Overactive Bladder Syndrome Treatments and Their Effect on Female Sexual Function: A Review

Gali Levy, MD,[1,2] and Lior Lowenstein, MD[1]

ABSTRACT

Introduction: Overactive bladder (OAB), the most common subtype of urinary incontinence, has a heavy price on quality of life, especially on sexual life. Unfortunately, most women rarely voice the worsening of sexual function, especially those who already suffer from OAB symptoms. It has been demonstrated that patients who suffer from OAB score lower on Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire and Female Sexual Function Index scores, meaning that their sexual function is debilitated. Therapies for OAB begin with traditional pelvic floor physiotherapy, advance to anticholinergic drugs, and become more invasive with intravesical injections of onabotulinumtoxinA (commonly known as Botox). Last, for patients resistant to conservative therapies, sacral neuromodulation is the treatment of choice.

Methods: This article reviews the current literature that sheds light on the above 4 treatments and their effect on sexual function. This topic is of great importance because of the under-reporting of sexual dysfunction in women who suffer from OAB, in hopes of raising awareness of sexual function for clinicians treating patients with OAB.

Results: This review found that the aforementioned 4 treatments for OAB (physiotherapy, anticholinergic drugs, intravesical injections of onabotulinumtoxinA, and sacral neuromodulation) do not have a detrimental affect on sexual function. On the contrary, the little data that do exist show that sexual function increases after these therapies are completed in women with OAB.

Conclusion: This review concludes with a positive outlook: physicians are helping women with OAB syndrome to improve their sexual function. However, not enough data exist, partially due to under-reporting of diminished sexual function. **Levy G, Lowenstein L. Overactive Bladder Syndrome Treatments and Their Effect on Female Sexual Function: A Review. Sex Med 2019;8:1−7.**

Key Words: Overactive Bladder; Anticholinergics; Sexual Function

INTRODUCTION

Overactive bladder (OAB) symptoms, urinary incontinence and sexual health are subjects many women find difficult discussing with their healthcare provider.[1] OAB is a condition defined by the International Continence Society as the manifestation of "urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence (UUI), in the absence of urinary tract infection (UTI) or other obvious pathology."[2] Urinary incontinence, although not a dangerous condition, detrimentally affects the psychological health of women and negatively affects quality of life.[3] Urinary incontinence (UI) is defined as involuntary or abnormal urine loss. UI is categorized by lower urinary tract symptoms (LUTS), including voiding and storage complications, and UUI is unintentional urine leakage associated with urgency.[3,4] Unfortunately, few people seek help for this symptom because of embarrassment and stigma.[5] Although highly under-reported, recent sources report that the prevalence of OAB in women is 16.9% and comparably increases with age.[6,7] Because of patients failing to report symptoms to their physician, the physical and economic burden of OAB is under-reported but is estimated to be up to 50% of women.[8,9] We found significant purpose in investigating this "silent" problem that affects so many women who do not discuss it.

According to the European Association of Urology, primary treatment for OAB includes behavioral (lifestyle) interventions and physical therapy such as pelvic floor exercises.[10] If these

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[1]Department of Obstetrics and Gynecology, Rambam Health Care Campus, Haifa, Israel;

[2]Tel Aviv, Israel

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conservative treatments fail, physicians continue to recommend pharmacologic treatment: either anticholinergics or beta agonists.[2] The last lines of treatment for OAB include invasive therapies: intravesical injection of botulin toxin, neurostimulation, or both.[2] Whether intravesical injection of botulin toxin should be given before attempting neurostimulation is still debated among physicians. Studies have found that patients diagnosed with UUI or OAB are afflicted with more anxiety and psychological distress compared with those with stress incontinence.[3] Barber et al[11] hypothesized that this burden is due to the erratic nature of detrusor muscle overactivity, which causes symptoms such as large volumes of urine leakage.

Women with psychological, physiological, and iatrogenic risk factors increase their chances of developing complications in sexual function. On the other hand, lower urinary tract symptoms are an independent risk factor for decreased female sexual function.[3,12] Sexual dysfunction is categorized into disorders of lubrication, arousal, desire, orgasm, and pain.[12] The amount of information pertaining to the effect of treatments used for OAB on sexual function of women is inadequate. To quantify these issues, well established guidelines are used to verify sexual history and permit assessment; the Female Sexual Function Index (FSFI) is a succinct, multidimensional "gold-standard" tool that is widely used for these measurements and is highly regarded.[12–14] In conclusion, OAB affects daily and sexual life severely.[15,16] It is under-reported and not discussed enough in the patient/provider setting. The aim of this article was to review the literature and shed light on how treatments for OAB affect sexual function in women.

METHODS

The search strategy we used for this review was to extract studies that investigated overactive bladder treatments, overactive bladder syndrome, and sexual function. The articles that were chosen for this review were found on the PubMed online database and were published between 1999–2019. In the search process, we used descriptors such as overactive bladder, treatments of overactive bladder, sexual function, and therapy overactive bladder. No restrictions were imposed on study selection. Study characteristics, such as language or publication status, did not exclude studies from being used in this review.

The number of studies screened was 58; however, after assessing them for eligibility, only 42 were included in the review. The reasons for excluding 16 studies were due to their irrelevance to OAB syndrome. Most of the studies that were excluded were not included in the review because they dealt with stress incontinence rather than OAB syndrome.

RESULTS

Conservative Treatment: Pelvic Floor Physiotherapy and Its Effect on Sexual Function

Pelvic floor muscle training (PFMT) is a widely accepted treatment for women with stress urinary incontinence (SUI) and also is used as a treatment for OAB.[17] Standard guidelines recommend PFMT as a first-line treatment for patients with OAB or UUI, but the evidence proving treatment success is insufficient.[18] The rationale is that increased pelvic floor muscle strength would allow better urge control by interfering with urethral/detrusor reflexes, thus inhibiting pathologic detrusor contractions.[19] A large meta-analysis published in the Cochrane Library compared the effects of different approaches to PFMT in women with UI.[17] The only significant conclusion that came out of the study was that women should be offered frequent appointments during the training period. Unfortunately, the review did not specify the effect of PFMT on OAB.[17] The most recent review published in April 2018 surveyed literature about effectiveness of PFMT in reducing OAB symptoms in women. This review shed light on a handful of small trials, with inconsistent outcome measures, and concluded with no standard recommendation.[20] A study by Zachariou et al[21] demonstrated that PFMT improved sexual function in women with stress urinary incontinence by using FSFI scores before and after therapy. Although the study focused on patients with SUI and not OAB, it showed that improvement in urinary incontinence symptoms after PFMT can improve sexual function. There are limited studies that shed light on whether PFMT (in OAB treatment) improves sexual function. An important aspect in OAB management is the patient's appreciation of her quality of life. A recent study published in *Female Urology* in 2018 compared the effects of transcutaneous posterior tibial nerve stimulation (TPTNS) and PFMT in women with OAB. Although this study did not focus on the effect PFMT has on sexual function, the Kings College Health Questionnaire results concluded significant improvement only in the group that received both PFMT and TPTNS: the women who underwent both therapies scored higher in categories of general health perception, role limitation, and physical and social limitations. There are several validated and reliable questionnaires to measure urinary symptom impact on quality of life. According to the European Association of Urology guidelines on urinary incontinence, the King's College Health Questionnaire is a valid and dependable tool to measure change over time. In this study, only the women treated with the combination of PFMT and TPTNS most effectively improved their quality of life, as illustrated in results of the King's College Health Questionnaire domains.[19] Based on the limited available data, evidence exists supporting the effectiveness of physical therapy for the treatment SUI in women; however, future studies are necessary to assess the effect of PFMT on patients with OAB and their sexual function.[22] The lack of contributory studies that investigate how PFMT affects sexual function in women who suffer from OAB makes it difficult to come to a definitive conclusion.

Pharmacotherapy Effect on Sexual Function

Initial pharmacotherapy for OAB consists of anticholinergics.[18] Anticholinergics are competitive bladder-selective muscarinic receptor antagonists that have been proven to treat

OAB. Mirabergon, a beta3-adrenergic agonist compound, is a novel oral treatment for OAB that improves storage capacity of the bladder without causing anticholinergic adverse events.[23] The safety and success of anticholinergics and beta-3 adrenergic agonists as treatments for OAB have been demonstrated in many clinical studies and meta-analyses.[24] However, there aren't as many studies or analyses that confirm the benefit that these medical treatments have on female sexual function.[1] Zachariou et al[1] conducted a prospective study with 85 sexually active women suffering from OAB, divided into 2 groups: a control group receiving no treatment and a group receiving mirabergon 50 mg/d for 3 months. By using FSFI evaluation, Zachariou et al[1] concluded that there was a significant increase in total FSFI scores in all domains in the group that received mirabegron. Cakir et al[25] prospectively enrolled 216 sexually active women with OAB and 165 healthy women (as the control group) in a study to test sexual function in women with OAB. Prior to treatment with anticholinergics and 3 months after treatment, women were asked to answer two questionnaires: the FSFI, an 8-item OAB awareness tool, and the Beck Depression Inventory form. At baseline, patients suffering from OAB conveyed significantly worse sexual function (in all FSFI questionnaire categories) compared with the healthy control group (21.47 ± 3.22 vs 26.79 ± 5.56, $P < .01$). The success of anticholinergic treatment was illustrated in positive results: >85% of participants reported clinical improvements in sexual function 3 months after beginning treatment. The mean FSFI scores increased drastically in the group receiving anticholinergic treatment.[25] Del Rosso et al[26] treated 33 women diagnosed with OAB with 5 mg solifenacin (an antimuscarinic agent). They were re-evaluated after 3 months: 70% of the patients described improvement in sexual function (by using FSFI questionnaires).[26] Another study that investigated the effects of tolterodine on sexual function was carried out by Zachario and Filiponi,[21] who studied 158 women with OAB. They divided their study population into 2 groups: 1 group received tolterodine, and the other group received no treatment. A follow-up evaluation after 3 months using FSFI questionnaire revealed a statistically significant increase in desire, arousal, lubrication, and orgasm. This key finding deserves attention because traditionally anticholinergic drugs have a drying effect on various mucosal tissue. Overall FSFI scores were higher in the group that received tolterodine.[21] An older study from 2008 illustrated similar findings with tolterodine.[16] Hajebrahimi et al[16] followed 30 sexually active women with OAB from ages 20−52 years by using the Arizona Sexual Experience Scale (ASEX) before treatment with tolterodine and at the end of each month of treatment until 3 months. The ASEX questionnaire is a 5-item rating scale. Each item explores an aspect of sexuality: sex drive, arousal, vaginal lubrication, ability to reach orgasm, and satisfaction from orgasm. The mean of the ASEX total score before tolterodine was 18.79. After each follow-up, the mean of scores for sexual desire, arousal, vaginal lubrication, and orgasm improved significantly. The study finally compared the scores with the baseline scores and concluded that after three months of treatment with tolterodine, ASEX evaluations portrayed that significantly more patients were free from sexual dysfunction.[16] Rogers et al[27] conducted a study on a more racially diverse, sexually active population, (a population younger than that typically embodied in OAB trials) and demonstrated an improvement in OAB symptoms after tolterodine treatment. In this study the evaluation included bladder diaries and 3 validated questionnaires: Sexual Quality of Life Questionnaire—Female (SQOL-F), Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ), and Hospital Anxiety and Depression Scale (HAD). Treatment with tolterodine showed statistically significant improvements in all 3 questionnaires compared with subjects receiving placebo. 3 months after beginning treatment, SQOL-F and PISQ total and all PISQ scores improved from baseline in both treatment groups. In addition, patients who received tolterodine reported statistically significant improvements in SQOL-F scores and PISQ total and Physical Domain scores vs patients receiving placebo. Compared with the group receiving placebo, there was significantly more improvement in HAD Anxiety scores in the tolterodine group. Specifically, the mean HAD Anxiety score declined to numbers beneath the cutoff range.[27] Key findings like these shed light on psychological factors such as anxiety and depression, which are important factors that influence sexual function and quality of life in women with OAB. In addition, women with OAB suffer from increased anxiety and depression.[15] Overall these studies illustrate that tolterodine significantly improves sexual function of women with OAB. Although there are no other studies investigating the effect of other antimuscarinic medications on sexual function, we can cautiously assume that other antimuscarinic medications might have the same effect of sexual function as documented in the case of tolterodine.

Intravesical Injection of Botulin Toxin Effect on Sexual Function

Few studies have been done to confirm the effect of intravesical botulin toxin injections on sexual function in women with OAB. Botulinum toxin type A (OnabotulinumtoxinA, or Botox) is the most commonly used type of botulinum and acts by blocking nerve activity in the detrusor muscles, causing a temporary reduction in bladder contractions.[28] In patients with OAB refractory to pharmacotherapy, intravesical injection of onabotulinum toxin type A has become the new treatment of choice.[29] In a distinct prospective observational study done in 2016, Miotla et al[30] investigated the impact of intravesical onaBoNT-A injections on sexual function in women with OAB, using the FSFI questionnaire. In this study, 56 women (age matched with a healthy control group) completed FSFI questionnaire before treatment and 12 weeks after receiving injections. The entire study group resumed vaginal intercourse during the month after receiving onaBoNT-A injections, and all the patients continued to be sexually active at week 12.

Treatment with onaBoNT-A injections demonstrated significant improvement in all FSFI domains. It is important to note that FSFI scores improved drastically compared with the control group (who were healthy women) because the scores before treatment were much lower in the study group. In other words, the control group did not have sexual dysfunction; therefore, significant improvement was observed in the study group. Additionally, safety assessments carried out by the investigators in the group receiving injections throughout the trial (during weeks 2, 4, and 12) did not illustrate adverse events after onaBoNT-A injections. The study concluded that onaBoNT-A treatment leads to increase in sexual function in women with OAB.[30] Balzarro et al[31] evaluated the impact of onaBoNT-A injection on sexual function in women with OAB. This prospective 3-center observational study followed 32 women diagnosed with OAB who were treated with onaBoNT-A injection. Sexual function was assessed using the FSFI before treatment and 3 months after onaBoNT-A injection. The study demonstrated significant improvement of most FSFI domains, except for desire and pain (no significant improvements). This study documented a significant correlation only between the reduction of episodes of urgency UI and improvement of FSFI. This most probably influenced the patients studied in a positive way that improved their quality of life. In other words, the psychological status of the patients drastically improved, and it was concluded that women who have better control of OAB symptoms concurrently have more gratification in sexual intercourse.[31]

Neuromodulation Effect on Sexual Function

Sacral Neuromodulation

Improvements in sexual function have been illustrated in women who underwent sacral neuromodulation (SNM) for lower urinary tract disorders. This has been proven in small, mostly prospective studies with underpowered sample sizes of on average 20 women, usually with a mean age of 60 years, by using a questionnaire (mainly FSFI) after a mean of 4 months after the implant procedure.[32–34] Van Voskuilen et al[35] carried out a study in lieu of routine follow-up visits of patients with SNM, reporting improvement in their sexual functioning. Although no statistically significant results were revealed after analysis, the results of this study demonstrated a tendency of improvement in orgasm scores. More specifically, all 3 patients showed increased vaginal pulse amplitude with the stimulator turned on during plethysmography studies (with both erotic and non-erotic stimuli).[35]

A shortcoming of this study was that there were not enough responses from the psychological questionnaires (The Questionnaire for Screening for Sexual Dysfunctions, the Golombok Rust Inventory of Sexual Satisfaction, the Symptom Checklist-90, the Maudsley Marital Questionnaire and the McGill-Mah Orgasm Questionnaire).[32,35] Similarly, Pauls et al[36] established significant improvement in the FSFI score in 11 female patients with a SNM implant for treatment of LUTS.[37] Another study on the effects of SNM for LUTS on female sexual function was done by Zabihi et al[38] and illustrated significant improvement in all and total FSFI scores; however, baseline FSFI scores were lower (average total FSFI of 9.2) and likely the reason for statistical significance.[34,35,37] Banakhar et al[39] performed a prospective, observational study on 23 women that demonstrated a statistically significant effect of SNM on FSFI: preoperative mean FSFI score was 15.49, and 4 months after surgery was 18.33.[39]

In 2013, Yih et al[40] studied the changes in sexual function among 167 women being treated with neuromodulation because of urological diagnoses. The study did so with the FSFI questionnaire at 3, 6, and 12 months after implantation. The study concluded that treating voiding dysfunction with neuromodulation can simultaneously treat sexual dysfunction. Overall FSFI scores increased from a preimplantation mean of 13.5, to a 12-month mean of 15.9. FSFI domains that improved included desire ($P = .047$), orgasm ($P = .0051$), satisfaction ($P < .0001$), and pain ($P = .011$). Most notably, of the 74 patients who began the study declaring that they were not sexually active, 10 became sexually active during the follow-up evaluation. The results of this study established an improvement in sexual function in a mixed population of women who were less sexually functional before implantation, compared with women who had higher preimplantation sexual function FSFI scores. Because of the significant improvement in all groups, the study raised questions about potentially treating women with primary sexual dysfunction with neuromodulation.[40] A recent review by Lombardi et al[32] concluded that, although many studies exist showing the benefit SNM (for treating OAB) has on sexual function, there is still not enough definite statistics that can ascertain the positive effect of SNM on sexual function.

In most of the recent studies investigating SNM and sexual function, the theory that SNM impacts neural pathways involved in sexual function is raised.[34,35] The potential benefits of SNM on sexual function have yet to be explored. By uncovering its maximal benefits, indications for neuromodulation are expanding. The current research, although underpowered, suggests that there is potential to improve sexual function after neuromodulation in women with various voiding dysfunctions. Unfortunately, large multicenter prospective controlled trials are yet to be carried out to determine whether SNM has a direct effect on sexual function compared with in control subjects.[32,38,41–44] In lieu of insufficient studies that are mostly underpowered, there is no significance and common consensus. In addition, patients who undergo sacral neuromodulation are usually those with more severe symptoms that are resistant to conservative treatments. Therefore, it is difficult to compare this treatment's effect on sexual function with other therapies.

The improvement in sexual function in women with urinary symptoms was credited to the reduction in OAB symptoms after SNM. More interestingly, the studies seem to support a direct action of SNM on sexual function.[32,45] It has been hypothesized that pudendal nerve function may play a role in female sexual

dysfunction; therefore, future research is necessary investigate the mechanism of the effect of SNM on pudendal nerve and, hence, on sexual function. A more recent study carried out by Parnell et al[41] assessed sexual function in a group of sexually active postmenopausal women by asking them to complete the PISQ-12 at baseline (score 24.7) and 6 weeks after undergoing first stage of InterStim1 implant (score increased to 30.9).[41] More notably, this study illustrated an inverse correlation between PISQ-12 and pudendal nerve terminal motor latencies (PNTML) at 6 weeks. In other words, as PISQ-12 scores improved, so did pudendal nerve function. On the other hand, the same study proved that FSFI scores (baseline and at 6 weeks) changed from 10.0−12.5, with the greatest statistical improvement found in the "sexual desire" category (1.5−2.3) but not in the other categories.

This study provided a relatively large cohort of sexually active women (compared with other studies); however, it was, unfortunately, not sufficiently powered.[41] Another hypothesis worth studying in the future is that permanent SNM may improve sexual function by increasing pelvic blood flow through the stimulation of parasympathetic fibers.[32,41,45] More research is required to conclusively explain the positive effect SNM has on sexual function: is it a direct one, mediated by the improvement in arousal, satisfaction and pain according to FSFI evaluations, or an indirect one mediated by changes in bladder and vaginal symptoms.

Table 1. Studies listed in chronological order (most recent at the top) and divided according to treatment

PMFT*
Randomized controlled trial, 90 patients[22]
Pharmacotherapy†
Prospective, 220 patients[21]
Prospective, 58 patients[26]
Prospective, 30 patients[31]
Randomized (1:1) in double blind, 330 patients[29]
Prospective, 85 patients[1]
Prospective, 216 patients[25]
Retrospective consecutive cohort, 177 patients[24]
Botulin toxin
Observational study, 68 patients[30]
Observational study, 32 patients[31]
Neuromodulation
Prospective, observational database study, 167 patients[40]
Observational study, 8 patients[35]
Retrospective, 33 patients[39]
Prospective, 41 patients[33]
Prospective, 36 patients[38]
Prospective, 31 patients[41]

OAB = overactive bladder; PFMT = pelvic floor muscle training.
The type of study, number of patients, and whether the treatment was found to be beneficial is shown, along with the reference number.
*No effect on sexual function.
†Positive effect on sexual function.

Percutaneous Tibial Nerve Stimulation

In a recent observational study performed by Musco et al,[33] women affected by OAB refractory to standard treatments who underwent percutaneous tibial nerve stimulation were evaluated by using the FSFI questionnaire. This study concluded that percutaneous tibial nerve stimulation benefited sexual function in women with OAB, by establishing significant increase in scores (FSFI) in overall sexual function, desire, and satisfaction in the groups with and without female sexual dysfunction. Overall, all FSFI scores portrayed statistically significant improvement.[33]

CONCLUSION

In the past, literature on OAB treatment focused on assessments of urinary frequency, urgency, and incontinence episodes. These domains were used to determine the extent to which treatments improved outcomes. However, today it is crucial to shed light on the patients' feelings and how OAB impacts quality of life and relationships. [3] While administering treatment for bladder syndromes, many clinicians neglect to address sexual function because they are focused on other outcome measures. Women undergo a double discomfiture; incontinence has a detrimental effect on quality of life, and, on top of that, they suffer the taboo complaints of sexual function. For this reason, we saw fit to evaluate the literature on the outcomes of treatments for OAB. Based on the small number of cases published, the overall trend portrays a global improvement in sexual function from OAB treatments (Table 1). The most striking improvements were after SNM. Most of the studies involving neuromodulation reported statistically significant improvements in all subsets of female sexual response.[32]

Overall, the therapies that exist today have been shown to improve sexual function in patients suffering from OAB. Although scant in number, several studies have confirmed that women who underwent successful intravesicle injection to treat OAB revealed an improvement in sexual function. A recent study (2018) demonstrated a significant correlation between the improvement of urinary urgency incontinence and a better gratification of sexuality.[31] Unfortunately, a shortcoming of our review was the lack of data pertaining the effect of PFMT on sexual function in women with OAB, but the few studies that do exist establish a positive improvement in FSFI domains. Last, SNM had such a profoundly positive effect on sexual dysfunction in women who were being treated for OAB that many of the studies predicted that SNM can not only treat OAB but also treat women with underlying sexual dysfunction, regardless of OAB diagnosis.

Counseling in urogynecology is crucial to improving the lives of patients suffering from OAB. Surgeons should be expected to explain their patients that sexual function can improve with the improving of OAB, and FSFI domains should be properly

explained. Physicians have a responsibility to lay out information about the different treatment options and explain the pros and possible cons of such treatments. The goal of urogynecology counseling is to clarify the clinical aspects of the treatment so that expectations become more realistic about what is achievable after the treatment of choice. This is clarification is even more critical when a procedure is chosen over a conservative method. Counseling is crucial and should include explaining pelvic floor physiology.[46] Recent protocols of counseling have been created to help physicians successfully lay out the various options that their patients have.[46] Balzarro et al[46] reported that most patients do not fully understand the complexity of their symptoms, clinical conditions, and potential sequelae. For instance, many patients falsely believe that their UUI is SUI. This may lead to dissatisfaction when SUI surgery does not successfully treat OAB symptoms. The take-home message in this review is to shed light on awareness for patients that certain treatments may potentially cause the development of new or worsening conditions, such as sexual function.[46] Patients suffering from OAB symptoms and other lower urinary tract symptoms deserve to know how the treatments they undergo will affect their sexual function.

The International Urogynecological Association and the American Urogynecologic Society provide leaflets that are useful as counseling tools (http://www.iuga.org/?page=patientleaflets; https://www.augs.org/ patient-services/patient-fact-sheets/). We hope this field will be explored in the future to improve the quality of life of countless patients.

Corresponding Author: Gali Levy, MD, Department of Obstetrics and Gynecology, Rambam Health Care Campus, 3 Avigur St, Apt 28, 1311502 Tel Aviv, Israel. Tel: 972 052 5982791; E-mail: Gali.levy88@gmail.com

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STATEMENT OF AUTHORSHIP

Category 1

(a) Conception and Design
Gali Levy; Lior Lowenstein
(b) Acquisition of Data
Gali Levy; Lior Lowenstein
(c) Analysis and Interpretation of Data
Gali Levy; Lior Lowenstein

Category 2

(a) Drafting the Article
Gali Levy; Lior Lowenstein
(b) Revising It for Intellectual Content
Gali Levy; Lior Lowenstein

Category 3

(a) Final Approval of the Completed Article
Gali Levy; Lior Lowenstein

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