

Dianette - a qualitative study of adverse drug reaction (ADR) reports from the public

Qualitative Study by Millie Kieve and Kathy Piccolo on behalf of APRIL www.april.org.uk

Aim :To find out if there is a link between Dianette and Depression

Introduction

This study was carried out to determine if there is a possible link between depressive illness and Dianette. What prompted this study is the significant number of emails APRIL (Adverse Psychiatric Reactions Information Link) receives from women on Dianette, who are or were suffering from depression and other serious psychological related symptoms they consider to be adverse drug reactions (ADRs) caused by Dianette.

APRIL charity provides information on ADRs via it's website. APRIL has helped a large number of people over the years, who have been searching for answers as to why they feel unwell. Patients have often reported that their doctor has not listened to them and refused to believe that these medicines could cause ADRs. One of the drugs on APRIL's website is Dianette.

APRIL has received a large number of complaints from women feeling unwell whilst taking Dianette. Over 150 reports have been evaluated for two qualitative studies.

Dianette, or Diane-35 as it is known in other countries, contains ethinyl-estradiol and cyproterone acetate an anti androgen. It is also known as Co-cyprindol, Acnecin, Cicafem and Clairette. Dianette is licensed for the treatment of acne, hirsutism and polycystic ovaries (PCOS) but also works as a contraceptive. However, Dianette is not licensed as a contraceptive pill alone due to the high risk of blood clots. Venous Thrombotic Embolism (VTE).

The manufacturer recommends that Dianette should be discontinued three to four months after the acne has cleared up. This normally takes about three to twelve months in the case of hirsutism.

On 8th May 2006 the Guardian Newspaper published an article and reported that 'The Medicines and Healthcare Products Regulatory Agency (MHRA) which licenses drugs is reviewing Dianette following the submission of a dossier from the charity APRIL (Adverse Psychiatric Reactions Information Link).

How APRIL persuaded the MHRA to listen to the patients' voices

Millie Kieve the founder of APRIL had persuaded the director of the MHRA, Dr June Raine of their need to read the details reports from patients who had contacted the charity. Millie had in years of correspondence and meetings with the MHRA expressed concern that women were not being told to stop taking Dianette, yet were prescribed antidepressants without regard to the possibility Dianette may be causing their depression. Her concerns that the only warning to doctors regarding the higher risk of VTE for women taking Dianette dated back to 2002, had also been expressed. APRIL had been contacted by bereaved relatives of young women who died following blood clots and a young woman who believed a stroke in her 20's was due to Dianette.

Dr June Raine agreed for the emails to be sent to the MHRA pharmacovigilance division and anonymised report from more than 100 women were dispatched in 2006.

These first 100 emails were from women who stated they had plunged into serious depression while on the drug. *Some of these young women had been on the drug for years, even though Dianette is only supposed to be prescribed for a short period'*. A qualitative study of the 100 emails has been done and the result transferred to a poster for presentation.

Following the Guardian article APRIL received another influx of emails from very anxious women. These women had read the article and related the cause of their adverse symptoms of depression, mood swings, crying and even attempted suicide to Dianette. They felt compelled to write in with their own stories of how Dianette had had a drastic affect on their lives.

56 of these emails are evaluated in this paper.

The emails APRIL received after the Guardian article mainly state how depressed the patients are as well as emotional, tearful and unhappy. Some patients felt they were losing their minds and others were suicidal with one patient sadly taking an overdose. After the information came to light some patients said they couldn't believe they were allowed to take Dianette for so long. Many patients reported how much better they felt when they stopped taking Dianette.

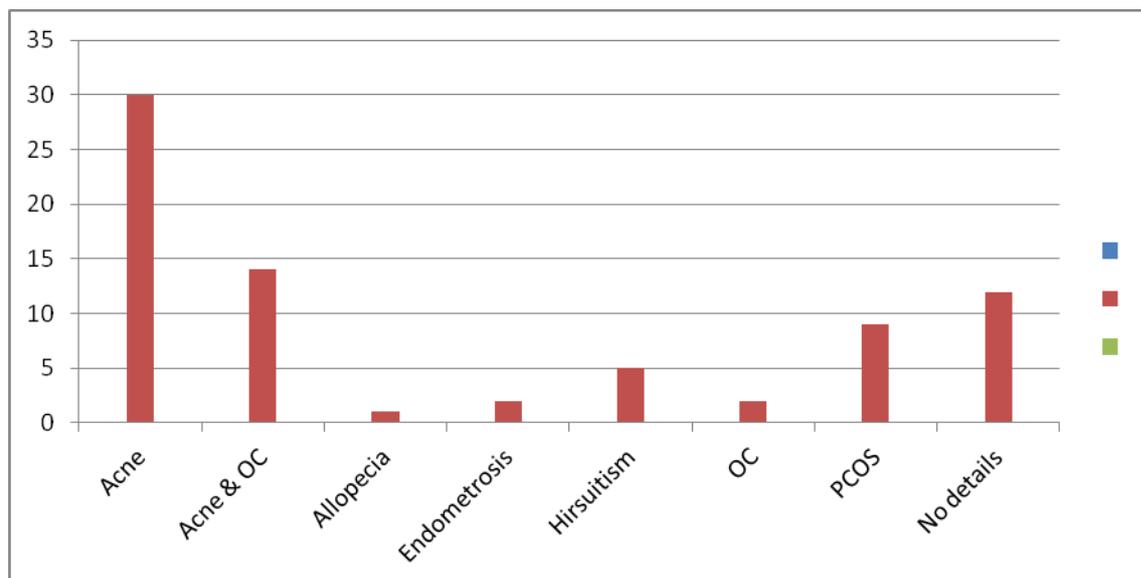
Method

For this study for APRIL we looked at Data from 56 emails received from women aged from 15 years to 38 years of age who had been taking Dianette from between 2 months and 18 years. These emails were received following an article in the Guardian newspaper Monday 8th May 2006. The article was about a link between Dianette and depression. The data from the emails was analysed and we recorded, from the emails, what Dianette was prescribed for, amount and type of symptoms, doctors response to patients complaints and for how long they were on the pill. There were limitations with the study, clearly APRIL only had the email data to evaluate and therefore important information may have been omitted due to the author of the email failing to report fully.

Results

There were 56 emails from women aged 15 years to 38 years old who were prescribed Dianette. The time spent on Dianette ranged from 1 month to 18 years. The data from the reports was collected and analysed with the results as below.

Bar Chart 1. Showing number of patients treated with Dianette in relation to different illnesses



The chart above shows that most patients are prescribed Dianette for acne alone and then for a contraceptive. Nine patients were being treated for Polycystic ovary syndrome, 5 for hirsutism, 2 with endometriosis and 1 for alopecia. There were no details for about 25% of patients;

17/56 Reports mentioned Doctor dismissed symptoms related to Dianette

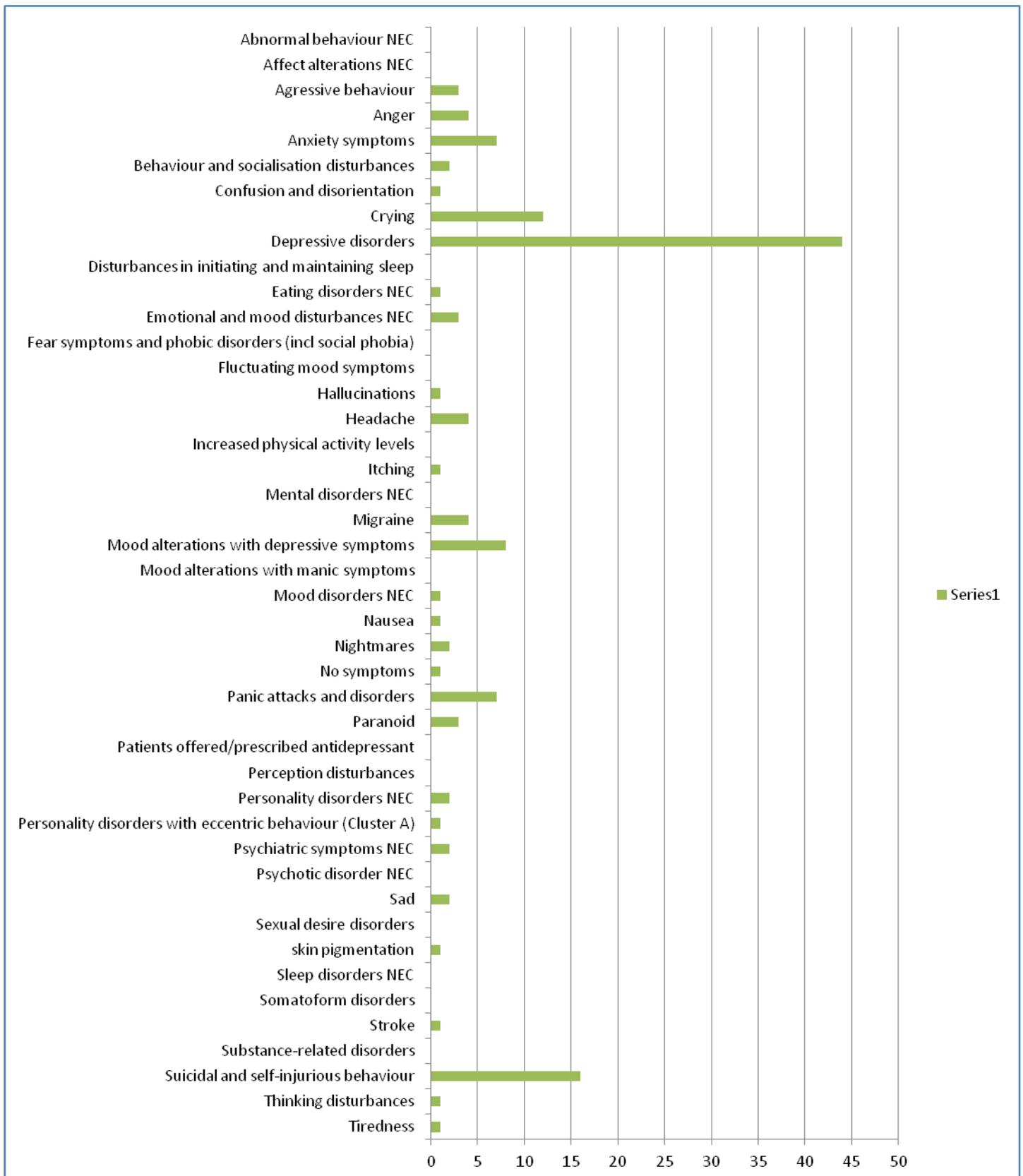
3/56 Reports Doctors didn't say anything; no reference to Dianette

2/56 Reports mentioned Doctors sympathetic

8/56 Reports mentioned Doctor s prescribed antidepressants

12/56 patients failed to mention doctors comments or had not seen their doctor

Bar chart 2. showing symptoms whilst on Dianette and severity of symptoms



The bar chart above shows the frequency of symptoms with nearly all the patients complaining of depression, followed closely by self harm (suicidal and self injurious behaviour) mood swings anxiety and crying.

Discussion

As a result of the Guardian article on Dianette, APRIL had an influx of emails from very worried females taking Dianette. Many patients were concerned that it took an article in the Guardian for them to realise that they may be suffering from ADRs. Some patients had already seen their GPs regarding feeling unwell and were concerned it could be Dianette causing their symptoms. All the patients but one complained of depression others complained they were suffering from depression, tearfulness, mood changes, self harming and suicidal thoughts. 15 out of 56 patients reported suicidal thoughts that is more than 25% of all the reports and were closely followed by complaints of crying, anxiety, panic attacks and mood changes. One patient took an overdose.

55 out of 56 patients who wrote in all believed that Dianette was responsible for their symptoms.

Patients reported that they were concerned that their doctors didn't listen to them. 17 of the reports mentioned that their doctors had dismissed what they were saying about their symptoms being related to Dianette and another 3 reports indicated that their GP showed no reaction when symptoms were described. Of these doctors 8, that is 14%, of the emails, mentioned that their GP prescribed them antidepressants for their symptoms. However two reports mentioned that doctors were sympathetic and took the patient off Dianette.

Two patients, reported that they were prescribed Dianette as a contraceptive pill, for which Dianette is not licensed in the UK.

One patient, a 21 year old woman, suffered ADR after 3 months. This the doctor dismissed, however after 6 months on Dianette she was rushed to hospital with a suspected stroke due to weakness on one side and poor mobility, this was later diagnosed as hemiplegic migraine.

One patient was prescribed Dianette at the age of 16 for a period of 18 months. She suffered depression during this treatment. When she came off Dianette her depression ceased. She went back on Dianette, a couple of years later, her depression returned and at the age of 24 she developed breast cancer. She is now concerned that there could be a link between taking Dianette, her breast cancer and the depression. Many patients have been on Dianette for a number of years.

Conclusion

APRIL was looking to find a link between Dianette and Depression. They found that over 95% of the reports received complained about depression and related symptoms of crying, mood swings, panic attacks, anxiety, self harm and 25% had suicidal thoughts. Following the Guardian article, 55 out of 56 patients who contacted APRIL believed that Dianette was linked or responsible for their symptoms. Patients mainly stated how depressed they are feeling, emotional, tearful and unhappy. Some patients felt they were losing their minds and others couldn't believe they were allowed to take Dianette for so long. Some patients reported how much better they felt when they stopped taking Dianette. Many patients felt so strongly after reading the article that they felt they had to write in and tell their own stories. Often patients felt very angry because they had been to the doctor about their symptoms and were led to believe, by the doctor, that how they felt was nothing to do with Dianette. In fact many reports complained that the patients' GP didn't listen to what they were saying and dismissed any link between Dianette and their symptoms. Of the doctors that dismissed the symptoms being related to Dianette, eight went on to prescribe anti-depressants for the patient at the consultation. After reading the article patients reported they were making appointments to see their doctors to change their pill. A variety of symptoms, some severe, were recorded most of which were related to depression. There were a few more serious physiological symptoms recorded. i.e. stroke and breast cancer. However, a large number of patients reported that as soon as they stopped taking Dianette their symptoms subsided.

The majority of the patients were on Dianette because of Acne followed by PCOS and hirsutism. A very small number of patients for Endometriosis and Alopecia were also treated with Dianette and two patients were prescribed Dianette solely as a contraceptive.

Based on the findings from this paper, there is significant evidence to expand on this piece of research by taking the findings to another level in proving that there is a definite link between Dianette and mental health disorders especially depression.

This could be achieved through doing another qualitative study and taking the following into consideration:

A larger sample size.

One to one interviews.

Looking at past medical history, medication and if the patients has a history of mental health issues.

Looking at world wide sources of evidence and comparing to the UK evidence.

Involve other clinicians for feedback i.e. Dermatologists, gynaecologists, endocrinologists, family planning doctors and Child and Adolescent Mental Health Services Camhns

Types of Psychiatric Symptoms

| | |
|--|----------|
| Tiredness | 1 |
| Thinking disturbances | 1 |
| Suicidal and self-injurious behaviour | 16 |
| Substance-related disorders | |
| Stroke | 1 |
| Somatoform disorders | |
| Sleep disorders NEC | |
| skin pigmentation | 1 |
| Sexual desire disorders | |
| Sad | 2 |
| Psychotic disorder NEC | |
| Psychiatric symptoms NEC | 2 |
| Personality disorders with eccentric behaviour (Cluster A) | 1 |
| Personality disorders NEC | 2 |
| Perception disturbances | |
| Patients offered/prescribed antidepressant | |
| Paranoid | 3 |
| Panic attacks and disorders | 7 |
| No symptoms | 1 |
| Nightmares | 2 |
| Nausea | 1 |
| Mood disorders NEC | 1 |
| Mood alterations with manic symptoms | |
| Mood alterations with depressive symptoms | 8 |
| Migraine | 4 |
| Mental disorders NEC | |
| Itching | 1 |
| Increased physical activity levels | |
| Headache | 4 |
| Hallucinations | 1 |
| Fluctuating mood symptoms | |
| Fear symptoms and phobic disorders (incl social phobias) | |
| Emotional and mood disturbances NEC | 3 |
| Eating disorders NEC | 1 |
| Disturbances in initiating and maintaining sleep | |
| Depressive disorders | 44 |
| Crying | 12 |
| Confusion and disorientation | 1 |
| Behaviour and socialisation disturbances | 2 |
| Anxiety symptoms | 7 |
| Anger | 4 |
| Aggressive behaviour | 3 |
| Affect alterations NEC | |

