consider the possibility of monotherapy. The guidelines strongly promote the importance of prevention which is a new aspect. Above all, the ISPD recommendations are very well referenced. Whenever possible, the guidelines have been annotated as opinion (O) or evidence (E) based. Some of the key updates/changes in these recommendations are highlighted here.



Prevention of PD-related infections

- Monitor infection rates at least once yearly^O
- No particular catheter has a definite advantage over standard Tenckhoff^E
- Prophylactic antibiotics at the time of catheter insertion decrease infection risk^E
- Prevention of exit site infection (ESI) reduces peritonitis. Antibiotic protocols against *S. aureus* are effective^E
- Spiking of dialysis bags is a high-risk procedure; flush-before-fill reduces the risk of contamination^E
- Training methods influence the risk of PD infections^E
- Invasive procedures may infrequently cause peritonitis^E
 - > Extensive dental procedures - Amoxicillin 2 Gm PO 2 hrs pre-procedure^O
 - > Colonoscopy with polypectomy - Ampicillin 1 Gm + aminoglycoside with or without metronidazole, IV prior to the procedure^O
 - > Drain peritoneal cavity prior to all abdominal or pelvic procedures^O
- There is an association between severe constipation and enteritis and peritonitis due to enteric organisms^E
- The majority of fungal peritonitis episodes occur following antibiotic treatment^E

Differential diagnosis of cloudy effluent

Consider the following:

- Culture-positive infectious peritonitis
- Infectious peritonitis with sterile cultures
- Chemical peritonitis (icodextrin)
- Eosinophilia of the effluent
- Hemoperitoneum
- Malignancy (rare)
- Chylous effluent (rare)
- Specimen taken from “dry” abdomen

Treatment principles

- Chronic antibiotic prophylaxis does not prevent peritonitis.
- Since peritonitis is a local infection, it is most important to achieve high concentrations of antibiotics intraperitoneally rather than systematically. Oral antibiotics are not usually recommended initially due to uncertain absorption and transit time.

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GEMS

CURRENT AND FORMER REIMBURSEMENT REGULATIONS FOR DIALYSIS IN GERMANY

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The reimbursement system for dialysis care has been revised in Germany during the past decade as expenditure for overall health care in general and for dialysis in particular has been steadily increasing. The percentage of peritoneal dialysis (PD) patients has declined from approximately 10% ten years ago to the current less than 5%, although the absolute numbers of patients on PD have not varied substantially. There are numerous reasons for this low utilisation of PD as a treatment modality in Germany. The number of new hemodialysis (HD) facilities proliferated during the past ten years and now services are available even in small cities, removing home dialysis

treatment - be it PD or home HD - from the nephrologist's spotlight. The unbalanced remuneration for PD has been an additional negative factor for the utilization of PD.

Prior to 2002 private and non-private health insurance companies were compensating for each treatment session, making more frequent HD sessions financially attractive. On the other hand, this regulation did not take into account the additional requirements imposed by the many comorbidities in the aging dialysis population.

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- Antibiotics given once daily, either parenterally or in the long dwell exchange, are often equally efficacious, less costly and less demanding than continuous administration.
- Refractory peritonitis, defined as failure to respond to appropriate antibiotics within 5 days should be managed by removal of the PD catheter to protect the peritoneal membrane^E.
- If catheter removal is necessary due to persistent peritonitis or mycobacterial, fungal or fecal peritonitis, parenteral antibiotic therapy should be provided.
- Simultaneous catheter removal and replacement can be performed under certain conditions and for susceptible organisms.



Exit site and tunnel infections

- *Staphylococci aureus* accounts for most exit site and tunnel infections (60-80%), with *S. aureus* and *pseudomonas aeruginosa* being the most serious^E.
- *S. aureus* nasal carriage is associated with increased risk of *S. aureus* exit site infections, tunnel infections, peritonitis and catheter loss.

- A single culture may give a false negative result as many patients are intermittent carriers.
- Diabetic patients and those on immunosuppressive therapy are at increased risk of ESI.



- Patients with persistent *S. aureus* nasal carriage should benefit from local gentamicin or mupirocin therapy.
- Empiric antibiotic therapy should be started immediately for tunnel and exit site infections, pending culture results. It should always cover Gram positive organisms and *pseudomonas*, if there is a history of previous infection.

The recommendations in this article are based on: Piraino B, Bailie GR, Bernardini J, Boeschoten E, Gupta A, Holmes C, Kuijper EJ, Li PK, Lye WC, Mujais S, Paterson DL, Fontan MP, Ramos A, Schaefer F, Uttley L. Peritoneal dialysis-related infections recommendations: 2005 update. *Perit Dial Int* 25:107-131, 2005. Refer to the full article for the complete recommendations and their associated references, as well as antibiotic dosing tables.

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Starting in 2003 the Physicians' Association and the non-private health insurance companies signed a complex contract regulating various aspects of dialysis care, mostly focusing on modality



reimbursement. In contrast to the former regulation, reimbursement is no longer based on the chosen modality alone, but also on the comorbidity and the age of the individual patient.

Providers are now paid for dialysis treatment on a weekly basis as well as relevant comorbidities such as diabetes mellitus or chronic viral infection for which an additional sum is provided. All in all, the total weekly reimbursement for standard hemodialysis has decreased, whereas PD reimbursement has increased substantially. The new contract also regulates various other aspects of dialysis care. It limits the number of patients a nephrologist is allowed to treat with HD, but imposes no limit on the number of PD patients. Despite this apparent support for PD, no significant increase in PD utilization has been noted. Many HD units have unused capacities for hemodialysis that perhaps explains the preferential selection of centre HD. We must also consider the lack of experience with PD by many German physicians as another important driver in the selection of HD. I personally hope that these changes in reimbursement will favour the growth of PD.

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INTERNATIONAL CALENDAR OF EVENTS

June 26-30, 2005 3rd World Congress of Nephrology; 18th Congress of the International Society of Nephrology; 10th Asian-Pacific Congress of Nephrology; 15th Renal Update of the Singapore Society of Nephrology. Singapore. Contact: 3rd World Congress of Nephrology - Congress Secretariat & Housing Bureau - C/o Ace: Daytons Direct (International) Pte Ltd - 2 Leng Kee Road #04-02 Thye Hong Centre Singapore 159086 - Website: www.wcn2005.org/home.htm; Email: admin@wcn2005.org; Phone: (65) 6379 5261; Fax: (65) 6475 2077

September 10-13, 2005 34th International Conference of the European Dialysis and Transplant Nurses Association/European Renal Care Association (EDTNA/ERCA) Vienna, Austria. Theme of conference - "Bridging the Gap between Patient and Technology". Contact: EDTNA/ERCA Head Office at Pilatusstrasse 35 Postfach 3052 - CH-6002 Luzern, Switzerland. Telephone: +41 41 766 05 80; Fax: +41 41 766 05 85 or visit their website at <http://www.edtna-erca.org/> for more information.

September 23-24, 2005 4th Annual Conference on Prevention in Renal Disease. Toronto, Canada. Contact: Prevention in Renal Disease, 399 Bathurst Street, ON M5T2S8 Canada, Telephone: (416) 603-7974 or visit their website at <http://www.nephrovention.com> for more information.

October 5-8, 2005 European Society for Artificial Organs (ESAO) XXXII Congress and the International Federation for Artificial Organs (IFAO). Palazzo della Cultura e dei Congressi, Piazza della Costituzione, 4/a-Bologna, Italy 40128. Email for Organizing Secretariat: info@omniameeting.com; Telephone: +39 06 4871366; Fax: +39 06 4815339 and Email for Scientific Secretariat: Sergio.stefoni@unibo.it; Fax: +39 051 340871 or visit the website at <http://www.omniameeting.com> for more information.

October 15-18, 2005 7th European Peritoneal Dialysis Meeting. Prague, Czech Republic. Contact: EuroPD Congress Secretariat c/o In Conference Ltd., 10b Broughton St. Lane Edinburgh, EH1 3LY, UK; Email: margaret@in-conference.org.uk; or visit their website at <http://www.europd.com/> for more information.

August 25-29, 2006 ISPD 11th Congress of the International Society for Peritoneal Dialysis, Hong Kong. The motto of the Congress is "Achieving PD Excellence". Contact: ISPD 2006 Congress Secretariat, International Congress Consultants, Limited; Telephone: (852) 2559-9973; Email: info@ispd2006.org or visit their website at <http://www.ispd2006.org/> for more information