The Holy Grail, Genes and Number Needed to Treat

"According to Christian mythology, the Holy Grail was the dish, plate, or cup used by Jesus at the Last Supper, said to possess miraculous powers." Wikipedia

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In this month’s WestJEM, Henderson and colleagues report on a preliminary study of the genetics of asthma therapy. It seems like a simple enough piece, short, to the point, preliminary, not earth-shattering, and yet it points to a brave new world, an emerging area of medicine that holds great promise. This is about targeting therapy, really targeting therapy, dropping the number needed to treat (NNT) as low as possible, and dreaming of a number close to one.

Today in medicine we accept that we must treat many patients with therapies to benefit just a few. We accept that of the many treated, many will have side effects and gain no benefit. We even accept that some therapies will kill patients almost as often as it cures them. We accept that with thrombolytic therapy for myocardial infarction we need to treat between 40 to 100 souls to benefit one person. In patients with hypertension we may need to treat hundreds of patients for many years before we prevent one death. We accept it, but we do not like it.

In Henderson et al’s paper, the target disease is asthma, the treatment is albuterol and the question is, “Can we determine with genetic testing which patients are likely to respond and which are not?” The study suggests that some patients are less or more likely to respond to albuterol and this can be predicted by their specific genetic profile. It could be argued, and indeed should, that the differences found in the study are of questionable clinical significance. Does a difference of 19% in FEV1 really matter? This was not the point of the study, but it will be an important question as these studies become more prevalent. Does knowing this patient’s genetic profile really change my management or similarly should it change my management?

It is no secret to the practicing clinician that some patients respond very well to a variety of therapies while others appear to gain no benefit. In asthma we have all seen the patient given multiple albuterol treatments to no avail. At the same time the patient about to have a respiratory arrest is given just a few treatments and responds remarkably well. There is clearly a variety of factors that predict response to therapy: the patient’s age, sex, race, prior therapies, smoking history, etc. At least part of what we are doing by collecting such data as sex and race is genetic profiling. We are searching for those patients with the right receptors to our therapy by using the blunt instrument of historical and epidemiologic data. Genetic testing promises to focus this effort.

While this area is still in its infancy (the human genome project was completed just four years ago), some remarkable data has been collected. In one study of heart failure, a specific genotype was associated with dramatic improvements in LV function when these patients were treated with beta-blockers, while others gained relatively little effect.

In the end this is all about NNT. Clinicians are crying out for new information that can allow them to target therapies to the specific groups likely to gain the most benefit. We long for the Holy Grail, the number needed to treat of one.

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REFERENCES