Follow-up Study: Protective Immunization in The Elderly

We previously reported that a group of elderly subjects given two doses of tetanus-diphtheria (Td) toxoid all achieved protective serum levels of antitoxin (≥ 0.01 AU/ml) to tetanus and diphtheria following a second dose.[1] A report describing the age-related decline in the synthesis of anti-tetanus antibody in humans[2] prompted us to follow up our study population.

From our previous study group, 14 persons (five males, nine females) were still alive four years following previous serum studies. Mean age at follow up was 78 years (range 65 to 98). Ten persons had received two doses of Td toxoid, two one dose, and two no vaccine. Sera were collected from all and antitoxin titers were performed as previously described.[1]

Protective antitoxin levels vs tetanus were present in seven of ten (70 per cent) sera from persons previously given two vaccine doses. Two persons who received only one dose of vaccine and two given no vaccine were below protective levels. Levels vs diphtheria showed that nine of ten (90 per cent) were still protective. Of two who received only one vaccine dose, one had fallen below a protective level; of two who never received vaccine, one remained below a protective titer.

A booster dose of Td toxoid was given to three persons who previously received two doses of toxoid and whose levels were below protection vs tetanus (two persons) or diphtheria (one) at follow up. None experienced any adverse reaction and all had protective levels four weeks after the dose.

These studies have implications for vaccinating the elderly against tetanus. The decline in titers to both vaccine components after four years suggests that two initial doses are not optimal for long-term protection, and a third dose is probably needed.

Tetanus continues to occur in the United States predominantly in elderly persons.[3] Any vaccine program for the elderly should take into account the reduced magnitude and duration of antibody responses of the elderly.

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Further Comments on Study by Morisky, *et al*

The recent article by Morisky, *et al*,[1] in this Journal was an important contribution to the health education literature, especially since it was a long-term follow-up study. However, the paper may mislead other investigators who emulate several of its approaches. First, the study not only evaluates the effect of the several intervention strategies on reduction of blood pressure, but also ascribes reductions in morbidity and mortality to these same interventions. Since the study was not originally designed to assess effects on morbidity and mortality, other important causal variables (family history of high BP, lack of exercise, smoking, salt intake, etc.) were not included in the study and differences in these factors between the intervened and non-intervened groups may be creating most or all of the apparent intervention effect.

Secondly, not all of the patients assigned to the various intervention groups actually received the scheduled interventions. In one group (E_1, E_2, E_3) only 13 out of 50 patients received the prescribed interventions. One would expect a considerable dilution of the intervention effect under such circumstances. Yet this study showed the second highest success in reduction in hypertension.

Thirdly, the data are presented in Tables 5, 6, and 7 at baseline, 3 years and 5 years. However, the number of individuals decreases over the follow-up period, allowing for selective drop-out of the less successful persons. A more appropriate analysis is the separate presentation of data for Baseline, 2 and 5 years for those followed 5 years, another analysis for B and 2 for those followed-up for less than 5 years but at least 2 years, and data for B alone for those who could not be followed for at least 2 years. This mode of analysis separates the selection effect from the intervention effect.

In summary, the health education intervention is credited with a marked reduction in hypertension, hypertension-related morbidity, hypertension-related mortality, and mortality from all causes. The size of the credited effect seems inappropriately large given the limited nature of the intervention techniques and may well be explained by the above mentioned methodological and analytical issues.

REFERENCE

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Authors' Response to Kirscht and to Tuthill, *et al*

We welcome the opportunity to address the issues raised by Tuthill, *et al*,[1] as well as respond to the commentary by Kirscht[2] on our study.[3] Both express skepticism about the fact that the results are more "positive" than in previous studies with even shorter follow-up intervals (implying that the longer interval should depress rather than enhance the benefits of health eduction).[4] Also, features of our design and data are questioned that deserve more discussion that we could possibly give in the space allowed for our article.

The problem of ruling out potential threats to internal validity has been resolved by the random allocation of individuals to experimental and control groups, thereby assuring the comparability of these groups with respect to *all* factors, known and unknown, except for the one being studied.[5] Analysis of variance on baseline measures confirmed the effectiveness of the randomization process. We agree that some skepticism is warranted until comparable results are available from "other settings with other conditions," but we do not see how Kirscht would offer "a somewhat more interpretable design." The fully crossed 2 × 2 × 2 randomized factorial design allows us to answer most of the questions he raises and many more he did not raise. Larger numbers, as always, would have helped, but longitudinal analyses of individual and subgroup histories of