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Review Article

Therapeutic Hemapheresis

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In the 1950s, Adams, et al (1) introduced the method of phlebotomy followed by selective removal of plasma and re-infusion of red cells for the treatment of hyperviscosity syndrome. When cell separators were introduced in the 1960s, hemapheresis procedures became less cumbersome and time consuming. By careful differential centrifugation, several liters of blood can be "processed" ex vivo, and the formed elements or plasma can be selectively removed. Because blood cell separators are efficient and relatively safe, the use of hemapheresis has markedly increased in the past decade.

In this communication we review important aspects of therapeutic hemapheresis which the clinician should consider when contemplating the benefit/risk ratio of this therapy and its effectiveness.

Terminology

"Apairesos" and "aphairesis" are Greek and Latin words, respectively, and mean to take away or separate. The term pheresis, although part of the jargon, is linguistically incorrect and should not be used. The correct term is apheresis, and, depending upon the constituent being removed, the terminology becomes plasmapheresis, leukapheresis, etc. When large quantities of whole blood or plasma are removed, replacement with whole blood or plasma becomes necessary; in these situations, the applicable terms are blood exchange or plasma exchange.

Equipment and Methodologies

Commercially available cell separators utilize two different designs: continuous flow centrifugation (CFC) or intermittent flow centrifugation (IFC). The CFC system allows continuous withdrawal of small volumes of blood from the patient, separation of the blood constituents, and re-infusion into the patient of the desired material. The IFC system requires a set amount of blood to be withdrawn from the patient to fill the centrifuge bowl (usually 250 ml), differential centrifugation, and then re-infusion. The intermittent flow centrifuge, however, can be used quite efficiently with a single access site, including catheters, and the equipment is relatively lightweight and much more portable. Disadvantages of each system are partially offset by other design features. However, both systems are fully acceptable, self-contained units which eliminate the risks of transfusion errors and minimize many of the problems encountered with cumbersome manual apheresis procedures.

Dynamics of Hemapheresis

If it were possible to remove all of a patient's blood at one time and replace it with donor blood, the pathologic material would fall to zero after one volume exchange. However, in practice, the efficiency of removing abnormal plasma constituents or formed elements depends upon the original concentration, mobility across intravascular and extravascular compartments, rate of synthesis of the constituent, and the mixing of the infused fluid. Theoretically, a one volume plasma exchange should reduce the original plasma components to 30% of the initial value and to approximately 10% after the second plasma volume exchange (2). However, this relationship is only rarely observed for plasma proteins because of the rapid equilibration between the intravascular and extravascular compartments; also, 55% of IgG and 25% of IgM are present in the extravascular compartment, and IgG is readily mobile across the two compartments. Further, since the efficiency of an exchange is greatest early in the procedure, many investigators perform limited exchanges of one volume per procedure in order to allow re-equilibration or new synthesis of abnormal constituents and to make the second exchange more efficient.

Replacement Solutions

The most commonly used replacement solutions are crystalloids, 5% albumin, 5% plasma protein fraction (PPF), and fresh frozen plasma (FFP). Crystalloid solutions may suffice when the exchange volume is small and when the patient is hyperproteinemic. In other situa-

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tions, it is essential to replace proteins to maintain colloid osmotic pressure and therefore the intravascular volume. Five percent albumin or PPF are easily available, do not require immunologic compatibility, and do not transmit hepatitis. However, because albumin or PPF do not provide essential coagulation factors, significant temporary reductions may occur after large volume plasma exchanges. After a four liter exchange using protein solutions, all coagulation factors are reduced; but within four hours, Factor IX, ristocetin cofactor, and Factor VIII procoagulant activity rapidly return to normal, while all other factors become normal within 24 hours (3). Also reduced are C3, fibrinogen, cholesterol, alkaline phosphatase, alanine aminotransferase, etc (4). Most of the constituent alterations are clinically inconsequential, and pre-exchange levels are restored within 72 hours.

Fresh frozen plasma does contain all the constituents, including coagulation factors and complement, but the availability of large amounts of FFP of the appropriate immunologic type can be a problem. In addition, immunologic transfusion reactions do occur with FFP, and the transmission of hepatitis is a risk. Another disadvantage is that since FFP contains a fair amount of citrate anticoagulant, hypocalcemia occurs regularly when it is used as a replacement fluid. However, this condition is readily reversed by slowing the infusion rate of FFP or by calcium supplementation.

In general, it is rarely necessary, except in cases of thrombotic thrombocytopenic purpura (TTP), to totally replace plasma by donor plasma. In our own protocol, 1,500 ml of crystalloid solution is given in lieu of the first 1,000 ml of plasma, followed by 5% albumin, volume for volume. At the end of the procedure, we transfuse two units of FFP to produce a modest increment of coagulation factors, including fibrinogen. Using this regimen, we have observed no volume or constituent-related problems in any of more than six hundred apheresis procedures.

Theoretical Basis for the Beneficial Effects of Hemapheresis

Hemapheresis is used in therapy for many diseases because it rapidly removes abnormal blood constituents, cellular or humoral, and leads to beneficial alterations in the "milieu intérieur." Antibodies, antigens, immune complexes, toxins, or an excessive number of cells can be removed efficiently if they are easily accessible via the vascular compartments, and normal blood components can also be infused, if warranted, at the same time. Removing noxious substances and replacing them by normal constituents may also induce immune modulation, improved reticuloendothelial function, expeditious, functional recovery of affected organs, or increased response to conventional therapy. However, in most instances, hemapheresis procedures do not eliminate the serious underlying etio-pathologic mechanisms, which must be treated by alternate means. Thus, hemapheresis should be considered an excellent adjunctive means for producing rapid alteration in the "milieu intérieur" in conjunction with conventional therapy.

Leukapheresis

In patients with acute myelocytic or lymphocytic leukemia, a rapidly rising white blood cell count above 100,000/μL can portend the development of the leukostasis syndrome, often with fatal involvement of the central nervous system and lungs. Cuttner, et al (5) have demonstrated that such patients benefit from cytoreduction therapy in concert with chemotherapy. Leukapheresis is very beneficial in the acute management of leukostasis complications, although the course of the disease is not altered (6).

In chronic myelocytic leukemia (CML), the leukostasis syndrome occurs infrequently, and the white blood cell counts are usually much higher. Two patients with CML and cerebral leukostatic symptoms, one of whom was resistant to chemotherapy, were treated with granulocytapheresis in our institution. The white blood cell count was reduced by 60% in both patients after three procedures in one week. One of the patients responded to chemotherapy after the procedure, and the other patient, who was resistant to chemotherapy, responded to intermittent granulocytapheresis during the next four months.

In CML patients, white cell counts can be managed effectively for long periods by cytapheresis, and symptoms such as sweating, malaise, and pain of splenomegaly can be rapidly relieved (6). Also, leukapheresis can significantly reduce organ size and control chemotherapy-induced hyperuricemia. However, since bone marrow remission, prevention of blast crisis, or improved longevity have not been observed (7), long-term management by leukapheresis is not indicated.

Long-term cytoreduction therapy of patients with chronic lymphocytic leukemia (CLL) in order to prolong life has produced equivocal results (8,9). It is interesting to note, however, that Cooper, et al (10) report considerable reduction in the size of the lymph nodes and spleen, as well as an increase in hemoglobin level and platelets in patients with CLL and lymphocytic lymphoma after treatment with intensive cytapheresis.

Treatment of Sézary syndrome with cytapheresis has produced encouraging results. Winkleman, et al (11) have demonstrated clinical remission in patients treated by leukapheresis alone or in combination with low dose chemotherapy. Although some patients with Sézary syndrome become refractory to leukapheresis therapy after an initial clinical remission, it has been suggested that younger patients who have the disease may be the best candidates (12). In these patients, weekly leukapheresis may be sufficient to maintain remission.

Lymphocytapheresis

Several difficult diseases are now being treated by immune modulation, including lymphocytapheresis or lymphoplasmapheresis procedures. In rheumatoid arthritis patients, Paulus, et al (13) have used thoracic duct drainage for short periods. Wright, et al (14) have shown that after such therapy the number of peripheral lymphocytes are decreased for several months, with specific reduction in the number of T-lymphocytes. In these patients, mitogen stimulation and skin reactivity are altered. Controlled treatment trials of rheumatoid arthritis patients by both lymphocytapheresis and lymphoplasmapheresis procedures confirm that significant, although modest, improvement occurred in the treatment group (12). In a larger study, Wallace, et al (15) treated 40 rheumatoid arthritis patients using plasmapheresis, lymphapheresis, and lymphoplasmapheresis and reported that morning stiffness and the Ritchie index of synovitis were significantly improved in the lymphoplasmapheresis group.

Multiple sclerosis is also difficult to treat by conventional therapy. In a recent cooperative study cited by Giordona, et al (16), 120 patients were treated by lymphocytapheresis; 46% showed improvement in their Kurtzke disability rating, 1% deteriorated, and 53% remained stable. These results are very encouraging.

Thrombocytapheresis

The danger of hemorrhage or thrombosis in patients with platelet counts in excess of 1,000,000/μL is real. Whether the thrombocytosis is secondary or due to an underlying myeloproliferative process, thrombocytapheresis procedures (17-19) can rapidly reduce platelet counts while other forms of therapy attack the underlying problem; a three-hour procedure can induce a 30-50% reduction in the peripheral platelet count. Apheresis used alone is less successful in maintaining normal platelet counts over long periods. It is now well recognized that prophylactic thrombocytapheresis for thrombocytosis is unwarranted, and this procedure should be reserved for patients who show marked thrombocytosis with impending thrombosis and hemorrhage.

Erythrapheresis

In sickle cell disease prophylactic or therapeutic red cell exchange has been attempted by many investigators (20-22). Prophylactic reduction of sickle hemoglobin in patients who are to receive general anesthesia is important. In one of our patients, the sickle hemoglobin level was reduced to a third by 1.5 volume red blood cell exchange. The patient subsequently underwent successful hip replacement surgery without intraoperative or postoperative difficulties.

Prophylactic erythrapheresis is also useful in children with sickle cell disease who have cerebral infarcts, since a second stroke can generally be prevented by this means (23). Exchange transfusions to abort sickle cell crisis have also been attempted, with encouraging results in some instances (12). We treated a young boy who developed priapism on two occasions. Automated erythrapheresis rapidly abated his symptoms, whereas other therapeutic measures were unsuccessful.

Plasmapheresis

Every new therapeutic modality goes through phases of enthusiastically expectant trials for management of a diverse group of diseases until, finally, a consensus is reached about its true efficacy. In the past five to seven years, plasmapheresis has been tried for many conditions in which conventional therapy has not been very effective or as a heroic last resort in grave conditions. However, consensus about its therapeutic effectiveness is now emerging, since the data base is rapidly increasing, comparative figures of efficacy are becoming available, and several well controlled trials are underway. Some of the conditions in which plasmapheresis is effective or shows considerable promise are described below.

Paraproteinemias

Symptomatic paraproteinemia is usually accompanied by systemic proliferation of immunocompetent clones of lymphoplasmacytic series (Waldenstrom's macroglobulinemia, lymphoma, multiple myeloma, heavy chain disease). Hyperviscosity syndrome, cryoglobulinemia, thrombocytopathy, inactivation of procoagulants, and acute renal failure are all caused by the unique physical, chemical properties of large asymmetrical paraprotein molecules. Since immunosuppressive therapy does not affect the immediate serologic concentration of paraproteins, it has limited usefulness in the acute management of hyperviscosity syndrome, whereas plasmapheresis can rapidly ameliorate all symptoms of the syndrome. A

review of three hundred procedures performed on 60 patients by Russell and his colleagues (24) concluded that plasmapheresis is generally effective in rapidly relieving subjective symptoms with minimal side effects. Since serum viscosity is not a linear function of paraprotein concentration, the removal of as little as 20% of the paraprotein volume may effectively reduce the viscosity by 50% or more (25). Removing larger quantities can promote prolonged, symptom-fee intervals, and patients have been maintained in symptom-free states for as long as 36 months using no other supportive therapy (26). Since most IgM is present in the intravascular compartment and has limited mobility across various compartments, most can be removed in one volume exchange.

Although plasma exchange is effective in reducing hyperviscosity, the paraprotein usually reaccumulates in the patient's blood, depending upon the rate of production. Therefore, most observers consider plasma exchange to be a temporizing strategy until definitive immunosuppressive therapy has taken effect. Optimal doses of cytotoxic agents are not well tolerated by some patients, who may require intermittent plasmapheresis in conjunction with cytotoxic agents. One of our patients with Waldenstrom's macroglobulinemia experienced a drastic reduction in the serum viscosity level (up to one fourth of the initial level) with obvious symptomatic relief after single volume exchanges (Fig. 1).

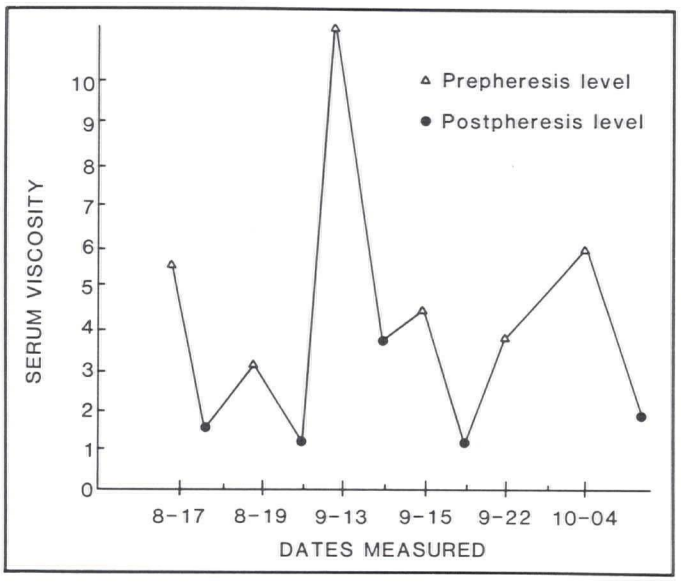

Fig. 1

Serum viscosity levels of patient with Waldenstrom's macroglobulinemia after plasma volume exchanges.

Hyperviscosity, vasculitis (gangrene and necrotic ulcers), dermatopathy, and Reynaud's phenomenon are symptoms of cryoglobulinemia and may be difficult to manage. Howert, et al (22) successfully used plasmapheresis on a patient who was refractory to conventional therapy; the remission lasted more than 18 months. McLeod and Sassetti (28) reported significant improvement for three cryoglobulinemia patients who underwent plasmapheresis; their plasma was returned after being rapidly cooled to precipitate cryoglobulin, and cryoglobulin-free plasma was returned to the patients. In another study, five patients with Reynaud's disease who underwent five treatments at weekly intervals showed marked symptomatic improvement; in all but one case, their digital ulcers healed completely (29).

Acute or chronic renal failure in multiple myeloma is essentially caused by precipitation of Bence-Jones proteins with destruction of the distal nephrons (30). Fifty percent of the circulating Bence-Jones proteins can be removed during a double volume plasma exchange. In renal failure patients who are unresponsive to diuretics, urine acidification, and chemotherapy, plasmapheresis can improve renal function (30). However, further long-term observations are needed to judge its therapeutic effectiveness and the prognosis of patients with myeloma kidney.

Autoimmune hemolytic anemia

Patients with autoimmune hemolytic anemia, primary or secondary, warm or cold antibody type, confront life-threatening situations if corticosteroids, immunosuppressive therapy, and splenectomy are not effective. Providing serologically compatible blood for these patients is extremely difficult, and the transfused red cells are readily exposed to the lytic effects of antibodies circulating in the blood. Intensive plasmapheresis to reduce the amount of circulating antibody has been attempted with some success in both the warm reactive and cold reactive antibody-mediated autoimmune hemolytic anemias (31-35). In the cold agglutinin disease, apheresis procedures are difficult to perform because of agglutination, sludging, and hemolysis of the red cells when the patient's blood is exposed to a lower room temperature in the centrifuge bowls; blood warmers along the in-flow and out-flow lines are beneficial in these instances. Although hemagglutinating antibody titers are significantly reduced, and the hemolytic process is improved, antibody titers return to previous levels rather rapidly unless immunosuppressive therapy begins to take effect.

Idiopathic thrombocytopenic purpura (ITP)

Because patients with ITP respond variously and unpredictably to corticosteroids and/or splenectomy, it is dif-

ficult to asess the role of plasmapheresis in their treatment. Branda, et al (36) described the response in two of three ITP patients. One was a 21-year-old man who had been in good health when he was admitted with a platelet count of 4,000/μL. The patient did not respond to high dose steroids (200 mg per day) and showed only a transient increase in his platelet count after splenectomy. Several days later, his hemoglobin level dropped, and there was evidence of intra-abdominal hemorrhage. He did not respond to treatment with vincristine and steroids, but his platelet count increased after plasmapheresis on two occasions. Thereafter, the platelet counts gradually became normal. Branda, et al (36,37) cited cases in which demonstrable antiplatelet antibody titers before plasmapheresis were reduced by 50% after a single session, and platelet counts increased by fifty to sixty-fold within several hours of the procedure. In a larger group of nine consecutive patients with acute ITP and five patients with chronic ITP, Marder et al (38) reported that the acute cases had a good response without the need for splenectomy, whereas the patients suffering from chronic ITP did not respond at all. In our institution four ITP patients, two of whom were considered chronic, received plasmapheresis (Fig. 2). It would thus appear that a trial of plasma exchange in ITP patients is warranted before splenectomy is performed.

Thrombotic thrombocytopenic pupura

The pathogenesis of this fascinating disease now revolves around the possibility of immune complex deposition on vessel walls and platelet membranes and the possibility that there is a missing plasma factor such as prostacyclin, PGI_2 (39,40). Absence of PGI_2, which is a potent inhibitor of platelet aggregation, leads to platelet consumption and underlying vascular endothelial damage. Conventional therapy using corticosteroids, antiplatelet agents, cytotoxic agents, and splenectomy has been tried for several years, but the mortality rates with conventional therapy still range between 72% at three months to 93% by one year (39). The use of plasma exchange as adjunctive therapy has been tried in more than 60 patients, and 67% achieved remission of three years or more. In these cases, recovery occurred after as little as one exchange of two liters of plasma, while other patients required up to 28 liters over several sessions.

Recent reports indicate that FFP infusion alone may be effective in the therapy of TTP (41), since normal plasma inhibits the platelet aggregating factor present in the plasma of TTP patients. However, it should be recognized that infusion of massive amounts of plasma will cause volume overload in most patients. Wenz and Barland (42) speculate that the plasma exchange is effective in patients with TTP, serving both to remove a pathologic plasma constituent while simultaneously providing the necessary therapeutic material in adequate doses. The availability of PGI_2 or other missing plasma factors in TTP patients would be of considerable benefit if the deficiency of such factors is the major contributing factor for TTP. One of our patients with central nervous system symptoms who was diagnosed as having TTP showed significant improvement of neurologic and other symptoms after plasma exchange with FFP. Later, the patient's platelet counts became normal with infusion of FFP.

Rh_o hemolytic disease

The rate of allo-immunization of childbearing women has markedly decreased since the introduction of Rh_o immunoglobulin injections. However, a number of allo-immunized women still remain at a high risk of fetal morbidity and mortality if intra-uterine hemolysis is confirmed by the 26th gestational week. Studies by Frazier, et al (43), involving 44 Rh-immunized patients, and by Graham-Pole, et al (44), involving eight severely affected women, are very encouraging in that most can be brought to term successfully. In both studies, ma-

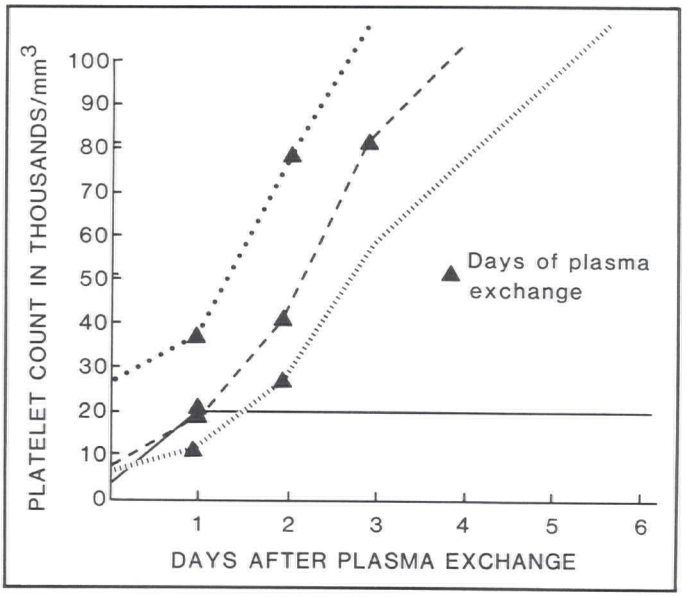

Fig. 2

Plasmapheresis in four patients with idiopathic thrombocytopenic purpura. • • Female, 83; one year duration; plasma exchange on day 1 and 2; normal platelet count on last visit. -- Female, 20; one month duration (steroids and vincristine); plasma exchange on days 1, 2 and 3. ||| Male, 46; one month duration (steroids); plasma exchange on days 1 and 2; platelet count normal after splenectomy. — Female, 69; five years' duration (steroids, oncovin, and cytoxan without effect); splenectomy done without beneficial effect; massive bleeding controlled by single apheresis; good response to steroids following apheresis; platelet count after four months - 100,000/mm³ and rising.

ternal antibody titers were significantly reduced after plasmapheresis.

Renal allograft rejection

Rifle, et al (45) have demonstrated the reduction of HLA antibodies using plasmapheresis in four of five patients with active rejection episodes. Circulating immune complexes were also removed, although titers of antibodies to B-lymphocytes did not change. In a large series of 37 patients, all patients were treated with corticosteroids and graft irradiation, and 15 were treated with plasma exchange also (46). Six patients in the control group and one in the plasmapheresis group rejected their grafts. Studies by Slapak, et al (47), Naik, et al (48), and Cardella, et al (46,49) show beneficial effects of plasma exchange therapy in conjunction with standard anti-rejection regimens. However, Power, et al (50) and Kirubakaran, et al (51) found no benefit from plasma exchange therapy in treating transplant rejection. Thus, it would appear that further, appropriately controlled protocols are needed to determine the cases in which plasma exchange can be beneficial.

Post-transfusion purpura

Two percent of the general population is PLA-1 antigen negative, and they may develop anti-PLA-1 antibodies if transfused with PLA-1 positive platelets. This antibody not only reacts with the transfused platelets, but it also produces immune complexes which bind to the recipients' own platelets. The antibody, which is IgG, is responsible for post-transfusion purpura, and plasma exchange therapy is the treatment of choice in these cases (52,53).

Myasthenia gravis

Autoimmune antibodies, usually IgG, to the neuromuscular acteylcholine receptors are responsible for most symptoms of the myasthenia syndrome. There is an inverse relationship between the acetylcholine receptor antibody levels and symptoms (54). Recently, patients with myasthenia gravis who have failed to respond to steroids, thymectomy, and anticholinesterase drugs have received plasma exchange therapy, with or without the continuation of steroids and immunosuppression (55). Among various studies, 75% of these patients showed a rapid clinical response lasting from three weeks to eight months (55-58). In Tindall's series of 57 patients, 43 showed good response (56). Tindall observed that the initial benefit was usually detectable after the second exchange, and the maximal benefit was usually seen two days after the sixth plasma exchange was completed. Patients whose disease was of short duration responded properly to the plasma exchange, but patients with chronic, severe disease, who may have developed postsynaptic destructive changes, responded only occasionally and were uniformly dependent upon exchanges for years. Of the 60 patients treated by Dau (55), 48 received corticosteroids, all but one received azathioprine, and plasma exchanges were done weekly. Of these patients, 39 had an earlier thymectomy, and 42 had received corticosteroid therapy. Only one of the 60 patients showed no improvement, 15 showed modest improvement, and 12 patients had no residual weakness.

Despite unanswered questions about the type of patient who would respond to plasma exchange therapy, the type of protocol, and the length of expected remission, the early use of plasma exchange in the therapy of myasthenia gravis will eventually be preferred to continued long-term use of corticosteroids or other immunosuppressive cytotoxic therapy.

Guillain-Barré syndrome

Several reports of dramatic, albeit short-lived, remissions induced by plasma exchange are in the literature (59-62). Recently, Tindall (63) analyzed his experience with seven patients with acute inflammatory demyelinating polyneuropathy who were judged to have Grade IV disease or worse. In three of seven instances, patients improved within the first 14 days after plasma exchange was initiated. All patients improved within six months. Six patients with relapsing inflammatory demyelinating polyneuropathy were also studied, and four of the six improved by two clinical grades. Two of the four responding patients became dependent on apheresis and required maintenance procedures at intervals of one to four weeks. Eight patients with slowly progressive chronic inflammatory demyelinating polyneuropathy were treated by plasma exchange, and two showed early response. In five of the eight, sustained control of the disease with plasmapheresis and/or immunosuppressive therapy could be achieved. Tindall concludes that in Guillain-Barré syndrome a trial with plasmapheresis is warranted, although failure to improve during an initial period of intense plasmapheresis precludes improvement during continued or subsequent exchanges.

Systemic lupus erythematosus (SLE)

Circulating autoreactive antibodies and immune complexes in this disease along with disengorgement of the reticuloendothelial system can logically be treated by plasma exchange therapy. In several published reports (64-67), 50% of the patients showed clinical improvement as a result of plasmapheresis, lasting between ten days and one month. Clinical and immunologic findings rebounded if no other therapeutic modalities such as

corticosteroids and/or azathioprine were used in conjunction with plasmapheresis. However, reports (68) indicate that plasmapheresis in conjunction with corticosteroids or cytotoxic agents produced considerable clinical and immunologic improvement, sometimes of a prolonged nature. Jones (68) believes that plasmapheresis might be considered a potentially valuable adjunct in the treatment of patients with severe SLE, when high doses of corticosteroids have failed. In these patients, the best results can be expected from a combined regimen of plasmapheresis and cyclophosphamide. Since there are many variables in the reported cases, a randomized prospective trial of plasmapheresis in patients with severe SLE glomerulonephritis has been initiated under Dr. E.J. Lewis of Rush Presbyterian-St. Luke's Medical Center in Chicago, which involves many other collaborating centers, including Henry Ford Hospital.

Renal diseases

Circulating immune complexes and/or glomerular basement membrane (GBM) antibodies cause severe and progressive immunologically-mediated inflammatory destruction of renal parenchyma. In a few patients with anti-GBM nephritis and Goodpasture's syndrome, the disease may be self limited, with rapid fall of anti-GBM antibody titers; but in 80% of the cases, end-stage renal insufficiency develops. In these cases plasma exchange has been used to: 1) remove circulating immune complexes and/or anti-GBM antibodies; 2) remove GBM antigens which may be released by the destructive inflammatory process and which, in turn, enhance autoimmune processes; 3) reduce plasma levels of inflammatory mediators such as fibrinogen, complement, etc; 4) disengorge the reticuloendothelial system and mobilize deposits from other areas such as the alveolar bed; 5) induce rebound proliferative activity of auto-antibody producing clones which may be killed by concomitant immunosuppressive therapy.

Several investigators have reported the usefulness of plasmapheresis in renal diseases due to antibodies or circulating immune complexes (69-73). Recent reports of controlled studies by Pusey and Lockwood (73) are encouraging. They studied 44 patients with anti-GBM disease; 22 were already oliguric or anuric and did not respond to plasma exchange, but 16 of the 22 remaining patients showed marked improvement. They also reported that 34 of 41 patients with immune complex rapidly proliferative glomerulonephritis improved on a plasma exchange regimen. Remarkably, 13 of 19 oliguric or anuric patients improved.

Other Diseases

Many other conditions have been treated by plasma exchange with varying success. Promising results are reported in conditions such as inhibitors to coagulation Factor VIII (74-76), Refsum's disease (77,78), familial hypercholesterolemia (79-82), diabetic hypertriglyceridemia (80,82), primary biliary cirrhosis (83,84), insulin resistant diabetes (85), pemphigus vulgaris (86-87), psoriasis (88), dermatomyositis (89), carcinomatosis (90-92), poisonings by Paraquat (93), by methylparathion (94), or by mushrooms (95,96).

Summary

Therapeutic hemapheresis procedures are increasingly being used to rapidly remove circulating and mobilizable deleterious materials. Procedures are safe and effective in appropriately monitored patients. Although in some instances the measurable parameters and the patient's condition change dramatically, the effects of hemapheresis are usually temporary, and concomitant specific drug therapy directed at the primary disease is necessary. Nevertheless, evidence is multiplying that apheresis procedures can benefit many previously therapy-resistant conditions. Immune modulation, the ability to interfere with re-introduction or resynthesis of substances, and the additional time the procedure allows for end-organ repair or regeneration, are compelling reasons for performing apheresis in carefully selected situations.

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