Protection of Animals and Animal Experimentation: A Survey of Scientific Experts

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This article summarizes information from a *survey of biomedical scientists, spe;-cifically pharmacologists and toxicologists, on the use of laboratory animals and the potential for replacing their use with alternative methods for the development and evaluation of pharmaceutical substances. The majority of those surveyed felt that the alternatives could supplement or complement animal tests, but not replace the tests a/together. However, most favored the use of nonsentient material in safety tests.*

Zusammenfassung

Dieser Artikel ist eine Zusammenfassung von Resultaten einer Untersuchung untel biomedizinischen Wissenschaftlern, insbesonders von Pharmakologen und Toxikologen, uber die Verwendung von Versuchstieren und ihres moglichen Ersatzes durch alternative Methoden in der Entwicklung und Auswertung pharmazeutischer Substanzen. Die Mehrzahl der befragten Wissenschaftler ausserten die Meinung, dass Alternativen wohl Tierversuche unterstutzen oder vervollstandigen, jedoch nicht ganzlich ersetzen konnten. Die meisten von ihnen sprachen sich jedoch zugunsten der Verwendung von nicht-empfindsamer Materie in Sicherheitstesten aus.

Introduction

To an increasing extent, animal experiments have become a subject of public discussion. There are some social groups who assert again and again that animal experiments are dispensable in many biomedical fields because they can now be replaced by alternative methods. We report how, for the first time in the German-speaking area, scientists of various disciplines, who hold different attitudes toward the problems involved, were surveyed by questionnaire on the subject of toxicological evaluation of pharmaceutical substances using animal tests. Information was sought on the value of animal experiments for safety evaluation in acute, subacute, chronic, mutagenicity, carcinogenicity, and embryotoxicity studies. The questionnaire also asked for the scientists' assessment of alternative methods and their reliability.

Method

Information was collected by means of a written questionnaire between the end of June to mid-August of 1980. The addresses of the persons to be. interviewed had been taken from lists of university lecturers, participants at various conferences, and the membership list of the German Pharmacological Society. Additionally, the questionnaire was sent to all medical societies and associations. Questionnaires were sent to a total of 1,526 scientists from the fields of pharmacology and toxicology, veterinary medicine, pharmaceutics, biology, genetics, biochemistry, and physiology. These scientists were affiliated with universities, industry, and governmental and private research institutions. There was a 60 percent (916 questionnaires) response, but only 682 questionnaires were evaluated; the rest arrived too late for analysis or were incomplete.

Disciplines, Experience in Animal Experimentation, and Fields of Activity

The majority of responses came from pharmacologists and toxicologists (53.6 percent), while scientists in pharmaceutics and biochemistry accounted for approximately 10 percent each. Veterinarians accounted for a further 3 percent, with the remainder (about 24 percent) coming from biology or other disciplines. Two-thirds of those responding used animals in experiments. The "typical" period of experience in animal research was found to be between 15 and 20 years, and the majority of these investigators came from the disciplines of pharmacology, toxicology, and veterinary medicine. Of the pharmacologists and toxicologists interviewed, approximately 48 percent of the respondents were affiliated with universities, and only 37 percent were affiliated with industrial establishments.

An analysis of the disciplines and place of employment of the 682 respondents showed that approximately 40 percent were employed by industry and 40 percent by universities. Approximately 9 percent were employed by other research institutions (e.g., Max Planck Institutes), 6 percent in hospitals, and some 2 percent in governmental regulatory bodies. Of the pharmacologists and toxicologists surveyed, approximately 48 percent were employed by industrial establishments and approximately 40 percent by universities, whereas approximately 61 percent of the pharmacists worked in industry, while only .26 percent were affiliated with university institutions. In contrast, most of the biochemists, veterinarians, and biologists surveyed were affiliated with universities and research institutions.

Results and Conclusions

It is important to note that those whose answers indicated insufficient knowledge were not included in the final calculations of percentages. Of those that remained, it was found that these respondents did not consider that animal experiments could be replaced by alter--natives in testing for toxicity at present. They felt that alternative methods, if applicable, could be used as supplements or complements, but not replacements. Also, the majority of those who were surveyed predicted that only small gains could be made in reducing the number of animal experiments. In fact, they argued for a need for more animal experiments and for longer periods of testing, which would result in the use of more experimental animals and an extension of pain and suffering. However, the majority of the respondents were in favor of using material incapable of feeling pain in special (short-term) toxicological studies.

There were some noteworthy differences of opinion on a number of issues. Scientists from industry and from universities differed, in some cases, over the length of time necessary for chronic studies: University scientists advocated more extended periods of animal testing. The LOSO statistic was considered to be of great importance by 48 percent of the respondents and of little or no importance by 35 percent of the respondents. A mere 34 percent of the respondents proposed that medical and scientific reasons be considered as the most important criteria in choosing appropriate animal models. Another 34 percent identified economic and regulatory requirements as being more important. Concerning the issue of the number of species required for testing, "two mammal species" was chosen as preferable by 67 percent of those who indicated some knowledge of the issues. However, 21 percent felt that three or more mammals should be used in testing. For acute toxicity testing, 42 percent felt that the follow-up period should be 2 weeks, while 31 percent felt it should be 1 week (or less), and 27 percent chose more than 2 weeks.

On the question of alternatives, the respondents were asked to comment on the application of clinical data and the utility of mutagenicity tests. A small proportion (7.7 percent) felt that data from chronic animal toxicity studies could be completely substituted by clinical data from human studies. Partial substitution was considered possible by 41.4 percent, and 25 percent considered that substitution of animal data was impossible. Concerning the issue of short-term tests for mutagenicity evaluation, 13.1 percent of the respondents expressed their opposition to these tests. Those who accepted short-term mutagenicity tests disagreed over when such tests should be conducted. Some (20.1 percent) felt that short-term tests should always be done, while others favored them only in cases of suspected mutagenic effects (24.0 percent) or in cases when it was anticipated that there would be long-term administration of a drug (17.5 percent).

Discussion

These examples indicate that there is considerable divergence of opinion among experts about the use of laboratory animals. This may be due to the lack of any real scientific basis for the design and selection of animal tests for toxicology testing. For various reasons, including concern about the ethical issues regarding use of experimental animals and the performance of animal experiments, there seems to be an urgent need to create a rational basis for animal experimentation in the field of drug safety. Therefore, it is recommended that appropriate committees to address this issue be formed within scientific societies. The present inquiry might provide a basis for such action.

These panels should explore the various kinds of approaches that might be taken to limit or partially omit animal experiments in toxicology in the future. It is important that the inquiry be conducted under carefully defined conditions for each individual field of application (e.g., acute toxicity or mutagenicity). The LDSO test can serve as an example. Experimental animals are undoubtedly needed to determine an LDSO. Nevertheless, the general importance of this parameter for risk evaluation is a matter of great controversy, especially in relation to drug testing.

Industrial drug research is already extensively using short-term tests, involving material incapable of experiencing pain, in the screening process of new drugs. Such tests contribute to a reduction in the consumption of experimental animals and to a limitation in the total number of animal experiments. Short-term tests may also be used to study the actions or toxicological profile of an active substance, and they are generally cheaper and quicker.

It is recommended that the importance of, and the conditions for, a more extensive use of alternatives be studied more extensively. This would include coordination of research activities and dissemination of experimental data, as well as the provision of funds to finance specific research projects. At the same time, efforts should be initiated to have the concept of alternative methods included in any new national and supranational legislation that deals with toxicology testing and research.