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OBSERVATIONAL MEDICAL THERAPY TRIALS ADD UP USEFUL INFORMATION AS COMPARED WITH RANDOMIZED CONTROLLED TRIALS: CASE MULTIPLE SCLEROSIS

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Background

Clinical practice guidelines (CPG's) are predominantly based on randomized controlled trials (RCT's). However, the number of published observational, non-randomized trials is high and yet, the information they contain is often excluded while compiling CPG's. Observational trials (OT) deal with effectiveness in a "real world" situation and patients, whereas RCT's deal with efficacy in strictly pre-defined clinical trial conditions.

Purpose

The aim was to find out whether valuable information for CPG's can be discovered by including OT's in source material. We compared randomized and observational clinical treatment trials, published within year 2012, using multiple sclerosis (MS) as a model. We wanted to evaluate whether important information is lost by using only RCT's in CPG's and whether OT's should be considered more often.

Methods

We searched all publications of MS treatment in Medline in year 2012, using Scottish Intercollegiate Guidelines Network (SIGN) search filters http://www.sign.ac.uk/methodology/filters.html without language or age restrictions. The searches were conducted 28th Dec 2012 with MeSH-term Multiple sclerosis restricted by subheading Drug therapy. A total of 137 RCT's and 90 OT's were found.

All the hits were reviewed using the following inclusion criteria: adults with MS in studies reported in English and focusing on treatments aimed at disease modulation with efficacy, safety, health economics, pharmacological or compliance endpoints, and the following exclusion criteria: case reports (<5 patients) and trials on symptomatic treatments or rehabilitation.

Results

A total of 24 RCT's and 44 OT's fulfilling the inclusion and exclusion criteria were found. Eleven RCT's and 4 OT's were performed using investigational, non-marketed treatments, respectively. The median number of participants in RCT's was 430 (range 66 to 2244) and in OT's 118 (range 5 to 22 255).

Twenty RCT's were efficacy trials, 2 evaluated health economics and one each safety and pharmacology. Twenty-seven OT's had efficacy as a primary end-point, 10 addressed safety, 5 compliance and one each pharmacology and health economics.

Of 20 efficacy RCT's, 14 were positive regarding the primary hypothesis, 5 were negative and one was unclear. For 27 efficacy OT's the figures were 16, 7 and 2, respectively.

The average impact factor of the journals publishing RCT's was 15.7 (n=24, range 1.2-51.7). For journals publishing OT's it was 4.9 (n=42, range 0.8-30.0).

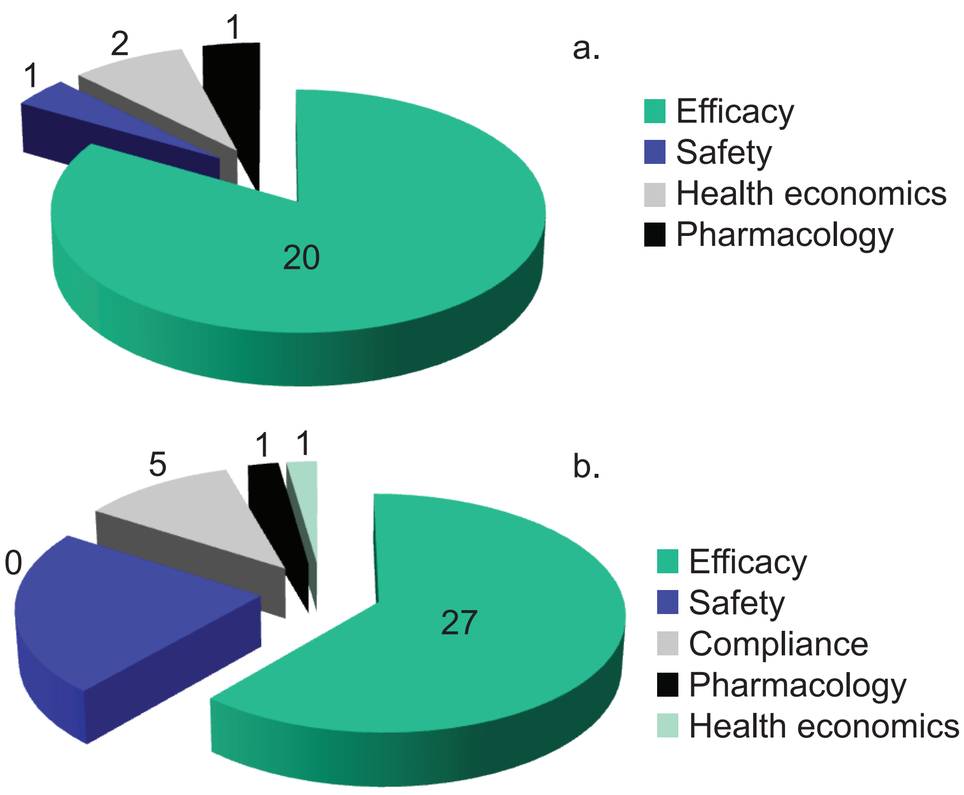

Figure 1. The portion of studies with different primary end points in RCT's (a.) and OT's (b.)

Discussion

Most trials addressing safety or compliance issues were observational, therefore important safety and adherence data could be lost by omitting them.

RCT's are published in journals with higher impact factor, which probably affects their penetrance in scientific community. Therefore RCT's get probably more publicity as compared with OT's.

The patients in OT's are more representative of the general MS population as compared with RCT populations with strict inclusion and exclusion criteria. Therefore their findings are more easily applied in everyday clinical practice, which should also be reflected in CPG's.

Implications for guideline developers

Despite their higher risk of bias, observational clinical studies should be considered while compiling CPG's. Especially the safety results can be missed when using only RCT's.

KEY NOTES

- OBSERVATIONAL TRIALS DEAL WITH EFFECTIVENESS IN "REAL WORLD" SITUATION, IN CONTRAST TO RCT'S, WHICH SURVEY EFFICACY IN PREDEFINED, STRICT CONDITIONS.
- IMPORTANT SAFETY AND ADHERENCE DATA CAN BE LOST BY EXCLUDING OT'S FROM SOURCE DATA.
- OBSERVATIONAL TRIALS SHOULD BE CONSIDERED WHILE COMPILING CPG'S.