Cardiac complications of vaccines

ARTICLE *in* JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY · MAY 2005

Impact Factor: 16.5 · DOI: 10.1016/j.jacc.2005.01.023 · Source: PubMed

4 AUTHORS, INCLUDING:

Serdar Kula

Gazi University

85 PUBLICATIONS **279** CITATIONS

SEE PROFILE

Fatma Sedef Tunaoglu

Gazi University

69 PUBLICATIONS **421** CITATIONS

SEE PROFILE

Rana Olgunturk

Gazi University

94 PUBLICATIONS **686** CITATIONS

SEE PROFILE

Cardiac complications of vaccines

Serdar Kula, Berna Canter, Fatma Sedef Tunaoglu, and Rana Olgunturk

J. Am. Coll. Cardiol. 2005;45;1309
doi:10.1016/j.jacc.2005.01.023

of diabetic patients enrolled. Ours was a prospective randomized study. By randomizing the patients prior to their procedure, the possibility of bias was negated. s noted in our Table 1, no significant differences existed between groups in any patient characteristic (including cardioplegia type, diabetes, and beta-blocker use) (3).

Both groups demonstrated an equal number of diabetics, use of beta-blockers, and cold or warm blood cardioplegia. Therefore, the differences between the groups seen at the conclusion of the study cannot be attributed to any of these factors. s Dr. Bisleri and colleagues state, there was an equal number of diabetics in both groups (35% vs. 31%; p NS) (3). lthough this number of diabetic patients is higher than expected for the general population, we were evaluating bypass patients in whom a higher incidence of diabetes is expected. s there were no significant differences in the patient characteristics, the effect on atrial fibrillation seen at the conclusion of the study is separate and significant.

Finally, the concern that "off-pump" bypass surgery decreases a "well-known" risk of atrial fibrillation is relevant to our study. During "off-pump" bypass, there is no cross-clamp applied, and minimal if any anterior fat pad dissection occurs. We agree that this may be one of the factors reducing the risk of atrial fibrillation using this approach.

In summary, the prospective randomized design of our study should address the concerns of Dr. Bisleri and colleagues. We agree that this study generates many questions regarding the mechanism of postoperative atrial fibrillation, and we look forward to future studies. The reality is that the sample size was small and although the patients were randomized, dogmatic conclusions are not warranted, at least not yet.

Jennifer E. Cummings, MD
Inderjit Gill, MD
Rami khrass, MD
Mark lain Dery, MPH, DO
Lee . Biblo, MD, F CC
***Kara J. Quan, MD, F CC**

*Heart and Vascular Research Center
MetroHealth Campus
Case Western Reserve University
2500 MetroHealth Drive
Cleveland, OH 44109
E-mail: kquan@metrohealth.org

doi:10.1016/j.jacc.2005.01.017

REFERENCES

1. Eagle K , Guyton R , Davidoff R, et al. CC/ H 2004 guideline update for coronary artery bypass graft surgery: Task Force on Practice Guidelines (update of the 1999 guidelines). Circulation 2004;110: 1168–76.
2. Eagle K , Guyton R , Davidoff R, et al. CC/ H guidelines for coronary artery bypass graft surgery: Task Force on Practice Guidelines (revision of 1991 guidelines). J m Coll Cardiol 1999;34:1262–347.
3. Cummings JE, Gill I, khrass R, Dery M , Biblo L , Quan KJ. Preservation of the anterior fat pad paradoxically decreases the incidence of postoperative atrial fibrillation in humans. J m Coll Cardiol 2004;43:994–1000.

Cardiac Complications of Vaccines

We read with interest the recent study by Eckart et al. (1) entitled "Incidence and Follow-Up of Inflammatory Cardiac Complications fter Smallpox Vaccination." lthough smallpox is the most common vaccine that is associated with myocarditis, other vaccines have also been linked with myocarditis, such as diphtheria–tetanus–polio vaccine, tetanus vaccine alone, cholera, typhoid–cholera, and variola vaccines (2–6). In order to assess any relationship between smallpox vaccination and myocarditis more accurately, it would be essential to know what other vaccines were administered to the military personnel in the study. Moreover, was there any relationship between specific lot numbers and myocarditis?

***Serdar Kula, MD**
Berna Canter, MD
Fatma Sedef Tunaoglu, MD
Rana Olgunturk, MD

*Gazi University
School of Medicine
06500, Besevler
nkara
Turkey
E-mail: kula@gazi.edu.tr

doi:10.1016/j.jacc.2005.01.023

REFERENCES

1. Eckart RE, Love SS, twood JE, et al. Incidence and follow-up of inflammatory cardiac complications after smallpox vaccination. J m Coll Cardiol 2004;44:201–5.
2. Dilber E, Karagoz T, ytemir K, et al. cute myocarditis associated with tetanus vaccination. Mayo Clin Proc 2003;78:1431–3.
3. Boccara F, Benhaiem-Sigaux N, Cohen . cute myopericarditis after diphtheria, tetanus, and polio vaccination. Chest 2001;120:671–2.
4. Driehorst J, Laubenthal F. cute myocarditis after cholera vaccination. Dtsch Med Wochenschr 1984;109:197–8.
5. Mittermayer CH. Lethal complications of typhoid–cholera-vaccination (case report and review of the literature). Beitr Pathol 1976;158:212–24.
6. postolski , Stankovic M, Romano M, nicic S, Popovic D. Myocarditis following administration of antivariola vaccine. Vojnosanit Pregl 1974;31:122–5.

REPLY

We appreciate the comments of Dr. Kula and colleagues regarding our publication on vaccinia-associated myocarditis (1). We agree with the need to consider the possible contributions of other vaccinations to myocarditis, and we recognize the potential for confounding. Our group recently published data revealing no statistically significant association of development of vaccinia-associated myocarditis in those with concomitant administration of other vaccines (2). Other vaccines in addition to vaccinia in cases of myocarditis may have included anthrax, typhoid, hepatitis , hepatitis B, influenza, meningococcal, MMR (measles, mumps, rubella), poliovirus, and yellow fever vaccines. No association was seen between specific lot numbers and development of myocarditis.

We note that all the available references cited by Kula and colleagues were isolated case reports relating to other vaccines (3–6). lthough they raise interesting questions, the reported observations are less persuasive than the extended case series we have reported (1,2). Recognizing that our experience is not within

the context of a prospective trial, we cannot exclude the possibility of multiple vaccine interactions; however, it appears unlikely at this time.

***Robert E. Eckart, DO**
J. Edwin twood, MD
John D. Grabenstein, RPh, PhD

*Cardiac rrhythmia Service
Cardiovascular Division
Brigham and Women's Hospital
75 Francis Street
Boston, M 02115
E-mail: robert.eckart@us.army.mil

doi:10.1016/j.jacc.2005.01.022

REFERENCES

1. Eckart RE, Love SS, twood JE, et al. Incidence and follow-up of inflammatory cardiac complications after smallpox vaccination. J m Coll Cardiol 2004;44:201–5.
2. rness MK, Eckart RE, Love SS, et al. Myopericarditis following smallpox vaccination. m J Epidemiol 2004;160:642–51.
3. Dilber E, Karagoz T, ytemir K, et al. cute myocarditis associated with tetanus vaccination. Mayo Clin Proc 2003;78:1431–3.
4. Boccara F, Benhaiem-Sigaux N, Cohen . cute myopericarditis after diphtheria, tetanus, and polio vaccination. Chest 2001;120:671–2.
5. Mittermayer CH. Lethal complications of typhoid–cholera-vaccination (case report and review of the literature.) Beitr Pathol 1976;158:212–24.
6. Driehorst J, Laubenthal F. cute myocarditis after cholera vaccination. Dtsch Med Wochenschr 1984;109:197–8.

Simple, Inexpensive, Rapid, and ccurate Preclinical Model for In-Stent Restenosis

With great interest we read the recent review by Schwartz et al. (1) regarding preclinical animal restenosis models. Detailed descriptions of the current available animal restenosis models, the pathophysiology of in-stent restenosis (ISR), and the usefulness of animal restenosis models to predict clinical outcomes are presented. In the final remarks it is concluded that preclinical models are important but imperfect standards. simple, inexpensive, rapid, and accurate preclinical model would be useful. However, in their description of available restenosis models, Schwartz et al. (1) overlooked two important and recently developed animal models of ISR. In these models, stents are implanted in the carotid artery (2) or in the abdominal aorta (3) of the rat. Pathophysiological processes of neoinitmal formation, such as thrombus formation, inflammation, and smooth muscle cell proliferation, evolve in an identical manner as seen in the rabbit iliac and pig coronary artery models. Moreover, in the rat abdominal aorta model, a positive correlation is found between the mean injury score and the neointimal area (2,3).

Rat ISR models enable thorough pathophysiological studies, as many antibodies to cellular proteins are available in the rat as compared to rabbits and pigs. By elucidation of the pathophysiology of ISR, more purposeful experiments to prevent ISR can be carried out. Rat models of ISR could provide important indications for the development of new anti-restenotic strategies (3). Generally, rat studies are preferable over rabbit or pig studies; only mainstream surgical equipment is required, animal facilities have large housing capacity for rats, and the costs for purchase are low.

Discrepancies between efficacy of anti-restenotic agents in preclinical and clinical studies have caused skepticism about the rat carotid artery model. For rat stent models this skepticism should be tempered, because differences in pathophysiological mechanisms between neointimal formation after balloon dilation alone and stent implantation are evident. Furthermore, rapamycin-eluting stents have been shown to inhibit neointimal formation in the rat abdominal aorta, a clear relation between preclinical and clinical outcomes in this model (3). In addition, these rat models enable stent research in transgenic diabetic and hypertensive strains. This offers a truer reflection of clinical settings in preclinical experiments, and might result in a better prediction of efficacy of anti-restenotic agents in clinical trials (2,3).

In conclusion, rat models are simple, inexpensive, rapid, and accurate preclinical models for ISR.

***Bas Langeveld, MD**
Wiek H. Van Gilst, PhD
Felix Zijlstra, MD, PhD

*Department of Clinical Pharmacology
University Hospital Groningen
ntonius Deusinglaan 1
9713 V Groningen
the Netherlands
Email: be.langeveld@med.rug.nl

doi:10.1016/j.jacc.2005.01.027

REFERENCES

1. Schwartz RS, Chronos N , Virmani R. Preclinical restenosis models and drug-eluting stents: still important, still much to learn. J m Coll Cardiol 2004;44:1373–85.
2. Finn V, Gold HK, Tang , et al. novel rat model of carotid artery stenting for the understanding of restenosis in metabolic diseases. J Vasc Res 2002;39:414–25.
3. Langeveld B, Roks J, Tio R , et al. Rat abdominal aorta stenting: a new and reliable small animal model for in-stent restenosis. J Vasc Res 2004;41:377–86.

REPLY

We read with interest the comments of Dr. Langeveld and colleagues concerning our recent review of preclinical restenosis models (1). These investigators write that stenting the rat carotid or abdominal artery provides a "simple, inexpensive, rapid, and accurate preclinical model for in-stent restenosis." We have several comments in response regarding the utility of the rat model.

useful in-stent restenosis animal model should accurately predict: 1) safety, 2) efficacy, and 3) pathophysiologic mechanisms. These are addressed as follows.

Safety. The major safety issues for stents are thrombosis (acute or subacute) and neointimal thickening causing luminal stenosis. lthough the rat model sometimes induces stent thrombosis, it does so to a lesser extent than the porcine and rabbit models. Total occlusion and severe stent stenosis do not generally occur in the rat model.

fficacy. Rat carotid restenosis models were abandoned years ago because virtually all therapies that were tested and effective in rats later proved ineffective in patients. Such studies included