Dr Luis A. Garcia Rodriguez

Aspirin Tributes

Luis A. Garcia Rodriguez is a Spanish pharmacoepidemiologist, who directs the Centro Español de Investigación Farmacoepidemiológica (CEIFE), in Madrid. The CEIFE, established in 1994, has pioneered use of automated computer-based data-bases to perform large-scale pharmacoepidemiologic research.

Pharmacoepidemiology, explains Garcia Rodriguez, explores utilization and effects of drugs in large populations, estimating probabilities of both beneficial and adverse effects.

In pharmacoepidemiology aspirin, says Garcia Rodriguez, represents one of the most widely studied drugs.

"*Aspirin has been off-patent for many years, with the result pharmaceutical companies no longer have any major economic interest in studying it. Therefore, much of the new clinical information derives from pharmacoepidemiology,*" explains Garcia Rodriguez. This, he adds, directly contrasts with new oral anticoagulants, such as apixaban and rivaroxaban, where much of the information has been derived from clinical trials.

INTERNATIONAL ASPIRIN FOUNDATION

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Celebrating the 125th anniversary of the synthesis of acetylsalicylic acid

Who is your aspirin hero?

"Over the years many scientists have contributed to knowledge about aspirin in the cardiovascular (CV) field, with notables including Felix Hoffman, Harvey Weiss and John Vane. But for me, Carlo Patrono, from the Catholic University of Medicine, Rome, represents the scientist who has made the greatest contribution to disentangling the molecular mechanisms behind the antiplatelet effects of low-dose aspirin.

Carlo conducted studies on the human pharmacology of platelet thromboxane inhibition by aspirin. In 1980, he published the first paper on the methodology of measuring serum thromboxane B2 (TXB_2), which in 1982 opened the way for his second paper describing the cumulative nature and biochemical selectivity of platelet TXB_2 inhibition by low dose aspirin.[1] Ultimately, it was this work that laid the foundations for establishing low-dose aspirin as a potential therapeutic strategy to prevent and treat CV disease (CVD).

Carlo, who chairs the Scientific Advisory Board of the International Aspirin Foundation, provides an example of a true Renaissance scientist who has mastered a whole range of disciplines from basic biology to clinical epidemiology. His work shows that once you understand the mechanisms involved you can achieve a far greater understanding of potential adverse effects, helping to identify relevant endpoints in clinical trials and observational research. Throughout his career, Carlo has been incredibly good at making complicated things simple."

What's the biggest difference aspirin has made in cardiology?

"Undoubtedly becoming one of the main pillars in secondary cardiovascular prevention for people who have already suffered a previous myocardial infarction (MI) or ischaemic heart disease. The first main study was The International Study of Infarct Survival-2 (ISIS 2), which between 1981 and 1985 randomised intravenous streptokinase, oral aspirin, both or neither to 17,187 patients with suspected acute MI.2 Results showed that low-dose aspirin once daily was effective and safe in reducing vascular mortality at five weeks by approximately one quarter.

For the last 20/ 30 years virtually everyone being discharged from hospital after an MI has been put on low dose aspirin. This strategy has undoubtedly resulted in saving a huge number of lives, although it would be difficult to tease out the exact contribution of aspirin since patients are also prescribed a multitude of other drugs."

What is the main research currently taking place with aspirin?

"Looking to see whether low dose aspirin might play a role in primary and secondary prevention of certain cancers. So far a primary prevention study of aspirin in cancer hasn't proved feasible due to the fact cancers aren't so common in the general population making it necessary to recruit an enormous number of patients over an extended period of time to show any difference between the arms.

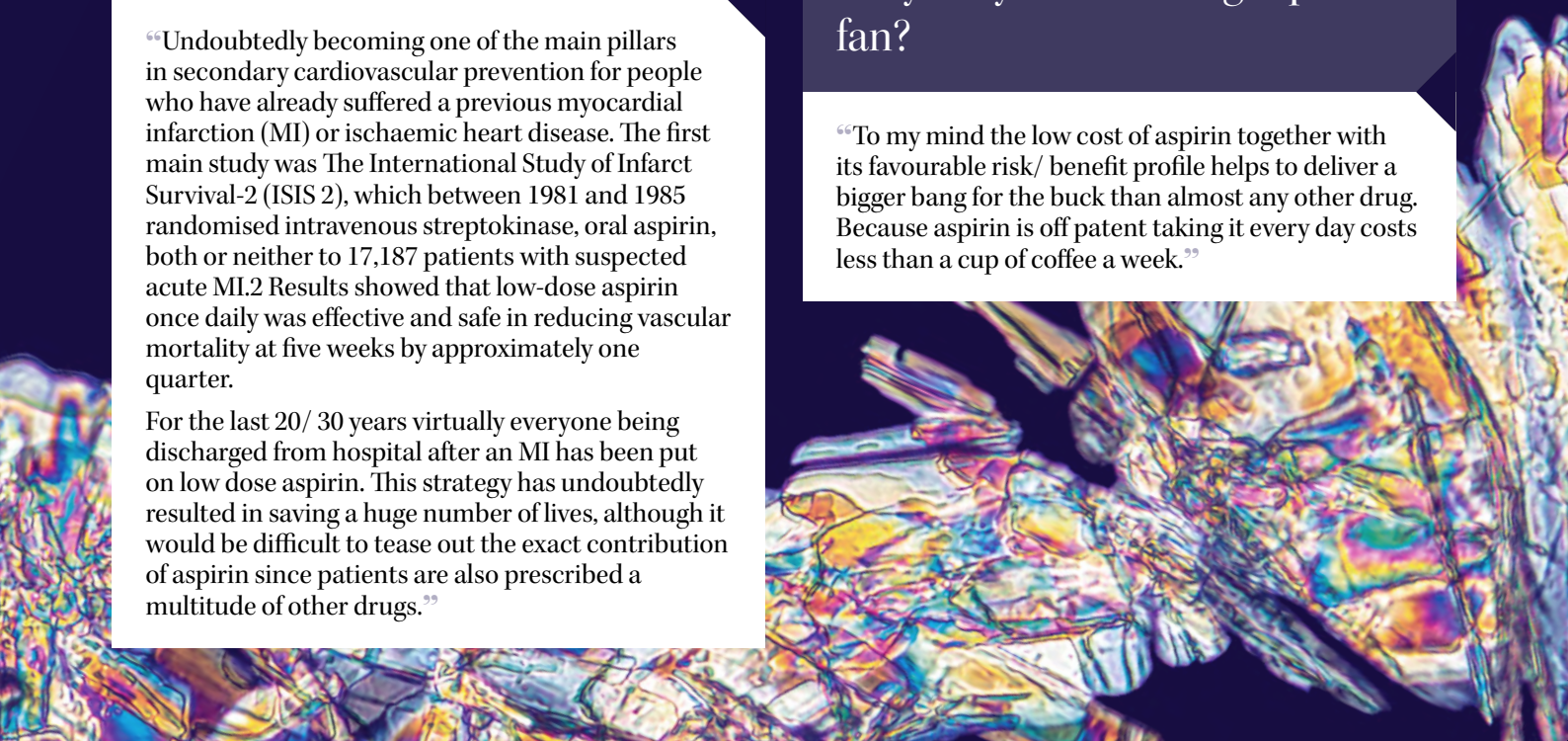
However, epidemiological studies have shown that individuals who chronically use aspirin (for both primary and secondary CVD prevention) reduce their risk of GI tract cancers (colon, stomach and oesophageal cancers) by around one third.

Carlo Patrono and colleagues developed a theory that aspirin worked in cancer prevention through a mechanism analogous to CVD prevention, through inhibiting platelet activation and downregulating participation of platelets in tissue repair, angiogenesis and immune response.

Currently, Ruth Langley (University College London) is running the secondary prevention Add-Aspirin trial to see whether after initial treatment for early-stage cancer taking aspirin every day for five years could help to prevent the cancer from coming back. Over 11,000 people who have been successfully treated for cancers of the breast, bowel, stomach/ oesophagus or prostate, are being recruited. If aspirin works in cancer prevention it would be marvellous because this would represent an additional benefit on top of CVD."

Why are you such a big aspirin fan?

"To my mind the low cost of aspirin together with its favourable risk/ benefit profile helps to deliver a bigger bang for the buck than almost any other drug. Because aspirin is off patent taking it every day costs less than a cup of coffee a week."



If you could do just one aspirin study what would it be?

"My ultimate aspirin experiment would be to perform a long-term observational study exploring all the major benefits and risks of low dose aspirin in the very same population. The usual approach is to say that in study A the benefit was X, while in study B the risk was Y and then combining the effects coming from different studies. The problem here is that we make the assumption that populations in study A and study B are the same, which is unlikely to be the case. If we looked at everything in the same population we'd be able to add and subtract all the different outcomes because they have the same denominator. To evaluate consistency of the findings the same study would need to be performed in different countries. Ultimately, this approach would provide us with an accurate risks/ benefits analysis for aspirin and the net impact of aspirin use in the general population.

For me this is the ultimate study because the overarching theme of my aspirin research has been to explore the different pieces that go into the overall risk benefit of aspirin in the general population.

Studies that I've undertaken with aspirin include looking at the role of aspirin in the primary prevention of MI in post-menopausal women[3], the effect of aspirin discontinuation, the bleeding risk of aspirin at different sites and looking to see whether low dose aspirin reduces progression of colorectal cancer as well as other cancer.[4]"

Tell us a surprising fact about aspirin?

"Virtually all worldwide production of acetylsalicylic acid, the main active ingredient of aspirin, comes from a factory in a town called La Felguera in Asturias, Northern Spain. The area was first selected to manufacture acetylsalicylic acid in 1942 because the nearby coal mines and iron and steel works provided carbon to make acetic anhydride and salicyclic acid. Even though the key ingredients have changed (to petroleum and acetic anhydride) production has remained at the same factory. From here Bayer transfers the powdered form acetylsalicylic acid to nearby Gijón, where it is shipped to centres around the world to be processed into pill form. For me personally, what's the biggest coincidence it that the acetylsalicylic factory happens to be just about 20 km south of Oviedo where I was born."

References

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