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Update of data from the world apheresis association (WAA) registry

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ABSTRACT

The WAA registry has been active since 2002. It allows bed side registration of safety and efficacy data. The data each center enters is accessible for its own use but also used for merged analysis. Most types of procedures are represented. Treatments of many severe diseases as well as the collection of autologous and donor cells for therapeutic use especially in oncologic diseases are recorded. Previous reports have shown a successive reduction in adverse events (AE) over the years. The aim of the present report is to update data of the risk for AE during the years from 2013 to Oct 2024. Contributions of 44 centers from 20 countries were analysed. Over these years, more than 169,000 apheresis procedures have been registered in more than 26,000 patients. During the study period the mean incidence of AE, merged for all types of procedures, was 1.6 /100 procedures for mild, 2.0/100 for moderate and 0.20/100 for severe AE, and reduced since 2013. Since 2002, death due to apheresis could not be excluded in one patient. There was an increased risk of hypotension during apheresis in patients with neurological diagnoses (ICD-10 chapter G) versus those with diseases of the musculoskeletal or connective tissue (ICD-10 chapter M) and vice versa for urticaria and tingling.

In conclusion, the present data show the risk for various degrees of AE in apheresis procedures. Many patients suffer from severe illness and apheresis is often offered as a rescue therapy. Although the risk of death due to the apheresis procedure is extremely rare the concomitant severe disease itself poses a risk for severe events.

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1. Introduction

The WAA-registry was initiated as an electronic registry in 2002 [1]. The registry is used for quality assessment of data of various types all relevant to the apheresis procedure. Application to access and to participate in the registry can be made on the site www.waa-registry.org The registration is free of charge. The data entered by each center can be downloaded for the submitting organization's own use such as for evaluation and publication at any time. Each center is invited to enter data after informed consent and the data should be entered as anonymous locally coded information not to be identifiable by others. Data is merged for overall comparisons and analyses. Subanalyses may be done between centers, within countries and between countries, while the intention is not to point out any specific center. The publications during the latest years are listed below [2–5].

The aim of the present report is to show updated data of the risk for adverse events (AE) during the years from January 2013 to October 2024.

2. Material

Until now we have registered more than 169,000 apheresis procedures. performed in more than 26,000 patients (42 % women).

Table 1 shows the 44 centers from the 20 countries that have participated or are participating in registering such data.

Statistical analyses for the trend of adverse events over time was estimated by the Spearman test (rho). The Mantel-Haenszel Chi-square test was used for larger figures and the Fisher exact test for small figures. Relative risk (RR) and confidence interval (CI) is given. A two-tailed p-value of < 0.05 was considered significant.

3. Results

Fig. 1 (below) displays AE (% of procedures) during the years 2013 to Oct 8, 2024. The AE are graded as mild (green column) when not needing supportive drugs, moderate (orange), when treatment was completed with supportive drugs, and severe (red), when treatment was interrupted due to AE. Out of all 169,000 procedures, so far, death due to apheresis could not be ruled out in one patient, as previously reported [4,6]. No other patient has been reported to have died due to the apheresis procedure.

Adverse events over the period 2013–2024 were lowered for moderate AE's (rho= −0.615, $p = 0.033$), but unchanged for mild (rho=-0.531, $p = 0.075$) and severe (rho 0.119, $p = 0.713$). When analyzing the period from 2015 to 2024 no significance was present.

Adverse events during therapeutic apheresis (TA) were compared between two frequently treated groups of patients: all ICD-10 diagnoses starting with G (neurological diseases) versus all diagnoses with M (musculoskeletal and connective tissue diseases including TTP). Mild AEs were more common when treating neurological diseases versus the M-group (RR 1.95 CI 1.64–2.33, $p < 0.001$) while moderate AEs were less common (RR 0.46, CI 0.39–0.54, $p < 0.001$) and severe AEs similar (RR 0.71, CI 0.49–1.005, $p = 0.065$).

Table 2 shows comparison of the most common AE during therapeutic apheresis (TA) for all neurological versus all M- diseases.

Hypotension was more common when apheresis was performed with the G-diagnoses (in 188 of 19,229 procedures) compared to those with an M-diagnosis (RR 3.76, CI 2.71–5.21, in 44 of 16,900 procedures, $p < 0.001$). The difference was significant for mild (RR 7.31, CI 3.91–13.7,$p < 0.001$), and moderate (RR 1.96, CI 1.30–2.95, $p < 0.01$), but not for severe AE.

Tingling was less common in those with a G-diagnosis, in regard to a mild (RR 0.35, CI 0.21–0.57, $p < 0.001$) and moderate AE (RR 0.35, CI 0.17–0.31, $p < 0.001$).

Urticaria was less common in those with a G-diagnosis in regard to a mild (RR 0.33, CI 0.17–0.66, $p = 0.001$), and moderate AE (RR 0.35, CI 0.26–0.48, $p < 0.001$).

Angiospasm was more common in those with a G-diagnosis and as mild AE (RR 8.49, CI 3.90–18.5, $p < 0.001$).

Other vascular access issues were more common in those with a G-diagnosis as mild AEs (RR 3.67, CI 2.48–5.42, $p < 0.001$), and moderate (RR 7.87, CI 0.997–62, $p = 0.036$).

A peripheral vein-to-vein access was more common for the patients with neurological diseases (57 %) than for those with M-diagnoses (12.8 %; RR 4.42, CI 4.24–4.61, $p < 0.001$).

Table 1
Listed are all centers that have been part of or still are active in registering apheresis procedures for the WAA registers. The names listed here represent the main responsible persons.

Country	Name and center	Registered through the years
Australia:	Newman E (Concord)	2007–2024
Austria:	Witt V (Vienna),	2005–2024
	Derfler K (AKH, Vienna)	2013-–2024
	Derfler K (Athos Institute, Vienna)	2017–2024
	Leitner G (Vienna)	2012
Belgium:	Eloot S, Dhondt A, (Gent)	2009–2013
	Deeren D (Roeselare)	2013-–2024
Croatia:	Bojanic I (Zagreb)	2016–2024
Czech Rep.:	Ptak J (Ostrava),	2005–2006
	Ptak J (Frydek-Mistek),	2006–2010
	Blaha M, Lanska M (Hradec Kralove),	2006–2024
	Gasova Z, Bhuiyan-Ludvikova Z (Prague),	2010–2024
	Blahutova S (Ostrava)	2011–2024
Germany:	Ramlow W, Prophet H (Rostock)	2002–2024
	Kielstein J (Braunschweig)	2018–2024
Indonesia:	Tehuteru ES (Jakarta)	2024-
Italy:	Liumbruno G (Rome), Mori (Livorno)	2003–2012
Kenya	Kiraka G (Nairobi)	2024-
Lithuania:	Audzijoniene J (Unit JA, Vilnius)	2006–2024
	Griskevicius A (Unit AG, Vilnius)	2004–2024
Macedonia Rep.:	Sikole A, Stojkovski L (Nephrology, Skopje)	2007
The Netherlands:	Vrielink H, Le Poole K (Sanquin, Amsterdam)	2005–2024
	Vrielink H (Sanquin, Groningen)	2011–2022
	Vrielink H, Le Poole K (Sanquin, Maastricht)	2016–2024
Norway:	Aandahl A (Oslo)	2013-–2024
Portugal:	Tomaz J (Coimbra)	2001–2014
Serbia	Lalic K (Belgrade)	2006–2007
South Africa	Poole C (SANBS Johannesburg)	2013–2017
	Skosana Y (SANBS Johannesburg)	2022–2024
	Glatt T (SANBS Johannesburg)	2018–2024
Spain:	Ortega Sanchez S (Barcelona)	2016
Suriname	Bihariesingh R (Paramaribo)	2022–2024
Sweden:	Strineholm V (Orebro)	2005–2024
	Brink B (Huddinge),	2006–2015
	Berlin G, Vasilache AM (Linköping),	2004–2024
	Dykes J, Smargianaki S (BC, Lund)	2015–2024
	Hellberg M (Nephrol., Lund	2011–2024
	Skoglund K, Toss F (BC, Umea),	2006–2024
	Stegmayr B, Ott M (Nephrol., Umeå)	2005–2024
	Nilsson T (Nephrol, Uppsala)	2006–2024
	Watz E (BC, Uppsala)	2006-–2024
	Welander G (BC, Karlstad)	2009–2024
	Ramsauer B (Nephrol., Skövde)	2009–2015
	Wallqvist C (Aph, Malmö)	2020–2021
Turkey	Seval GC, Ilhan O, Toprak SK (Ankara)	2009–2024
	Korkmaz S (Kayseri)	2018

4. Discussion

The apheresis centers reporting data to this registry are fairly

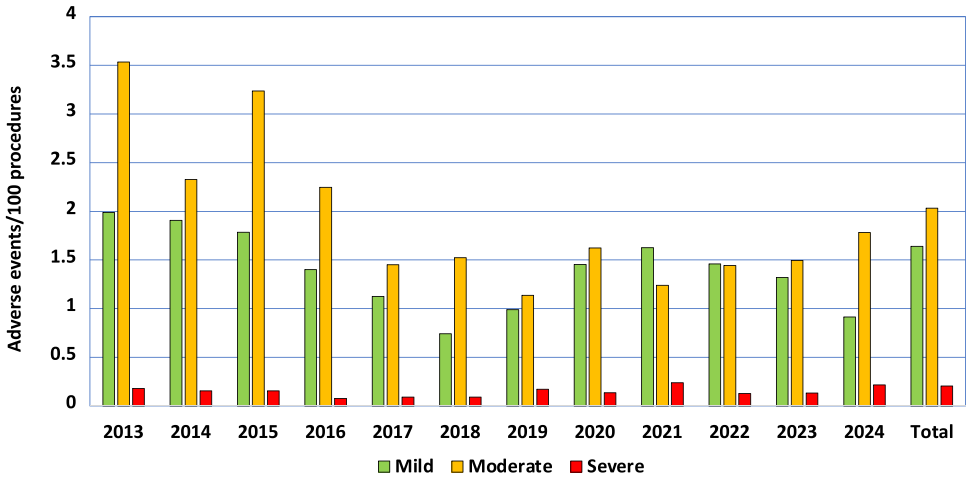

Fig. 1. Annual percentage of mild, moderate, and severe side events during apheresis procedures.

Table 2
displays the most frequent types of adverse events (in % and total numbers of AEs n =) by ICD-10 diagnosis.

Main AEs	G-Mild (n = 393)	M-Mild (n = 176)	G-Moderate (n = 217)	M-Moderate (n = 432)	G-Severe (n = 56)	M-Severe (n = 69)
Hypotension	23.4	6.3	34.1	7.6	39.3	17.4
Tingling	5.3	30.1	22.1	42.1	1.8	2.9
Urticaria	2.8	16.5	25.3	31.9	26.8	27.5
Flushing	0.8	1.7	1.4	4.2	1.8	8.7
Angiospasm	17.3	4.0	0.0	0.2	3.6	0.0
Access issues	33.1	17.6	4.1	0,2	1.8	8.7
Technical issues	6.6	5.1	0.0	0.2	3.6	0.0
Other	10.7	18.7	3.0	13.6	21.3	34.8
Total	100		100		100	

constant through the latest years. Although participation in the registry is without any cost, there seems to be an overall global resistance for centers to report data. However, we are happy to welcome the latest new centers registering their procedures in the WAA registry. They are from Paramaribo Suriname, supervised by Bihariesingh R; from Nairobi, Kenya by Kiraka G; and Jakarta, Indonesia by Tehuteru ES.

Within the frame of the WAA registry, AE decreased during the latest 20 years [4]. Even during the latest ten years a reduction was noticed, while during the latest years no further reduction was seen. The registry data show that there are substantial differences in adverse events between different groups of diagnoses treated [7].

In the present study we found that patients with neurological diseases have a significant higher risk of hypotensive episodes during TA compared to those with musculoskeletal diseases. Urticaria and tingling were more common when treating the M-diagnoses. Since the patients treated for M-diagnoses more often receive plasma as replacement fluid, these side effects may be related to the substitution fluid. The hypotension in the G-patients could also be due to the substitution fluid as, in regard to replacement of albumin, especially of lower concentration, this will cause a lower colloid osmotic pressure. In a previous study, we noted that replacement with albumin only (no plasma) or an albumin concentration of 35 g/L versus 50 g/L ($p < 0.001$), resulted in more (RR 4, CI 1.5–10) frequent occurrences of hypotension [7]. A reduction in vascular tonus may be present in several of the neurological diseases, reducing the ability to compensate for a hypovolemic condition by vasoconstriction. Notably, angiospasm at the access site was a more prevalent AE in these patients. However, the peripheral vein-to-vein access was the main access in this group compared to those with the M-diagnoses. Further investigations of the registry data will help to discriminate risk variables.

In a previous report we also presented rare but severe side effects in relation to the procedures and suggested that safety is increased by regular vital sign measurements, cardiac monitoring and by having emergency equipment nearby [8].

Currently, a report of the change in neurological diagnoses treated by therapeutic plasma exchange over the years is in preparation.

In conclusion, the present data show the risk for various degrees of AE in apheresis. Many patients suffer from severe illness and apheresis is often offered as a rescue therapy. Although the underling severe disease may pose a risk for severe AEs, apheresis itself poses a low risk of severe AEs (0.20/100) and death.

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