LETTERS TO THE EDITOR

To the Editor:

The recent publications by Ferries et al in JECT entitled "The Effect of Methylprednisolone on Complement Activation during Cardiopulmonary Bypass" concluded: 1) That corticosteroids did not reduce C3a activation and 2) That a membrane oxygenator (TMO) was not associated with less activation of C3a than a bubble oxygenator.

In contrast to these findings, a recent study presented at the meeting of the American Heart Association in November, 1984 from the Mayo Clinic demonstrated significant reduction in C3a activation and pulmonary sequestration of leukocytes when corticosteroids (Solu-Medrol 30 mg/kg) were given 20 minutes prior to cannulation. A significant reduction in C3a activity and leukosequestration was also demonstrated when the bubble oxygenator was compared to the Sci-Med membrane oxygenator.

There are two differences in the design of these studies which lead to apparently conflicting results. First, our study clearly demonstrates that high-dose (30 mg/kg) Solu-Medrol reduces complement activation as measured by C3a levels. In vitro studies have shown that corticosteroids depress the functional and immunological titre of the first four components of the complement cascade; corticosteroids also inhibit complement-mediated red cell lysis and mast cell histamine release. The ability of corticosteroids to inhibit complement activation experimentally appears to be independent of glucocorticoid activity and may be due to the cyclohexylethylamine (steroid) ring structure. Controversy exists whether corticosteroids other than methylprednisolone possess the ability to inhibit the complement cascade. In vitro studies show that corticosteroids inhibit the fluid phase formation of a neutropenia-inducing substance (a low molecular weight moiety formed when complement is activated experimentally) if given before complement activation, but have no effect once complement is activated. The reduction in complement activation and leukosequestration in our patients who received corticosteroids may be related to the pretreatment (20-30 minutes prior to cardiopulmonary bypass) and the large dose (30 mg/kg).

Corticosteroids given in the prime do not result in decreased C3a activation as shown by Ferries et al.

Secondly, the comparison of a bubble to a membrane oxygenator (TMO) in Ferries article demonstrated no significant reduction in C3a activity. However, we demonstrated lower complement activation, as measured by C3a levels, with silicone membrane oxygenators compared to the bubble oxygenators. In fact in a study presented in March 1985 at the AmSECT Meeting, Clancy et al demonstrated a significant reduction in C3a activity in the Sci-med membrane oxygenator compared to the Travenol oxygenator. It seems inappropriate to extrapolate data obtained from studies of the TMO to all membrane oxygenators. The silicone membrane provides a surface through which oxygen diffuses on a molecular level similar to that found in the human lung. The lack of a direct blood gas interface may minimize C3a activation and thus reduce C5a aggregation of PMN in the pulmonary microvasculature.

Sincerely yours,

Nicholas C. Cavarocchi, M.D.

References

Response

To the Editor:

Thank you for referring the Cavarocchi correspondence to us for response. We found it unprofessional, peculiar, and aggravating that Cavarocchi did not reference our article in his letter to the editor, yet he wants to discuss our work in print in the *Journal of Extra-Corporeal Technology*. Moreover, his paper is not in publication so we are at a loss to make meaningful comparisons. Furthermore, we find it rather disconcerting that the paper presented at the AmSECT meeting by Clancy is being distributed by the SciMed representative before it appears in print, or presumably, is even reviewed. Distressingly, the Clancy paper also fails to reference our work. Other than hearing Clancy’s presentation at the AmSECT meeting, we really have no official knowledge of either paper.

Reviewing the unofficial Clancy paper brought to mind some questions:

1) During his presentation, Clancy stated a number of consecutive patients were run on one type of oxygenator, then they switched and ran a consecutive number of patients on another oxygenator. Yet, his paper says it was a prospective randomized study and at two different centers. What was it, prospective or retrospective?

2) Which groups were done at what center? Did one center do all of one group, or was there a mix?

3) C3a levels on bypass in all groups were not significantly different. Off bypass, when we have no knowledge of what was being done or drugs given, is when C3a levels rose in groups II, III, and IV, but surprisingly not in group I. How is this explained?

4) Leukocyte counts, as an indicator of leukosequestration, also were only reported pre and post bypass, rather than sequentially throughout bypass. Why?

There may indeed be differences in the biological activity of different types of membrane materials. Cavarocchi and coworkers, as demonstrated by O’Flaherty et al, may indeed have made some legitimate observations concerning time dependence on the effect of corticosteroids. We feel very strongly though that using letters to the editor is not an appropriate forum to present and discuss unpublished data.

The three papers in question are of quite different design but do have enough similarities to make for some interesting dialogue once the other two papers are published. At this point, dialogue comparing results of the three papers would be inappropriate and unfair to the readers.

Sincerely,

Leroy H. Ferries, B.S., C.C.P.

References

