Letter

The effects of IgM-enriched immunoglobulin preparations in patients with severe sepsis: another point of view

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We read with interest the paper by Tugrul *et al*. [1] regarding the effects of IgM-enriched immunoglobulin preparations in patients with severe sepsis managed in their intensive care unit. Apart from the global interest of reading a paper in the field of the treatment of severe sepsis and septic shock, we have an almost similar project in progress.

It is well known that the immunotherapy in sepsis is still a gray zone, and it will remain so as long as the relevant literature presents conflicting results [2]. From our understanding and the interim analysis of our data, it seems that we could expect some definitive immunotherapy information in the near future.

In our study, we have presently included 34 patients in the treatment group (IgM + IgG + IgA) and 34 in the control group. Analyzing our data in a manner comparable with that of Tugrul *et al*. [1], we reach a different conclusion regarding the results.

The only difference that exists between our protocol and that of Tugrul *et al*. regarding the study design and the inclusion criteria is that we include only adults older than 18 years old (the lower age limit of Tugrul *et al*.'s study is 10 years, and adolescents are probably included).

The number of patients needed per arm of the study in order to achieve a safe conclusion (statistical power analysis, 80%; $P < 0.05$ for a mortality decrease of 17%, which was the mortality decrease in our preliminary analysis) is 120 patients in each arm. In a study with a smaller number of patients, therefore, such as those of Tugrul *et al*. (21 patients in each arm) or ourselves (34 patients in each arm to the present time), any conclusion may be unsafe.

Although the data in both studies (in our opinion) are so far not sufficient, a significant difference trend is recorded. The mean age in Tugrul *et al*.'s study is 42.0 ± 18 years in the IgM + IgG + IgA group and 49.3 ± 20.6 years in the control group. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score in that same study is 10.5 ± 4.6 in the IgM + IgG + IgA group and 14.0 ± 8.5 in the control group. Although there is no statistically significant difference, there is a strong tendency for the two means to become different ($P = 0.10$).

In our preliminary data analysis, the mean age is 50.5 ± 3.33 years in the IgM + IgG + IgA group and 50.7 ± 7.36 years in the control group. The APACHE II score in our study is 21.27 ± 7.23 in the IgM + IgG + IgA group and 23.5 ± 7.91 in the control group.

The 28-day mortality rate in Tugrul *et al*.'s study is 23.8% in the IgM + IgG + IgA group versus 33.3% in the control group. In our preliminary data analysis, the mortality rate is 22.35% and 40.0% in the IgM + IgG + IgA group and the control group, respectively. Although this difference is a statistically significant one, the analysis of the mortality rate of the subgroups according to the APACHE II scoring of inclusion to the study day is more interesting. The mortality rate in our preliminary data for the IgM + IgG + IgA group with an APACHE II score ranging between 20 and 29 was 22.22%, and that of the control group with the same APACHE II score range was 55%.

APACHE II = Acute Physiology and Chronic Health Evaluation II.

As we pointed out earlier, in order to demonstrate the clinical effectiveness of immunotherapy in severe sepsis and septic shock, a number of 120 patients is necessary to be included in each arm of our study. Using our preliminary results in the same manner as those in Tugrul *et al*.'s paper [1], we could conclude that it is sometimes possible to present the data in such a way resulting in delusive conclusions. Analyzing the data by means of definitions of sepsis and septic shock, and assuming the patients to be a uniform group, we cannot demonstrate the special subgroups of patients in whom the administration of IgM-enriched immunoglobulin preparations may have highly beneficial effects. By grouping the patients according to some characteristics (such as APACHE II score or Simplified Acute Physiology Score II score), the beneficial effect of immunoglobulins could be shown. Using such an approach, a beneficial effect of IgG immunotherapy in a special subgroup of septic patients has already been shown in the study by Dominioni *et al*. [3].

In conclusion, it seems that there is a subgroup of patients with severe sepsis or septic shock in which the delivery of IgM-enriched immunoglobulin preparations may have a beneficial effect. Further study with more patients, either in our study or that of Tugrul *et al*., is necessary before we decide whether to use this type of immunotherapy in the treatment of severe sepsis.

Competing interests

None declared.

References

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