In-Vitro Diagnostics: An Under-Utilized Tool

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Abstract:

With the spread, and impending pandemic, of antimicrobial resistance, public health agencies from around the world are promoting a multifaceted approach to limit the use of necessary antimicrobials. Multiple studies have concluded that increased use of diagnostic tests to diagnose patients, as well as the development of innovative diagnostic tools, have the potential to curb antimicrobial resistance. In a presentation at the Knowlex National Infection Prevention and Control Conference in Manchester, England in 2016, Barbara Fallowfield discussed the use of *in vitro* diagnostics as a primary tool to curb the use of antimicrobials in the clinic.

Main Article:

Antimicrobial resistance (AMR) is a global issue, requiring collaboration to address both the causes and solutions to the problem. Currently, 85 companies across 18 countries have signed a 'Declaration on Combatting AMR.'[1] This pledge bands together a consortium of clinicians, researchers, governing bodies and industry representatives to reduce the impact of antimicrobial resistance today. In this fight, one primary consensus is that without diagnostics, medicine is blind. In a recent study, it was found that 70% of all clinical decisions were based off of *in vitro* diagnostic (IVD) tests.[2] At the Infection Prevention and Control Conference in Manchester, England in 2016, Barbara Fallowfield discussed the importance of more thorough use of these critical tests.

The British *In Vitro* Diagnostics Association (BIVDA) is the official diagnostic association of the United Kingdom. Representing over 8,000 employees across the UK, it was reported that over 900 million tests were performed, and over £730 million spent on diagnostics.

Antimicrobial resistance (AMR) is a global problem, requiring collaboration to address these problems. In the UK, a five-year AMR strategy (2013) was adopted to reduce the impact that AMR will have in the future.[3] In the report, the use of diagnostics was indicated as the key to addressing AMR. Currently, BIVDA is involved in developing new diagnostics to improve these strategies. The O'Neill review (2016) also concluded that IVD is crucial for this development. It recommended the development of rapid point-of-care diagnostics to support clinical decision making.[4] However, it also found a lack of consensus when determining what evidence is sufficient when using IVD to diagnose a patient. For new IVD technologies, they must undergo a compulsory assessment process, which can take up to two years to be approved. This delay can render the technology obsolete by the time it is approved, not including the time period required for introduction of the product into the healthcare system.

There Is A Ten Million Pound Prize

Known As The Longitude Prize To Develop And Commercialize A Rapid Point Of Care Test

Currently, there is a ten million pound prize known as the Longitude Prize (Nesta) to develop and commercialize a rapid point of care test.[5] These tests should address antimicrobial resistance, and must have a global impact. To win, teams must meet the Prize criteria, but there is little restriction placed on entrants to empower innovation of new technologies. Currently, 262 teams, from 37 countries have signed on to take part in this competition.

A Wellcome-Trust institute workshop was held with the goal of bringing together multiple IVD experts to improve patient care. From this workshop, four defined roles were developed for IVD technologies, which had to be satisfied prior to their adoption. These included:

1) Avoiding antibiotic use;

2) Optimizing patient treatment and antibiotic use;

3) Identifying high-risk patients; and

4) Improving drug development and stewardship.

One recent example illustrating the need for IVD is a frequent conundrum for doctors when differentiating between viral and bacterial infections. In 2014, a survey of 1,000 general practitioners in the UK revealed that 90% felt pressure from patients to prescribe antibiotics, and 70% of these still prescribed antibiotics, even if they were unsure if the illness was bacterial or viral in nature.[5] Twenty-four percent of respondents stated that this was due to the lack of appropriate diagnostic tools.

New IVD technologies are being developed, and are capable of differentiating between bacterial and viral infections within seconds, but they have not entered the market as of yet. Currently, there is a test for C-reactive protein (CRP), a biomarker for inflammation.[6] Identifying biomarkers can also identify high risk patients. Originally used to differentiate between infectious and non-infectious patients, procalcitonin levels in sepsis patients can be easily measured. Lower levels of procalcitonin are associated with favourable outcomes in these patients. Countries that have adopted this point of care test have already seen reduction in antibiotic prescription tests. In the UK, use of this test is extremely limited, due to lack of funding and distrust of current evidence supporting the CRP test. Fallowfield, stated that to optimize patient treatment, the main response of general practitioners should be to determine the appropriate treatment for the patients' illnesses. Tests such as real time polymerase chain reaction (RT-PCR) can be implemented in the clinic to quickly diagnose tuberculosis (TB). Other tests, such as mass spectrometry, or MALDI-TOF can provide rapid information about the species involved, but are still expensive to perform within clinics and require specialized training.

There is no holy grail of IVD test. Ideally, there would be one test that works in 5 minutes, determines if the infection is bacterial or viral, identifies the microorganism, and provides a sensitivity profile for an affordable price. For the most effective use of resources, companies should work towards identifying high priority illnesses, and their associated biomarkers, which can guide the future development of *in vitro* diagnostics.

Currently, our IVD tools are effective, but imperfect. More adoption and evaluation of current and new technologies has already shown to provide benefits to patients. Continuing this trend in improving diagnostics is crucial for our future fight against global antimicrobial resistance in the near future.

Watch the presentation here: https://youtu.be/M2vL-yclAKY

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