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Title: A systematic review of publicity interventions to increase awareness amongst healthcare professionals and the public to promote earlier diagnosis of type 1 diabetes in children and young people.

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Abstract (249 words)

Background: Children with new onset Type 1 diabetes are at risk of developing the life threatening condition ketoacidosis if they have a delayed diagnosis. The rate of children presenting in ketoacidosis remains high in a number of countries worldwide. To ensure interventions to raise awareness of symptoms are effective a systematic review was conducted to evaluate previous publicity campaigns.

Methods: A range of databases were searched using search terms relating to Type 1 diabetes, publicity campaigns, symptom awareness. Identified articles were checked against the inclusion criteria, ensuring interventions were designed to target individuals prior to diagnosis of Type 1 diabetes. Papers were independently assessed under the criteria specified within the Critical Appraisal Skills Programme checklist.

Results: The initial search retrieved 1537 papers and following screening 20 were identified for full consideration. Thirteen did not meet the inclusion criteria, leaving seven to be assessed. Of these seven, two observational case control studies reported a reduction in the rate of ketoacidosis following a publicity campaign using posters and providing glucose testing equipment to primary healthcare professionals. Four observational cohort studies, utilised posters and media campaigns; two reported a reduction in the rate of ketoacidosis and two reported no difference following their interventions. A feasibility study, not designed to evaluate effectiveness, reported some anecdotal evidence of a more timely diagnosis.

Conclusion: Due to the methodological limitations of the studies identified, it is not possible to make a definitive conclusion on the effectiveness of the interventions reported.

MeSH Headings: Type 1 diabetes, Childhood, Publicity campaigns, Healthcare professionals

Background:

Type 1 diabetes (T1D) is the most common chronic condition in childhood, affecting 26 per 100,000 in the UK (1). The incidence rate of T1D is reported to be rising, with an expected increase rise of 3.9% between 2005 and 2020 (2,3). Left undiagnosed and untreated, children with new-onset T1D will develop life threatening diabetic ketoacidosis (DKA). DKA is mostly avoidable with a reduced risk should children experience an earlier diagnosis. The proportion of children with DKA at diagnosis of T1D varies across the world between 13–80% (4). In the UK, the rate is currently 23% (5) and although small fluctuations occur from year to year, rates have remained unchanged over the past 20 years despite efforts to promote awareness of diabetes (6,7). Children who present in DKA at diagnosis have an increased risk of mortality and long term morbidity (8,9) and younger children (<4years old) are at greatest risk (5).

In order to develop effective future interventions to promote an earlier diagnosis of T1D, it is important to evaluate the effectiveness of previous publicity interventions. Previous literature suggests that interventions should be designed and developed that target both parents and primary healthcare professionals to raise awareness of T1D. This systematic review therefore aimed to assess the effectiveness of population and primary healthcare professional awareness campaigns to raise awareness of early symptoms of T1D in children, to promote an earlier diagnosis and reduce morbidity and mortality in children with newly diagnosed T1D.

Methods

This systematic review was performed following the development of a protocol, registered with PROSPERO (registration number CRD42017062250) and in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidance.

Literature Search

We searched a range of databases (Table 1) and undertook a comprehensive grey literature search for any studies reporting an intervention which could raise the awareness of symptoms of T1D to promote an earlier diagnosis.

The search strategy used a combination of Medical Subject Headings and free text for articles published in English language from inception to March 2017.

In addition to the electronic databases, we searched electronic table of contents (eTOC) of key journals (*Pediatric Diabetes, Diabetic Medicine and Diabetes Care*) and websites recommended by two review authors (JG and JT) who are experienced in the field of childhood diabetes. Furthermore, a generic 'Google' search was carried out to ensure we had captured all relevant information.

Also, reference lists were reviewed, authors contacted for additional data where necessary. Full details of dates and all search terms are reported in appendix 1.

Study Selection

The search identified 1537 records. RD and JT then independently screened the titles and abstracts, followed by full text papers. Any disagreements were resolved through discussion and after removing duplicates and those that did not meet the inclusion criteria, 7 remained for analysis (PRISMA flow chart in Figure 1). Reasons for study exclusion are highlighted in

Table 2; two were excluded as the topic was not relevant to the review upon reading full text, six because there was no formal analysis or research, three due to the English-language only restriction, one as the research focused on children who already had diabetes as opposed to diagnosis of diabetes and one as the research did not focus on the effect of a publicity campaign.

Study Eligibility

Any intervention with the purpose of raising awareness of symptoms of undiagnosed diabetes was considered relevant, for example, a healthcare intervention, poster or media campaign. Studies focusing on an intervention for children who were already diagnosed with diabetes did not fit the inclusion criteria. For the purposes of this review we defined children and young people as anyone aged under 21 years and limited the search to T1D. Only English language articles were included. From our understanding prior to undertaking this systematic review, there are limited data on this topic so all types of studies were included to ensure that all relevant data were found. No restrictions were applied to the date of the study.

Primary and secondary outcomes

The primary outcome was defined as the rate of diabetic ketoacidosis in areas where an intervention was delivered compared to no intervention.

Secondary outcomes were the length of time to diagnosis and knowledge of the campaign (for healthcare professionals capillary blood testing and for the public greater symptom awareness).

Critical Appraisal

RD and JT evaluated the methodological quality of included studies using the criteria based upon the CASP (Critical Appraisal Skills Programme) checklists (10).

Data Extraction

A data extraction table was created based on key factors relevant to the review and pilot tested on a sample of papers. Key aspects of the table included study design, participants, intervention and key conclusions as well as other key details pertinent to the review. RD and JT performed the data extraction independently of each other. JG and MM reviewed their findings and resolved any disagreement.

Results

Study Characteristics

Table 3 summarizes the data of all included studies. No randomised controlled trials were identified. Two studies were observational case control trials, one a qualitative study and the remaining papers observational cohorts. Most studies involved longitudinally comparisons of rates of DKA before and after intervention, while studies by King et al (11), Vanelli et al (12) and Lansdown et al (6) included data from a control area. All articles were published on or after 1999 and the duration of the interventions ranged from one to eight years. We found articles from a variety of different countries; UK, Italy, Turkey, Saudi Arabia, Australia and Austria.

One study developed a new intervention in the form of a reusable shopping bag (13), but all other studies used posters as the main intervention (6,11,12,14–16). Three studies provided glucose and ketone testing equipment to doctors as part of the intervention (11–13) and

three studies included a media coverage element to raise awareness, for example press coverage and television broadcasts (6,14,15).

Results of studies

During the critical appraisal of the studies the methodological weakness of their study design was identified, namely that all studies were observational. However, the two studies with a more rigorous design, observational case control, did report a reduction in the rate of DKA following the delivery of their interventions.

Primary Outcome Measures

Six studies included rates of DKA as part of their results (6,11,12,14–16) (Table 4). Due to the study design, Townson et al (2017) did not provide data for rates of DKA pre-and post-intervention, although anecdotal and qualitative evidence suggested that the intervention did have impact, including two reports of parents receiving the intervention and recognizing symptoms in their children. These six studies used rate of DKA as their primary measure of success for the intervention (6,11,12,14–16). Using this measure, four studies were deemed successful (11,12,15,16) whereas the remaining two found that the intervention did not influence incidence rates of DKA (6,14). Ahmed et al (15) carried out an observational cohort to evaluate the effect of an awareness campaign involving posters, leaflets, educational activities, primary healthcare professionals and school nurses being reminded of a same day referral system for children with newly diagnosed diabetes and parents and teachers being reminded of the hazards of alternative therapies (popular in this culture) to insulin. These measures were found to be successful with DKA rates dropping from 48% in 2010 to 39% following the campaign in 2014. There was noted to be a statistically significant decrease in the frequency of DKA during the campaign period from 47.2% to 41%, p<0.01. Ucar et al

(16) by means of an observational cohort, also analysed the effect of an awareness programme on DKA frequency. The intervention involved displaying a poster in approximately 60,000 schools and providing information on websites. The results of this study showed a statistically significant drop in DKA incidence post intervention from 49.3% to 23.9%, p<0.0001.

There were only two observational case control studies in this systematic review and both reported a drop in DKA incidence following their interventions (11,12). Vanelli et al (12) reported an impressive drop in DKA incidence from 78% to 12.5% post intervention. In fact, during this eight year study, only three cases of DKA were reported in the intervention region, with no cases of DKA reported after 1992 following the intervention which started in 1991. King et al (11) carried out a similar study, which concluded that the rate of DKA at diagnosis decreased by 64% following the intervention; baseline incidence of 37.5% DKA reduced to 13.8% following the intervention, p<0.03, χ^2=4.74.

On the contrary, two studies found no statistically significant difference in DKA rates after an awareness programme (6,14). Lansdown et al (6) carried out an observational cohort study to determine the prevalence of DKA at diagnosis. Their intervention involved sending posters to every pharmacy, school and GP surgery in Wales, television and radio broadcasts, press coverage and internet links. Despite these efforts, there was no significant change in DKA rates; 25% presented with DKA before the intervention, 26% after the intervention, p=0.72, χ^2=0.65. Fritsch et al (14) sent posters both for adults and children to all kindergartens, primary schools, secondary schools and pharmacies in Austria. In addition, they also sent posters and articles to all Austrian paediatricians and GPs, offered medical education, published articles in newspapers and made broadcasts on Austrian television.

There was no significant change in the DKA rate after the intervention; 37.8% prior to the intervention and 36.9% post intervention.

Secondary outcome measures

There were limited data on the effects of interventions on our previously defined secondary outcomes. Two studies reported a reduction in the duration of symptoms prior to diagnosis; the first reduced from a mean of 14 days (SD 10-20) before to 8 (SD 5-14) days after the intervention (p = 0.0001) (16) suggesting the intervention led to an earlier diagnosis and the second found a statistically significant difference in the duration of symptoms for the intervention group compared to control group (mean 5 ± 6 days and 28 ± 10 respectively (12)). Townson et al (13) assessed the impact of their intervention using qualitative methods, including semi-structured interviews from parents with a child diagnosed with T1D, as well as GPs and Practice Nurses. Analyses suggested the intervention led to parents seeking health care advice earlier and primary health care professionals changing their practise and performing more point-of-care tests for T1D. These qualitative data suggest that the intervention increased awareness in public and healthcare professionals.

Discussion

This systematic review identified six observational studies, of which four were cohort and two were case-control studies. In addition, one feasibility/qualitative study was included. Four of the six observational studies reported a drop in the rate of children presenting in DKA at onset of T1D following the initiation of an intervention to raise awareness of the symptoms of T1D. There were no studies identified where an intervention had been fully evaluated using a randomised controlled trial. Due to the methodological issues that

observational studies pose, it is therefore not possible to draw definitive conclusions over the effectiveness of the interventions delivered to reduce the rate of DKA at diagnosis.

However, all of the studies included in this systematic review demonstrate that it is both feasible and acceptable to deliver large scale population and primary healthcare interventions to raise awareness of the symptoms of T1D, to ensure a timely diagnosis. The two case-control studies offer the most reliable evidence and suggest that a campaign targeting both primary healthcare professionals and parents, through schools, could be effective. The first and earliest study to describe an intervention to raise awareness of the symptoms came from Parma, Italy (12). This intervention concentrated on raising awareness through schools (teachers, parents and children) and paediatrician's offices using posters, cards, blood glucose testing equipment and a direct toll free telephone number to the hospital diabetes clinic. The use of a toll-free telephone system was a unique component to the intervention, not adopted by subsequent campaigns, and may have allowed parents or paediatricians the freedom to call for advice, without feeling that they were "wasting" the hospital's time. The reported fall in the rate of DKA post intervention is dramatic but interpretation of these results is limited due to the small numbers of children involved (3 per year) and the exclusion of children less than 6 and older than 14 years. The interventions delivered in other countries after this, largely mirrored the Parma intervention, adapting posters but dismissing particular components.

The Australian study (11) also showed a decrease in the rate of DKA following a population and primary healthcare targeted campaign. The interpretation of the results however are limited, as with the Parma study, due to small numbers of children diagnosed in the intervention area (40 at baseline and 29 post intervention).

In contrast, in a national study carried out in Wales, there was no effect on the rate of DKA, following a 12 month publicity campaign, supported by Diabetes UK (Cymru), where posters, based on those in the Parma study, were sent to every pharmacy, school and GP practice (6). This study also demonstrated the variability in annual national rates of DKA (ranging from 33% in 1993 to 22% in 1994) emphasising the need for longer term studies and the uncertainties of analysing data from interventions that report success based on small numbers and only one year of follow-up post intervention.

Indeed, one of the main challenges to effectively evaluate interventions to raise awareness of the symptoms of T1D is to design and deliver an adequately powered, randomised study due to the relatively small numbers of children who develop T1D. However, there still remains an urgent need for an intervention to be developed informed by guidance provided for the development of complex interventions by the Medical Research Council (17).

In addition to the studies included in this systematic review there have been a number of national campaigns which have been implemented but have not been formally evaluated. In the UK this includes Diabetes UK's 4 Ts campaign that comprised posters for the general public and another for clinicians, flyers, a video and web page (7). Other similar campaigns worldwide include the "Test One Drop" (18), "Defeat DKA and save lives" (19) and "You are never too young to have diabetes" (20) campaigns, involving posters and information via web pages. However, the rate of DKA at diagnosis over the past 20 years has remained constant at 25% in the UK which suggests that an effective campaign is still warranted.

To the best of our knowledge, no previous systematic review has evaluated the effects of publicity interventions to increase awareness amongst healthcare professionals and the public to promote earlier diagnosis of type 1 diabetes in children and young people. The

strengths of this study are that it was rigorously conducted and performed following a protocol published prior to commencing the data extraction. A limitation this study was that many of the papers identified, reported studies of poor quality or which were poorly described, thus limiting interpretation. In addition, we were only able to evaluate studies in English, though we do not believe this excluded any relevant studies.

In conclusion, there have been numerous attempts across the world to develop and evaluate interventions designed to raise awareness of T1D, to reduce the number of children presenting in DKA at onset. Most of these interventions have focussed on raising awareness with primary healthcare professionals and parents through schools, using posters, leaflets and media campaigns. Results suggest that it is possible to reduce the rate of DKA through publicity campaigns and the interventions within studies reporting the greatest success included common components, namely provision of capillary blood testing meters, diabetes educators, as well as posters and leaflets. Further research should be conducted to build on these findings using a randomised study design.

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