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**Comparison of treatment strategies for anaemia of prematurity in  
extremely low birthweight infants between 1997 and 2011**

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LETTER

## Comparison of treatment strategies for anaemia of prematurity in extremely low birthweight infants between 1997 and 2011

Anaemia of prematurity (AOP) is a common sequela of preterm birth.<sup>1</sup> It remains largely unknown how individual neonatal intensive care units (NICUs) manage AOP and whether treatment strategies have changed over time. We present the results of a standardised multicentre survey to assess the alterations in the treatment of AOP in NICUs caring for extremely low birthweight (ELBW) infants comparing Germany in 1997 (n=125 NICUs) to German-speaking countries in 2011 (n=129): Germany (n=110), Austria (n=10) and Switzerland (n=9).<sup>2</sup> Preparation strategies for red blood cells (RBCs), transfusion volume, and rate and protocols for erythropoietin

administration were analysed. High response rates (63.6%, 1997; 66.2%, 2011) make our results representative for German-speaking countries: Treatment strategies for AOP in ELBW infants have changed significantly from 1997 to 2011 regarding RBC transfusion volume, rate and preparation (table 1). In 2011, the transfusion of large volumes (15 and 16–20 mL/kg) of RBCs had increased significantly compared with 1997; 45% vs 27% (p=0.010) and 27% vs 16% (p=0.042) of subjects, respectively. Only 26% ELBW infants received 10–14 mL/kg vs 51% (p<0.001) in 1997. Furthermore, transfusion rates were significantly faster; 27% of subjects received blood products at a rate of 5 mL/hour vs 10% in 1997 (p<0.001) and only 19% at a rate of <3 mL/hour vs 42% in 1997 (p<0.001). Finally, matching subgroup RBCs (p<0.001), cytomegalovirus negative (p<0.001), filtered (p=0.002) and consanguineous blood products (p<0.001) were administered less frequently in 2011 whereas the use of irradiated products (p<0.001) had increased. No significant

changes of erythropoietin administration were observed. Our results show a significant increase of both volume and rate of RBC transfusion, increased administration of irradiated products over time and, conversely, less frequent use of matching subgroup RBCs, cytomegalovirus negative, filtered and consanguineous blood products. Even though all countries visibly aim to reduce the risk for bloodborne infections and immunological reactions in ELBW infants, there is paucity of universal international transfusion guidelines for this target group.<sup>3 4</sup> The strength of our study lies within the large sample size from Germany (1997), consolidated with pooled data from Germany, Austria and Switzerland (2011), which allows us to plausibly describe the changes in treatment strategies of AOP over 14 years. We therefore assume that our results represent actual current clinical practice and are not merely recommended treatment strategies. Further studies are warranted to examine the ideal volume and rate of RBC transfusion, time and quantity of erythropoietin administration as well as immediate and long-term transfusional adverse events.

**Table 1** Comparison of treatment strategies in ELBW infants between 1997 and 2011

	1997 (n=125) (%)	2011 (n=129) (%)	Difference (%)	95% CI	p Value
<b>Preparation RBC</b>					
Only O negative	34	37	3	-10% to 14%	0.750
Similar subgroups	65	41	-24	-36% to -11%	<0.001
CMV negative	94	79	-15	-24% to -7%	<0.001
Washed	26	15	-11	-21% to 0%	0.050
Irradiated	45	75	30	18% to 42%	<0.001
Filtered	85	67	-18	-28% to -7%	0.002
Satellite packs	73	73	0	-11% to 12%	0.995
No blood relationship	79	98	19	12% to 27%	<0.001
<b>Volume RBC (mL/kg)</b>					
<10	5	1	-4	-10% to 1%	0.091
10–14	51	26	-25	-37% to -11%	<0.001
15	27	45	18	4% to 30%	0.010
16–20	16	27	11	0% to 23%	0.042
>20	1	1	0	-5% to 4%	1.000
<b>Rate RBC (mL/h)</b>					
<3	42	19	-23	-34% to -10%	<0.001
3	11	16	5	-5% to 14%	0.326
3–5	25	26	1	-11% to 12%	0.947
5	10	27	17	7% to 27%	<0.001
5–10	12	12	0	-9% to 9%	1.000
<b>EPO</b>					
Use EPO	37	27	-10	-22% to 2%	0.095
<b>Dose EPO</b>					
<750 IU/kg/week		15			
750 IU/kg/week		51			
>750 IU/kg/week		24			

CMV, cytomegalovirus; ELBW, extremely low birth weight; EPO, erythropoietin; IU, international units; RBC, red blood cell.

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**Contributors** AW analysed the data, performed the literature research and wrote the first draft of the manuscript. TA was responsible for development and realisation of the first survey. HK supervised the development and contributed to the realisation of the first survey. RG was involved in the design of the second questionnaire, centre recruitment and data analysis, and reviewed the manuscript for intellectual content and approved the final version. HM designed the second questionnaire, developed the database, was responsible for data management and centre recruitment. SA was responsible for centre recruitment, development of the database of the second questionnaire. MN supervised the development and realisation of the second survey and acquired hospital funds for the incentive. RML critically reviewed the manuscript for important intellectual content and approved the final version. All listed authors on the manuscript have seen and approved the submitted version of the manuscript and take full responsibility for the manuscript.

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## REFERENCES

- 1 Strauss RG. Anaemia of prematurity: pathophysiology and treatment. *Blood Rev* 2010;24:221–5.
- 2 Gerull R, Manser H, Küster H, *et al*. Increase of caffeine and decrease of corticosteroids for extremely low-birthweight infants with respiratory failure from 1997 to 2011. *Acta Paediatr* 2013;102:1154–9.
- 3 *Cross-Sectional Guidelines for Therapy with Blood Components and Plasma Derivatives*. 4th revised

edition. Bundesärztekammer (German Medical Association).

- 4 Guideline for transfusion of blood and blood products, Austria 2005. [http://www.oegbt.at/wp-content/static/Richtlinien\\_Empfehlungen/KAV\\_Wien\\_Leitlinie\\_Transfusion\\_von\\_Blut\\_und\\_Blutprodukten\\_v3\\_2005.pdf](http://www.oegbt.at/wp-content/static/Richtlinien_Empfehlungen/KAV_Wien_Leitlinie_Transfusion_von_Blut_und_Blutprodukten_v3_2005.pdf)



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