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METHADONE AND LUNG TRANSPLANTS

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SUMMARY

Objectives: *The aim of this article is to better understand the role of the liason psychiatrist regarding the pulmonary pre-transplantation assessment for a patient treated by methadone.*

Method: *At the beginning, we collected data concerning the different habits of patients requiring pulmonary transplantation. Through a literature review, we studied the possible guidelines related to this subject, the effects of methadone, the side-effects explaining the psychiatrist's concerns. Finally, this problem is involved in the bio-psycho-social model to underline the influence of methadone on post-operative prognosis.*

Results: *In our database, only 4.3% of patients were treated by methadone. However, this addiction is one of the most important stresors for psychiatrists and involves a great deal of multidisciplinary staff time. There are absolutely no guidelines on this topic. Due to the action of methadone, the pulmonary, cardiac, urologic, drug and immune side effects are more understandable. Thanks to clinical labels, we are able to handle this dual problem. Different parameters are considered such as patient's history, drug addiction, deterioration of physical condition, possible surgery and its consequences, choice of treatment to better estimate the post-operative prognosis.*

Conclusion: *Until now, there is nor indication or contra-indication regarding the duration of treatment by methadone for patients requiring pulmonary transplantation. The main advantage is the patient's stabilization by minimizing possible relapses. This advantage is to compare the following major inconvenients: increased confusional risk, delicate management of the post-operative pain, negative impact on the immunity. The support, a double psychoeducation and the patient's decision making are to be encouraged.*

Key words: *methadone - lung transplants - liaison psychiatry - side-effects – confusion – anesthesia - post-operative pain - immune response - biopsychosocial model*

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INTRODUCTION

In liaison psychiatry, the psychiatrist is conventionally and regularly asked to take part in multidisciplinary evaluations of potential lung transplants. In addition to the absolute or relative counter-indications which must be identified, the main difficulties essentially concern the phenomenon of dependence. We have observed that methadone was the substance which caused most concern about consumption and it monopolised discussion time in multidisciplinary meetings.

We have decided to investigate the potential need to stop methadone treatment for lung transplant candidate patients, the conditions under which treatment would be stopped and the role that liaison psychiatry plays in this treatment.

To do this, we examined the different consumptions found in patients taking part in the pre-lung transplant evaluation, as well as guidelines on the attitude to adopt in this type of case, the mechanism of action and side-effects of methadone which explain the concern surrounding this medication and finally the different roles of the liaison psychiatrist with the other members of the multidisciplinary team.

METHOD

In retrospect, we were mainly interested in the different consumptions of patients in the context of the pre- lung transplant assessment over the years from 2004 to 2010. We counted a total of 93 patients - 43 women and 50 men.

RESULTS

As the table above shows, we observed that the most commonly-used substance is tobacco. 85 patients out of 93 were affected (91.4%), of which 82 patients were

Table 1. Different consumptions of patients in the context of the pre-lung transplant assessment over the years from 2004 to 2010

Consumption	Number of patients
None	7
Tobacco	2
(Tobacco)	59
Alcohol	0
(Alcohol)	1
Tobacco - Alcohol	0
Tobacco - (Alcohol)	1
(Tobacco) - Alcohol	13
(Tobacco) - (Alcohol)	6
Opiates	0
(Opiates)	0
(Opiates) - Methadone	0
(Opiates) - Methadone - (Tobacco)	1
(Opiates) - Methadone - (Tobacco) - (Cocaine)	2
(Opiates) - Methadone - (Tobacco) - (Cannabis)	1

Legend: ( ): former consumption

teetotal (88.2%). However, other substances are also mentioned, such as alcohol, heroin, cocaine, cannabis and methadone. 4 patients out of 93 (4.3%) were on methadone treatment (Table 1).

DISCUSSION

Paradoxically, methadone is used much less than tobacco, yet it is methadone which monopolises the agenda during multidisciplinary meetings. At these meetings, lung specialists show concerns about its overall side-effects, while intensive care physicians wonder about complications with anaesthesia and analgesia. The issue of whether to stop the use of methadone is regularly discussed.

Guidelines, mechanism of action and side-effects

Although the side-effects of alcohol and tobacco have been well established within the context of a potential lung transplant, this is not the case for methadone treatment.

To date, there are no guidelines on the issue. From a clinical, psychiatric point of view, we know that coming off methadone is a process which should not be done quickly. The matter must be approached like a set of scales, with the potential risks of taking methadone on one side, and arguments supporting the potential importance of continuing treatment on the other.

First of all, we will give a brief recap on methadone's mechanism of action in order to better understand its side-effects (Corkery et al. 2004).

As a reminder, methadone is a synthetic narcotic. Its main indications, other than chronic pain treatment and palliative care, include the relief of opiate withdrawal syndrome during detoxification and its long-term use as an opiate (particularly heroin) replacement treatment. It is used to stabilise the patient and reduce risks - such as those linked to injecting substances intravenously or snorting them, risks of overdose and risks linked to the illegal activities which are performed in order to obtain heroin.

Table 2. Methadone's mechanism of action and potential side-effects

Receptor	Sub-type	Location	Effect
delta (δ) OP_1 (I)	δ_1, δ_2	Pontine nuclei Amygdal Olfactory bulbs Depth of the cerebral cortex	Analgesia Antidepressive effects Physical dependence
kappa (κ) OP_2 (I)	κ_1, κ_2, κ_3	Hypothalamus Periaqueducal grey substance Claustrum Gelatinous substance	Spinal cord analgesia Sédation Myosis Hallucinations (reduced release of dopamine in these same regions) Inhibition of the ADH hormone
Mu (μ) OP_3 (I)	μ_1, μ_2, μ_3	Cerebral cortex Thalamus Striatum Periaqueducal grey substance Gelatinous substance Gastrointestinal tract	*μ_1:* Supraspinal analgesia Physical dependence *μ_2:* Central depressive action Antitussive action Bronchoconstriction (histamine) Choking when swallowing Low blood pressure Bradycardia Long QT syndrome and wave burst arrhythmia Myosis Euphoria Reduced motility of the gastrointestinal tract Urinary retention Renal failure Physical dependence *μ_3:* ?
Récepteur nociceptif OP_4	ORL_1	Cerebral cortex Amygdal Hyppocampus Septal nucleus Hypothalamus Spinal cord	Anxiety Depression Increased appetite Development of a tolerance to mu (μ) receptor agonists

Briefly, its characteristics are as follows:

- Taken under controlled medical prescription, the euphoriant effect is nil. Therefore, this stabilisation phase does not eliminate dependence, but is aimed at abstinence from seeking the euphoriant effect.
- Its first analgesic effects appear after 30 to 60 minutes.
- It essentially differs from morphine (a natural opiate) and heroin (a semi-natural opiate) because of its long-lasting effects (6 to 8 hours).
- If it is administered repeatedly, the effects last longer and the half-life (15 to 55 hours) increases.
- Phenomenon of tolerance and dependence.
- Acts as an opioid receptor antagonist. (Reminder: an opioid can interact with the different receptors either as an agonist, partial agonist or an antagonist, hence the different possible effects) (Table 2).

It is important to mention that the side-effects of methadone can be exacerbated by stressful situations, such as an operation. Nevertheless, they are generally only observed when treatment starts or when the dose is increased, and not when methadone is taken chronically.

However, clinically speaking, we also get the impression that the risk of peroperative confusion increases in patients who are treated beforehand with methadone. This observation fits in with withdrawal syndromes which unfortunately, are sometimes inevitable. These withdrawals are generally the result of either a temporary stoppage of treatment (for example transfer from the theatre block to intensive care) or different drug reactions. These should not be underestimated and explain the concern of anaesthetists and intensive care physicians (Weinrieb et al. 2004):

- Cross-tolerance, leading to increased post-operative anaesthetic and analgesic treatments.
- Interactions with tranquilisers, sleeping pills, analgesics and antibiotics, which can hasten a withdrawal and/or overdose.
- Interactions with antidepressants, neuroleptics, barbiturates and anxiolytics, which can exacerbate respiratory depression.

Finally, methadone is suspected to be involved in immune disorders (Van der Laan et al. 1996), particularly a disorder of the humoral and cellular immune response, which can increase the likelihood of certain infections. By contrast, it should be emphasised that some studies show that methadone decreases the activity of T Natural Killer lymphocytes, which play a major role in transplant rejection.

Biopsychosocial model and roles of the liaison psychiatrist

In light of the issues mentioned above, the lung transplant medical team is bound by major necessities.

However, the patient is not only a set of malfunctioning organs. Already weakened by his or her life history, drug addiction and the deterioration of their physical state, they are forced to make a choice, not only relating to a serious operation, but also relating to medication which he or she generally considers to be their saviour.

The liaison psychiatrist is thus faced with a two-faceted problem: a team which must assess a risk, and a patient who must make a choice. After stating the risk of a relapse in consumption to the patient and to his or her colleagues, the liaison psychiatrist's role is to be vigilant of the danger of the "drug addict" label and of the negative representations of these patients by the medical world and also support the patient in their reflections.

It is obviously important to create a link between the patient, the physicians and the psychiatrists in order to take the proper time and not rush into a decision. In liaison psychiatry, our work will focus on the need for regular support prior to transplant and the need to formulate an intermediate treatment plan with gradually smaller doses.

Along these lines, it has been shown that a premature stoppage in methadone treatment was an ominous prognosis factor. Let us remember that it is recommended that the daily dose of methadone is reduced by 10% every month in order to avoid withdrawal symptoms, to reduce the risk of relapses and to leave room for the psychotherapeutic work. It is obvious that this decrease must be decided upon with the involvement of the patient. It is easy to understand how a premature, unplanned or forced stoppage in treatment could unfortunately result in a consumption relapse, disqualifying the patient from being a transplant candidate.

Likewise, some studies (Weinrieb RM et al. 2007) go even further by stating that patients undergoing methadone treatment for several years have a better prognosis thanks to a better compliance to post-operative revalidation.

Finally, some studies (Liu Lawrence U et al. 2003, Hensel M. et al. 2000) are still contentious as to the risk of post-operative relapse encountered by patients who are still dependent on a substance. In fact, some describe increased alcohol abuse, relapses back to heroin use or even back to the daily dose of methadone after the transplant, while others underline the localised nature of the figures obtained.

CONCLUSION

The particular nature and the wealth of liaison psychiatry allow a link to be established between the physician and the psychologist, as well as a partnership with not only our physician colleagues, but particularly with patients. This is fully reflected in the multi-disciplinary evaluations. We chose to investigate whether methadone treatment should be stopped prior to a lung transplant, but we were unable to produce a unidirectional treatment. At the current time, there is no indication or counter-indication. The advantage of this

replacement therapy is that it stabilises patients by limiting relapses. Its disadvantages, however, cannot be dismissed: heightened risk of confusion, delicate management of anaesthesia and post-operative pain, impact on immune responses.

Despite the concerns, and the convictions of each party, it is important to establish a three-way link. We also need to investigate the matter by refocusing our thoughts on the patient him or herself. What risks does the patient weigh up when making such a decision? What risks is the patient willing to take? What risks do we think are acceptable?

Despite all this, if we had to write our own guidelines, they would be as follows:

- Regular support is indispensable prior to transplant.
- Psychoeducation at two levels: anticipate patient relapses and counteract the negative image of drug addicts among medical teams.
- Motivational interview to help the patient make a decision.
- Leave sufficient time to plan for the gradual decrease in methadone doses in partnership with the patient.

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