

Reply to Arends and Harkisoen

TO THE EDITOR—We thank Arends and Harkisoen [1] for their thoughtful comments relating to our article on the efficacy of polyspecific intravenous immunoglobulin (IVIG) in streptococcal toxic shock syndrome (STSS). As detailed in our article [2], 75 STSS patients were identified through a national Swedish active surveillance study of invasive group A streptococcal (GAS) infections, in which a total of 746 invasive cases were included [3]. The study was designed to focus entirely on STSS cases and not on the heterogeneous group of patients with invasive (GAS) infections, the rationale being that IVIG has been suggested as adjunctive therapy in STSS with a beneficial effect on survival in these patients with pronounced systemic toxicity. The mortality often exceeds 40% in STSS cases compared with <15% for invasive cases. Among the 746 invasive GAS cases, 26 patients in total received IVIG, and as expected, the vast majority had an STSS diagnosis (n = 23).

Table 1. Timing of Intravenous Immunoglobulin Administration in Patients With Streptococcal Toxic Shock Syndrome

Time of IVIG Administration ^a	All Cases	NF Cases	Non-NF Cases
Within 24 h	14	9	5
Within 48 h	3	1	2
Data missing	6	3	3

Abbreviations: IVIG, intravenous immunoglobulin; NF, necrotizing fasciitis.

^a As related to time of streptococcal toxic shock syndrome diagnosis.

The question of whether the timing of IVIG administration differed between STSS patients with or without necrotizing fasciitis (NF) and therefore could be a confounder influencing mortality is a valid concern. The reported timing of IVIG administration in patients with or without NF showed that the majority of patients received IVIG within 24 hours after their STSS diagnosis (Table 1). However, as we acknowledge in the article, presence of NF might lead to a more rapid diagnosis and consequently a more rapid aggressive therapy including also IVIG.

In the article, we discuss the fact that although the IVIG and non-IVIG groups were well matched with respect to several baseline characteristics, including among others the Simplified Acute Physiology Score (SAPS II), they did differ significantly with respect to age (60 vs 65 years), presence of NF (56.5% vs 13.6%), and erysipelas (4.3% vs 34.1%). As Arends and Harkisoen point out, the data also show some differences, albeit nonsignificant, in underlying conditions. However, the number of patients affected by specific underlying conditions was too small to allow for further statistical analyses. In addition, the SAPS II score, in which some chronic underlying conditions such as metastatic cancer, hematological malignancy, and AIDS are represented, was included in the analytical plan as a possible confounder. Even when clindamycin treatment, surgery, and SAPS II scores were taken into account, IVIG remained a significant factor for survival with an odds ratio of 5.6.

Notes

Potential conflicts of interest. All authors: No potential conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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