Management of chronic abdominal wall pain: A one-year study

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Abstract:
Objectives: This study was designed to determine the prevalence of chronic abdominal wall pain (CAWP) in the gastroenterology clinic unit (GCU) and investigated the criteria of CAWP patients. Therapeutic trials to control such annoying problem were investigated. Methods: The study had two stages; the first stage was a cross-sectional analysis of the adult patients who were suffering from chronic abdominal pain. Patients reporting a score ≥ 10 on the Questionnaire of CAWP in addition to a positive Carnett’s sign were included in this study. Included patients were subjected to study the criteria of CAWP. The second stage was a randomized clinical trial where anti-neuropathic drugs (e.g. pregabalin-carbamazepine-amitriptyline) were used. Results: CAWP was diagnosed in 30.6% of the screened patients. 76% were female. Upper right quadrant pain was reported in 48.1%. Delay in diagnosis was reported to be 9.1±8.9 months. Misdiagnosis as cholecystitis, peptic ulcer disease and irritable bowel syndrome was reported. 94.4% of treated patients showed a satisfactory response to anti-neuropathic medications. 5.6% was successfully controlled by local injection. Conclusion: Lower Visual Analogue Scale (VAS) was reported after 2 weeks and 1, 2, 3, 4, and 6 months of the treatment plan implementation compared to the basal value (p. < 0.001). Conclusions: CAWP was identified in 30.6% of the patients complaining of chronic abdominal pain. Multiple physician consultations, delayed diagnosis, misdiagnosis with subsequent mistreatment were common. While, anti-neuropathic drugs are an effective tool in most cases of CAWP, trigger point injection represents an alternative line of treatment.

Keywords: Undiagnosed chronic abdominal pain, chronic abdominal wall pain, abdominal wall myofascial pain, Carnett’s sign, anti-neuropathic medications and trigger point injection.

Introduction
Although chronic abdominal wall pain represents about 10-30% of the patients complaining of chronic abdominal pain¹,². Yet, it received minimal attention in daily clinical practice. CAWP is studied sparsely in most textbooks of medicine, surgery and gastroenterology with subsequent lack of knowledge for health care providers². Patients complaining of CAWP have commonly undergone multiple diagnostic examinations and investigations up to sophisticated minimally invasive procedures; like gastrointestinal tract (GIT) endoscopies. These tests are sorrowfully almost often inconclusive. Therefore, the common diagnosis of functional GIT disorders has been adopted. Exhaustion of the health care system resources in addition to patients and doctor’s dissatisfaction is common³,⁴,⁵. The estimated direct cost of failure to recognize CAWP was near $700 per patient in 1994⁶. It increased in 2004 to exceed $1,100 per patient, for physician visits and imaging procedures for abdominal pain, during one year³. Therefore, earlier diagnosis of this relatively forgotten disease could reduce these charges³. Myofascial pain and radiculopathy are rare examples of a CAWP syndrome. However, CAWP is commonly caused by the entrapment of one or more of the anterior cutaneous branches of 7-12th thoracic intercostal nerves and known as anterior cutaneous nerve entrapment syndrome (ACNES)⁷. In ACNES, the most common site of pain is located at the lateral edge of the rectus abdominis muscle, where the nerves make a double right angle; in order to travel from the inner to the outer part of the abdominal wall and to continue along the abdominal wall⁸. Although different treatment modalities for CAWP had been used, including medical therapy, injection and surgery, the outcome of the pharmacotherapy was not justified³,⁵,⁷. This study was designed to determine the prevalence of CAWP in the gastrointestinal clinic and investigated the criteria of CAWP patients concerning: its sites and severity, duration before definitive diagnosis, number of previous physicians consulted during the process of diagnosis and treatment, misdiagnosis and mistreatment. We also evaluated the effectiveness of different treatment modalities in the management of CAWP.

Methods
This study comprised two stages; the first 12 month stage was a cross-sectional analysis of the
adult patients who were suffering from chronic abdominal pain. This stage included two phases: the screening phase and the inclusion phase. The second stage, which extended for another 6 months, was a randomized clinical trial that included the third phase of the study which was the treatment and the follow-up phase. After approval from the institutional ethical committee and obtaining a written informed consent from the patients, the study was conducted in the GI clinic at the Specialized Medical Hospital, Mansoura University from 23rd August 2014 until the end of February 2016. The institutional gastrointestinal clinic is a tertiary clinic serving about 8 million in the province and nearby areas. A four week pre-inclusion pilot study demonstrated that the weekly range of patients fulfilled the criteria of CAWP in the GI clinic was estimated to be about 3-4 patients. Therefore, the expected number of patients to be included in this study was about 150-200 patients.

**Inclusion criteria**

The approached participants were the referred adult patients who had been suffering from chronic abdominal pain (> 3 months) of unknown etiology, despite the use of multiple investigations; and who did not respond to multiple treatment modalities. In addition, the newly diagnosed patients (complaining of chronic abdominal pain of more than 3 months duration) during the period of recruitment were also screened. Only patients reported a score value ≥ 10 on the screening Questionnaire of CAWP in addition to positive a Carnett’s sign (where the leg-raising test is performed and the abdominal pain tenderness should remain the same or get worse to be considered positive) were included.

**Exclusion criteria**

Patients who had organic chronic abdominal pain (e.g. chronic cholecystitis), renal impairment, chronic liver diseases, psychiatric illness, pregnant female patients, and those who refused to participate in the study were excluded.

**Study Team**

The study protocol was suggested by a team from the Internal Medicine Department and the Anesthesiology and Surgical Intensive Care Department. Each member of the study team had a unique role. Firstly, an internal medicine residence was responsible for the screening for the prevalence of CAWP using the Questionnaire of CAWP and continuous follow-up of the patients throughout the study follow-up period. Secondly, two senior staff from internal medicine department were responsible for the exclusion of organic GIT disorders; hence, they enrolled only patients with chronic abdominal pain due to CAWP. Next, a combined team of above mentioned staff and pain physician were responsible for the treatment plan suggestion and pharmacotherapy for pain. Finally, the injection therapy was done by the pain physician.

**Patient Evaluation**

The patients in our study were subjected to 3 phases:

**Phase 1 (Screening Phase)**

Phase 1 included patients who asked for consultation in the GI clinic, complaining of chronic abdominal pain (> 3 months) of unknown etiology. During the first visit to the GI clinic, after taking an adequate medical history; reviewing their files and initial clinical examination by an internal medicine residence, the patients were evaluated for pain severity using Visual Analogue Scale (VAS), (100 mm unmarked line in which 0 = no pain and 100 mm = worst pain imaginable). Screening for the prevalence of CAWP was done using the Questionnaire of CAWP consisted of 18 items.

**Phase 2 (Inclusion Phase)**

Patients reported a score value ≥ 10 on the screening Questionnaire of CAWP were subjected to a standardized history taking and physical examination including the presence of positive Carnett’s sign, by two senior staff from internal medicine department. The diagnosis of CAWP was considered if the patient reported a score of ≥ 10 /18 on the Questionnaire of CAWP and positive Carnett’s sign. Patients who fulfilled the criteria of CAWP were subjected to studying the clinical features including the delay in diagnosis (due to the previous misdiagnosis), mistreatment, the site of pain, the performed investigations (especially spine x-ray) and the number of previous physicians consulted because of the same complaint.

**Phase 3 (Treatment and follow-up Phase)**

Pretreatment randomization of the patients into two groups was done using a computer-generated random number table. Therapeutic modalities included a trial of anti-neuropathic drugs (e.g. pregabalin – carbamazepine - amitriptyline). Pregabalin was started as the first line treatment with a dose, starting from 75 mg twice per day for 3 days. It was up-titrated by increasing the dose by 75 mg every 3 days; up to 150 mg twice per day, if there was no satisfactory response. Thereafter, patients were assessed after 2 weeks of pregabalin therapy. In the case of failure to achieve improvement; defined as more than 50% reduction of pain score, a second anti-neuropathic drug was added. The patient received a closed envelope, which determined his allocation into one of two groups. Firstly, the carbamazepine group received carbamazepine in a dose...
of 100 mg/12 hours, which could be increased up to 400 mg/day in a divided dose. Secondly, the tricyclic antidepressant (amitriptyline) group received amitriptyline in a dose of 25 mg at night. Medical treatment was continued throughout the study duration. The treatment team reviewed the drug therapy for each patient. Medications were stopped if there were any contraindication or serious adverse effects, and the patient was excluded from the study. Injection of the tender points was done if there had been a persistent pain after one month of the medical treatment (VAS >30). Pre-injection ultrasound was used to estimate the depth of the posterior rectus sheath in order to avoid deeper needle penetration. The injection was performed using 3ml of 0. 25% bupivacaine (diagnostic blockade) by a 26 gauge 1.5-inch needle passed perpendicularly through the skin mark drawn at the most tender spots. A therapeutic blockade; using 2.5ml of 0. 25 % bupivacaine and 20 mg of methylprednisolone acetate, was done after 2-3 day, if there was a good response (>50% reduction of pain score). This was repeated after 2 weeks if needed. Both diagnostic and therapeutic injections were performed in the outpatient pain clinic by 'freehand technique' without ultrasound control. Follow-up for all patients was done every week for 1 month and then every 2 weeks for another five months with pain assessment using a visual analog scale. The Telephone consultation was allowed for patients who cannot attend the follow-up clinic, those who encountered an increase in pain and those whom needed an earlier booking of appointments.

**Statistical analysis**

The statistical analysis was carried out using SPSS version 16 (SPSS Inc., Chicago, IL). The descriptions of data were done in the form of mean (±) standard deviation for quantitative data and in frequency and proportion of qualitative data. Chi -square test was used to compare categorical variables. For quantitative data, paired-samples t-test was used to compare with basal values. For all tests, statistical significance was considered when p <0.05.

**Results**

The study was conducted at the gastrointestinal clinic in a Specialized Medical Hospital, Mansoura University, where the patients had been being recruited for one year from 23th August 2014 to the end of August 2015. With additional 6 months follow-up of treatments, the study was completed by the end of February 2016. Meanwhile, 353 patients complaining of chronic abdominal pain of unknown etiology were subjected to screening using Questionnaire of CAWP. The diagnosis of CAWP was suspected in 138 patients based on the screening questionnaire of CAWP among the studied group members. Thirty patients had been excluded from the study (19 patients declined to participate in the inclusion phase, 10 patients reported a negative Carnett’s sign and one patient was proved to be pregnant). Hence, the total number of patients fulfilled the criteria of CAWP and were included in the study and under statistical analysis was 108 patients, which represented 30.6% of the screened patients, fig. (1).

**Figure 1.** Flow chart of studied patients

As regards, the demographic data, the mean age of the studied patients was 43.4±14.1 years, tab. (1). There was a significantly higher prevalence of CAWP encountered in females in comparison to male gender (76% versus 24% p. 0.029) , tab. (1). The mean body mass index (BMI) of the studied patients showed a tendency towards mild obesity 25.95 ± 3.7 Kg/m², tab. (1). The delay in diagnosis reported to be 9.14±8.9 months, tab. (1). Meanwhile, misdiagnosis was reported. For example, patients were misdiagnosed as cholecystitis in 12%, peptic ulcer disease (PUD) in 31.5%, irritable bowel syndrome (IBS) in 19.4%, IBS or PUD in 9.3% and cholecystitis or PUD in 10.2% of the studied patients. In contrary, 17.6% of the studied patients were diagnosed from the start (Naive) as CAWP, tab. (1). The previous mistreatment included antibiotics and NSAIDS in14.8%, proton pump inhibitor (PPI) in 44.4 %, digestive enzymes and spasmyotics in 23.1%, tab. (1). We found that 53.7% of the patients visited less than 5 physicians for the same complaint in last year while 28.7% visited ≥ 5 physicians in last year, tab. (1). The site of pain varied in the studied patients; as 48.1% of them reported pain in the upper right quadrant, while in 28.7% of the sample the pain was located in the upper left quadrant, tab. (1). Degenerative changes of the spine were reported in one third of the x-ray of the studied patients, tab. (1).
Table 1. Demographic data and patients’ criteria of the studied group; Values are means (SD) and in number (%).

<table>
<thead>
<tr>
<th></th>
<th>108 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>43.4 ± 14.1</td>
</tr>
<tr>
<td>Male / Female</td>
<td>26 / 82</td>
</tr>
<tr>
<td>Body Mass Index (Kg/m²)</td>
<td>25.95 ± 3.7</td>
</tr>
<tr>
<td>Delay in Diagnosis (months)</td>
<td>9.14 ± 8.9</td>
</tr>
<tr>
<td>Previous Misdiagnosis</td>
<td></td>
</tr>
<tr>
<td>Naïve</td>
<td>19 (17.6%)</td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>13 (12%)</td>
</tr>
<tr>
<td>PUD</td>
<td>34 (31.5%)</td>
</tr>
<tr>
<td>IBS</td>
<td>21 (19.4%)</td>
</tr>
<tr>
<td>IBS or PUD</td>
<td>10 (9.3%)</td>
</tr>
<tr>
<td>Cholecystitis or PUD</td>
<td>11 (10.2%)</td>
</tr>
<tr>
<td>Previous Mistreatment</td>
<td></td>
</tr>
<tr>
<td>No previous treatment</td>
<td>19 (17.6%)</td>
</tr>
<tr>
<td>Antibiotics and NSAIDS</td>
<td>16 (14.8%)</td>
</tr>
<tr>
<td>PPI</td>
<td>48 (44.4%)</td>
</tr>
<tr>
<td>Digestive enzymes as well as spasmolytic</td>
<td>25 (23.1%)</td>
</tr>
<tr>
<td>Number of physicians consulted in last year</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>19 (17.6%)</td>
</tr>
<tr>
<td>Yes &lt; 5 physicians</td>
<td>58 (53.7%)</td>
</tr>
<tr>
<td>≥ 5 physicians</td>
<td>31 (28.7%)</td>
</tr>
<tr>
<td>Pain location of the CAWP syndrome</td>
<td></td>
</tr>
<tr>
<td>Upper right quadrant</td>
<td>52 (48.1%)</td>
</tr>
<tr>
<td>Upper left quadrant</td>
<td>31 (28.7%)</td>
</tr>
<tr>
<td>Lower right quadrant</td>
<td>12 (11.1%)</td>
</tr>
<tr>
<td>Lower left quadrant</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Upper right quadrant and middle line</td>
<td>6 (5.6%)</td>
</tr>
<tr>
<td>Upper left quadrant and middle line</td>
<td>6 (5.6%)</td>
</tr>
<tr>
<td>Back X – ray (Degenerative changes)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>72 (66.7%)</td>
</tr>
<tr>
<td>Abnormal</td>
<td>36 (33.3%)</td>
</tr>
</tbody>
</table>

Regarding the severity of pain in the studied patients, the Mean VAS at the time of diagnosis of CAWP (basal) was 55.5 ± 10.2. Furthermore, a significant lower VAS was reported after 2 weeks and 1, 2, 3, 4 and 6 months of the treatment implementation (when compared to the basal value (p. Value < 0.001), fig. (2)). Regarding the responses to different treatment modalities used in the current study, fig. (3), 65 patients (60.19%) reported satisfactory pain relief with the use of pregabalin alone. 28 patients responded to pregabalin at a dose of 260±52 mg/day while 37 patients needed 300 mg/day. Unfortunately, 43 patients (39.81%) showed an unsatisfactory response to pregabalin 300 mg/day. The combination of pregabalin and carbamazepine at a dose of 303±78 mg/day was an effective treatment modality in 29 patients. Fourteen patients received a combination of pregabalin and amitriptyline. Eight patients reported adequate pain relief while 6 of the studied patients (5.6 %) showed poor response to medical treatment (VAS > 30), so they underwent injection therapy. None of the patients showed contraindications or serious adverse effects to drug therapy. Patients with poor responses to medical treatment were reexamined by the pain physician at the pain clinic. They were suspected to have ACNES as a cause of CAWP based on the presence of chronic localized abdominal pain on the lateral borders of the rectus abdominis muscle which increase after abdominal muscle tensing (+ve Carnett’s test). Therefore, after a positive diagnostic blockade using a local anesthetic, four patients received a single therapeutic injection session for the tender points and two patients received two therapeutic injection session. They experienced satisfactory pain relief throughout the study follow-up period. Fortunately, apart from some self-limiting drowsiness reported in 23 patients (21.3 %) during the initiation of medical treatment, no serious adverse effects were reported in the current study.
Figure 2. The therapeutic modalities and patients’ responses
* Two patients with response > 50% after local injection still unsatisfied and required a second injection after 2 weeks.

Figure 3. Visual analog scale (VAS) during follow-up

Discussion
The results of the current study address an important issue about the anticipation of CAWP as a cause of pain in patients complaining of chronic abdominal pain of unknown etiology. It was found that 30.6% of the screened patients fulfilled the criteria of CAWP. Multiple physician consultations, delayed diagnosis, misdiagnosis with subsequent mistreatment were common findings
in screened patients fulfilling the criteria of CAWP. Medical treatment was an effective modality in most of the cases. Injection therapy provided an improvement in patient resisted medical treatment. The majority of the studied patients with a positive diagnosis of CAWP were females (76%). The results are in agreement with many earlier studies stating that female gender represented 77% to 83% of the cases proved to have CAWP. The increase of CAWP among females might be due to the influence of sex hormones, which may affect pain perception. Moreover, the increase in the frequency of obesity among females causing entrapment of the nerve endings and previous pregnancies stretching abdominal wall with an injury of nerve endings are contributing factors (especially in the community where multiparity is a common finding). Previous studies reported that increased BMI was another risk factor for CAWP. The results of the current study showed that the prevalence of CAWP increased among the overweight (BMI was 25.95±3.7), a finding that may be ascribed to the entrapment of nerve endings. The mean age of the studied patients with a positive diagnosis of CAWP was (43.4±14.1) which matched the results of Boelens and his colleagues who reported an age of 47±17 as the mean age of CAWP. In the current study, the prevalence of CAWP among the screened patients complaining of chronic abdominal pain was (30.6%). The prevalence of CAWP varied depending on the criteria of the studied group of patients. It represented 2-3% of the unselected patients presenting with chronic abdominal pain in the out-patients and in the emergency room. A recent review reported that the prevalence of anterior wall pain is as high as 30% among patients in whom prior diagnostic evaluation yielded negative results. Being a tertiary hospital, most of the patients in the current study were referred cases with a long history of chronic abdominal pain and negative investigations. The newly diagnosed patients as CAWP (Naïve) represented about 5.38% of the screened patients. The delay in diagnosis and multiple physician consultations are common findings among CAWP patients, which may be due to lack of knowledge about the existence of CAWP. A Dutch survey involved surgeons and residents reported that more than 85% of the survey responders never heard about ACNES as a cause of CAWP and only 18% of the expert surgeons were aware of this syndrome. The present study displayed that the mean duration of delay in diagnosis was 9.14±8.9 months. Meanwhile, 28.7% of the patients complaining of chronic abdominal pain asked for consultations by five or more physicians in the last year. Boelens and his colleagues reported a median duration of 13 months of delay before the accurate diagnosis of ACNES as a cause of CAWP. Therefore, in accordance with similar results reported in the previous studies, it is not surprising that the delay in diagnosis of CAWP is substantial, hence, most of ACNES patients remain undiagnosed or misdiagnosed. Globally, diagnosis of CAWP (especially ACNES) has been a challenge. Misdiagnosis and subsequent mistreatment supposed to be due to the lack of knowledge about the CAWP among general practitioners and even senior specialists. Therefore, unfamiliarity and unawareness of CAWP as a cause of chronic abdominal pain were clear in the present study. We found that more than 80% of the patients fulfilled the criteria of CAWP, referred from other physicians, were misdiagnosed as cholecystitis, PUD and IBS. A confusing factor in diagnosis is that CAWP patients frequently reported ‘pseudo-visceral’ symptoms similar to functional abdominal disorders as IBS and dyspepsia (nausea, bloating, change in bowel habits and pain related to eating). Those complaints look seemingly unrelated to an abdominal wall problem. A misdiagnosis as PUD occurred in (31.5%) of the patients, while IBS was reported in (19.4%) of them. The misdiagnosis of cholecystitis also was recognized in the studied patients. Consequently, mistreatment by PPI was reported in 44.4% and by digestive enzymes as well as spasmyloctics in 23.1% of the sample. While, antibiotics and NSAIDS were prescribed for 14.8% of our patients. This result is in agreement with the previous studies reported IBS in 16.7 to 21.8% of patients and misdiagnosis of functional dyspepsia in 27.1%.

Regarding the anatomical location of CAWP, right sided abdominal wall pain was more common than the left sided one (59.2% vs 29.6%), which is in accordance with previous studies. Treatment modalities for CAWP include medical therapy, injection and surgery. In the current study, regarding treatment of accurately diagnosed CAWP, the majority of the patients responded to medical treatment (94.4%). Local injection with bupivacaine and steroid was used in a minority of patients (5.6%), who failed to respond adequately to medical treatment. The results of medical treatment in the previous studies was not clear. Pregabalin can be used alone or in combination with other drugs. Pregabalin binds with a high affinity to α2δ1- subunit of voltage- gated calcium (Ca2+) channels and attenuates the neuronal calcium influx, causing inhibition of the release of several excitatory neurotransmitters. Hence, it attenuates the neuronal hyper-excitability and interferes with the nociceptive signal transfer, resulting in analgesic effects on neuropathic pain. Amitriptyline relieves neuropathic pain, because it inhibits the presynaptic reuptake of norepinephrine and sero-
tonin, increasing their level and enhancing the activity of the descending inhibitory neurons. In addition, other mechanisms such as N-methyl-D-aspartate receptor and ion channel blockade could probably play a role in their pain relieving effect. Carbamazepine is an antiepileptic agent that is generally used as a third-line treatment for neuropathic pain. Carbamazepine stabilizes presynaptic neuronal membranes by inhibiting sodium channels, resulting in a reduction of neurotransmitter release and action potential conductance in nociceptive fibers. Carbamazepine can also potentiate GABA receptors, interrupt the glutamatergic function via N-methylD-aspartate receptors, and block calcium channel-modulated central sensitization, which is related to its anti-nociceptive, but not its anticonvulsant effects. The present study demonstrated that medical treatment was the first line of management. Pregabalin was used as a monotherapy and showed a good response in (60.19%) of patients. Pregabalin plus carbamazepine had a superior analgesic effect to amitriptyline. They are more effectively ameliorates neuropathic pain synergistically. This is because carbamazepine blocks voltage-dependent Na (+) channels, while pregabalin blocks voltage-dependent Ca (2+) channels. Local anesthetics are thought to "break" a chronic pain cycle and produce a rapid pain relief. The inclusion of steroid into the block might decrease neuronal inflammation and may exert a membrane stabilizing effect on the c-fiber transmission. They also have been found to reduce the development of ectopic neural discharges. Steroid presumably results in the thinning of connective tissue around the painful nerve. The injection was successful in all cases of the current study. The modification of the neuro-signature of pain in the brain by prior medical treatment may decrease the strength of chronic pain and could improve the injection results. A previous study reported higher efficacy and better quality of the injection therapy, if the injection was preceded by a short course of pharmacotherapy. The main limitations of the present study were that the patients were recruited from a single center, the relatively small number of patients involved and that the study was not powered. Furthermore, relatively short follow-up duration was another limiting factor. The previous limitations make back generalization difficult for this study. Hence, a large multicenter study is needed to confirm these results. The Authors recommended that, the inclusion of CWP in continuous medical education may reliably enhance early accurate diagnosis of this disorder, reduce misdiagnosis and mistreatment, can lead to an effective treatment, which markedly reduces the patient suffering and medical costs. Good history taking, full abdominal examination including Carnett’s sign in addition to increasing the awareness of the physicians about this globally underestimated problem are the keys to proper diagnosis of CWP.

Conclusions

CWP was identified in 30.6% of the screened patients complaining of chronic abdominal pain. Multiple physician consultations, delayed diagnosis, misdiagnosis with subsequent mistreatment were common. Medical treatment was an effective modality in most of the cases. Injection therapy provided a significant improvement in patient resisted medical treatment.

References