CASE REPORT

Successful treatment of a patient with severe atopic dermatitis and severe asthma by centrifugal therapeutic plasma exchange

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SUMMARY

This is a case of a 42-year-old atopic man with severe atopic dermatitis and asthma who despite long-term immunosuppression was not well controlled. He had a very high IgE at 7897 lu/mL prior to treatment. He underwent two therapeutic plasma exchanges (TPEs) through two peripheral lines in our outpatient department, which led to an absolute decrease of 44.1% and 37% in his plasma IgE for each exchange, and immediate sustained improvement in shortness of breath, and atopic dermatitis, and hence led to a vast improvement in his quality of life. TPE offers a new exciting adjunctive treatment option for severe atopic individuals, where it may provide a novel role to reduce health burden and improve clinical symptoms. Further studies need to be performed to establish an optimal protocol and potential maintenance with recently available targeted anti-IgE biologics.

BACKGROUND

Therapeutic plasma exchange (TPE) removes large molecular weight substances from the plasma.¹ Through two peripheral cannulas in our outpatient unit, a preselected plasma volume from the body was replaced with 4.5% human albumin solution. One plasma volume removes 66% of an intravascular constituent.¹ TPE is well known as a treatment within the medical specialties of neurology, renal and haematology; however, it is rarely used in dermatology practise for inflammatory dermatosis. The prevalence of atopy in the Western World continues to rise, with the annual cost to the National Health Service (NHS) of treating atopic eczema in the mid-90s being £465 million.² The NHS spends around £1 billion a year treating and caring for people with asthma.³ Currently the refractory symptoms of atopy, in particular, in atopic dermatitis (AD) are managed with immunosuppression with treatment such as intravenous immunoglobulin (IVIG) or biologics in secondary care, both of which are expensive.

CASE PRESENTATION

A 42-year-old atopic man with severe AD, asthma and hay fever underwent two TPEs for the treatment of his recalcitrant atopy.

His medical history also included type II diabetes. Since childhood he remained on immunosuppression, and control as an adult remained challenging requiring alternate day 5/10 mg prednisolone, azathioprine 150 mg once daily, Seretide

inhaler twice a day and salbutamol inhaler seven times a day. His mean peak flow was 290 L/min. He required prophylactic itraconazole for pulmonary aspergillus and aciclovir for eczema herpeticum. He remains on bone protection and regular topical emollient and steroid.

He struggled with walking his dog particularly with walking up hills, having to stop halfway up the hill to use his salbutamol inhaler midway and then again at the top of the hill. He had used topical steroids for his eczema for particularly troublesome areas on his wrists, nipples and knee flexors, which had never cleared despite long-term oral steroids and azathioprine. He had found weeping from his nipple eczema difficult to manage as they regularly stuck to his shirt.

On examination, he has moderate eczema around his nipples, his wrists and mild eczema of his knee flexors. He was short of breath after walking 100 m.

TREATMENT

He underwent TPE of 0.9 of his total plasma volume over a 3 h time period in our dermatology outpatients at day 0. He subsequently underwent a further repeat 0.3 of his total plasma volume 34 days later over 2 h. His plasma was exchanged for 4.5% human albumin solution. This was performed via two peripheral cannulas.

The TPE procedure performed was on a continuous flow centrifugal aphaeresis device which allows for immunomodulatory removal of inflammatory mediators (eg, antibodies and cytokines) based on specific gravity.

Using continuous flow centrifugal plasma exchange allows a higher extraction efficacy while running at lower flow rates, thus allowing for peripheral venous access. Comparing this with filtration plasmapheresis, which requires high flow rates to achieve a transmembrane pressure, needs larger veins (therefore typically central, femoral or fistula), and has a lower extraction efficiency (86% for centrifugal vs 35–40% filtration).⁴ Filtration TPE is via a membrane of a set pore size, therefore larger molecules will not be removed, for example, IgM.⁵ With centrifugal plasma exchange, this is negated as gravitational forces allow for removal based on specific gravity, rather than molecule size. This is of great benefit to our patient because it allows peripheral venous access and it is an outpatient procedure.

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Table 1 IgE, SCORAD and DLQI values post first plasma exchange (0.9 of total plasma volume)

Days post-TPE	Day 0	Day 2	Day 16	Day 21	Day 28	Mean value post-TPE (IU/mL)	Percentage reduction (%)
IgE (IU/mL)	Pre: 7897 Post: 4393	4260	6076	6441	6954	5624.8	28.77 (mean) 44.1
SCORAD	23.2	15.2	7.1	30.4	19.7	18.1	21.98
DLQI	6	4	1	4	4	3.25	45.83
Weight (kg)	116.8		116.5	116.5	116.1		

DLQI, Dermatology Life Quality Index; SCORAD, SCORing Atopic Dermatitis; TPE, therapeutic plasma exchange.

The first procedure was performed exchanging 0.9 plasma volumes. One volume of plasma equals total blood volume minus haematocrit, utilising Nadler and Allen's formula for total blood volume.^{6 7} This is calculated by the devices software. For the device, we only need to input patient gender, height and weight as well as the patients' haematocrit. The device then requires information regarding how many plasma volumes are to be exchanged. This is a fully automated system. The 0.9 plasma volume exchanged of our patient therefore equates to exchanging approximately 60% of his total plasma volume. This is based on the hypothetical efficiency curve previously reported.^{4 8} The curve is based on the following assumptions: the patient's plasma volume remains constant; the substance is only intravascular, or there is no equilibration with the extravascular compartment; synthesis and catabolism can be ignored. In these conditions, approximately 63% or 86% of the substance is removed, when one or two plasma volumes, respectively, have been exchanged.⁹ The second procedure exchanged 0.3 total plasma volume (TPV) which equates to approximately 25% of our patient's total plasma volume.

At no point was his medication altered. He remained on the same dose of oral prednisolone and azathioprine throughout. He was however able to alter the frequency of his topical steroids that he applied and the number of times he took his salbutamol inhaler throughout the day, as he deemed appropriate for symptomatic control of his AD and asthma.

We used the DLQI (The Dermatology Life Quality Index) and SCORAD (SCORing Atopic Dermatitis) to assess the severity of his AD. DLQI is a questionnaire used to assess the impact of skin disease on quality of life,¹⁰ and SCORAD is a clinical tool to assess the extent and severity of a patient's atopic eczema.¹¹ These tools together help us to form both a subjective and objective measurement of how well our patients' AD is being controlled at a given time point.

OUTCOME AND FOLLOW-UP

Following the first TPE, our patient had an immediate decrease in his total plasma IgE, and an improvement in his DLQI scores as well a generalised improvement in his SCORAD. In

particular, he was less self-conscious with regard to his skin, and it interfered less with his day-to-day life (tables 1 and 2).

Furthermore, he became less steroid dependent, indeed following TPE he did not use any topical steroids for 3 weeks, and in the last week before his next TPE he was using minimal low-potency topical steroid for troublesome areas.

Our patients mean peak flow was 290 L/min. Following TPE there was an immediate substantial increase in his peak expiratory flow rate (figures 1 and 2). More importantly for him it meant that he could walk his dog including up hills without needing to use his salbutamol inhaler. This is more than supported by his personal statement below.

His improved symptoms of asthma and AD correlated well with IgE levels.

DISCUSSION

Previous studies using plasma exchange have shown improvement in both drug-resistant bronchial asthma and recalcitrant AD.^{12 13} Our treatment in a severe atopic adult male with TPE has also shown clear immediate but surprisingly sustained benefit both subjectively and objectively. Moreover, the improvement has been mirrored by the plasma IgE levels.

Potential side effects during the procedure include vasovagal episodes, symptoms of hypocalcaemia due to intravenous citrate, fluid overload or under-replacement; however, these are all carefully monitored. Rarely patients can be allergic to the citrate or to the human albumin. As TPE can cause a transient fall in blood clotting factors, there is a very small risk of bleeding, or bruising from venepuncture sites.¹ Our patient had an uneventful course.

Recent trials report the anti-IgE antibody omalizumab to be effective in recalcitrant adult AD.¹⁴ It is also in National Institute for Health and Care Excellence (NICE) guidance for the treatment of severe persistent allergic asthma.¹⁵ Omalizumab is a humanised recombinant monoclonal antibody that binds free and membrane-bound IgE.¹⁶ TPE non-selectively removes IgE from plasma as illustrated by our results.

A recent German study analysed IgE-specific immunoadsorption for treatment of recalcitrant AD. Immunoadsorption was performed on two patients showing a mean SCORAD

Table 2 IgE, SCORAD and DLQI values post second plasma exchange (0.3 of total plasma volume)

Days post-TPE	Day 0 (day 34 post first TPE)	Day 11	Day 18	Day 25	Day 32	Mean value post-TPE (IU/mL)	Percentage reduction (%)
IgE (IU/mL)	Pre: 7175 Post: 4495	5833	6758	6729	7692	6301.4	12.18 (mean) 37.4
SCORAD	33.9	14.2	14.2	10.7	8.95	12.01	64.56
DLQI	3	1	1	0	0	0.5	83.33
Weight (kg)	116.3	116.5	117.5	116.9	117.5	116.7	

DLQI, Dermatology Life Quality Index; SCORAD, SCORing Atopic Dermatitis; TPE, therapeutic plasma exchange.

Figure 1 12-month peak flow diary (TPE, therapeutic plasma exchange).

improvement by 33%, 37%, 54%, 53%, 55% and 49% at weeks 3, 5, 9, 13, 17 and 25. Their mean reduction in IgE for each immunoadsorption cycle was 92% and they also found similar IgE levels which relapsed over a similar 3-week time period as our study.¹⁷

As with treatment with omalizumab and IgE-specific immunoadsorption, our study has shown that by reducing IgE symptoms of atopy improve, which can significantly improve quality of life. Indeed a reduction in IgE by TPE lends itself to the role of its suitability in reducing IgE levels of such recalcitrant

Figure 2 Peak flow graph in detail for first and second plasma exchange (TPE, therapeutic plasma exchange).

patients to potentially benefit from omalizumab as an adjunctive therapy once their IgE has been reduced.

We believe, contrary to existing literature,¹³ that centrifugal TPE is more cost-effective and time efficient in comparison to other methods of plasma exchange (double filtration and immunoadsorption). Puppe and Kingdon¹⁸ highlight the difficulties using membrane methods of plasmapheresis in that it required the use of additional disposable sets, high doses of heparin and nursing time as well as a longer procedure length. More importantly, our removal of IgE is greater than other methods previously reported and the rebound rate of IgE is lower, thus giving more clinical benefit to the patient.

Currently research in AD is investigating the roles of targeted biologics and IVIG; however, these medications are expensive, and long-term side effects are unknown. Even in comparison to current treatment regimes in AD, TPE has the potential to be safer, in particular potentially sparing high doses of immunosuppression and long-term known risk of lethal cancer from chemo phototherapeutic agents.

Patient's perspective

- ▶ Plasma exchange equals freedom.
- ▶ When Professor Cerio first asked me to take part in the trial I was nervous as not a big fan of needles. But as I have known Professor Cerio for over 30 years and trust him completely I quickly agreed.
- ▶ The day came, and after signing some forms and having the treatment explained fully we started. Soon the worse bit was over and the needles were in and the plasma exchange started. The rest of the treatment was painless and the few hours it took to be completed soon passed with Professor Cerio, Louise, Benit and Neil all making sure I was comfortable. After the treatment, I made my way home and it was only when I got home that evening, that I realised I had not used my inhaler once getting home.
- ▶ The next day I took my dog Chloe for her normal walk and found for the first time, I realised I was not getting wheezy or tight chested.
- ▶ Over the next week or so I was having surprises everyday as I was feeling better and stronger.
- ▶ During the next few weeks I never used my inhaler once, and I was able to walk Chloe further and for longer without needing my inhaler, in a word 'freedom'.
- ▶ My skin also started to clear and became less red and sore. No more scratching or being itchy—it was wonderful.
- ▶ Slowly after about 3 weeks, my symptoms returned, but I still was only using 2–3 inhalers a day instead of my normal 6–8 before the treatment.
- ▶ After my second treatment, I lasted longer and went around 4 weeks before using my inhaler and my symptoms returned.
- ▶ Hopefully with more trials this treatment could give freedom and a much better quality of life to hundreds, if not thousands of asthma and eczema sufferers.

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Learning points

- ▶ Plasma exchange is a novel treatment for atopy in an outpatient setting.
- ▶ Plasma exchange by reducing plasma IgE substantially improves symptoms of atopy including asthma and atopic dermatitis.
- ▶ Further studies using plasma exchange in atopy need to be performed to determine an optimal treatment protocol and it also may allow maintenance with new adjunctive anti-IgE agents which are not currently available under National Institute for Health and Care Excellence (NICE) guidance for these patients.

Competing interests BM and NI are employed by Terumo BCT (manufacturers of apheresis devices) and acted here solely as clinical and procedural advisors, respectively.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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